Recurrent Postpartum Anaphylaxis With Breast-Feeding

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BACKGROUND: Anaphylaxis associated with breast-feeding is a rare but potentially life-threatening event.

CASE: This woman reported anaphylaxis with three previous pregnancies while breast-feeding. With her fourth pregnancy she was treated with corticosteroids and antihistamines after delivery. Despite treatment, she developed urticaria, facial edema, and throat tightening, less severe than prior episodes. Her symptoms resolved with epinephrine and antihistamine but recurred with subsequent breast-feeding. On postpartum day 4 she had no symptoms while breast-feeding.

CONCLUSION: Three cases of postpartum breast-feeding anaphylaxis have been reported. Although the pathophysiology is unclear, it may involve the decrease in progesterone and rise of prolactin causing mast cell degranulation. Avoidance of nonsteroidal antiinflammatory agents and prophylaxis with corticosteroids and antihistamines may offer the best protection.

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CASE

A 35-year-old gravida 4 para 3 had a history of anaphylaxis on postpartum day 3 with all three previous pregnancies. Three days after delivery of her first neonate, she developed hives, swollen eyelids, choking, coughing, and wheezing, which lasted overnight. The second pregnancy was significant for hives, shortness of breath, and cyanosis on postpartum day 3, which required epinephrine injection and intensive care unit admission. Codeine was used before this reaction. She had a similar reaction again 3 days after delivery of her third neonate, which required repeated epinephrine injections over 24 hours. All three episodes were associated with breast-feeding. Other medical history was notable for mild asthma and gestational diabetes. Because of her previous postpartum anaphylaxis history, she was referred to the Allergy Division for an evaluation. Workup at that time included negative skin tests to common aeroallergens and latex. Her lung function was normal on spirometry. A recommendation was made that she receive prednisone 30 mg twice daily and cetirizine 10 mg once daily beginning immediately after delivery in an attempt to prevent postpartum anaphylaxis. This recommendation was directly passed on to her obstetrician before delivery.

The prenatal course of her current pregnancy was significant for gestational diabetes controlled with glyburide and a history of genital herpes on acyclovir suppression beginning at 35 weeks. She presented in labor at term and was started on penicillin for group B streptococci prophylaxis. She received an epidural anesthesia and had an uncomplicated spontaneous vaginal delivery of a healthy male neonate. As per the above recommendation, she began prednisone and cetirizine prophylaxis. Postpartum days 1 and 2 were unremarkable, and breast-feeding occurred without difficulty. Ibuprofen and acetaminophen were provided for pain control. Three days after delivery, while breast-feeding, she developed raised, erythematous, pruritic patches on her arms, chest, and back, with periorbital and oral swelling. The rash worsened after each episode of breast-feeding. She had received a total of six doses of 800 mg ibuprofen before the first onset of hives, and was subsequently discontinued. Her symptoms began to diminish after intravenous diphenhydramine, but with each attempt to breast-feed, the facial edema and rash returned. She was subsequently also given an epinephrine injection and ranitidine for control of her symptoms, which subsided overnight. Her symptoms did not return despite continuing to breast-feed throughout the rest of her hospital stay. Upon discharge, the patient was given strict instructions that if her symptoms returned to use the epinephrine auto-injector and to go immediately to the emergency department. The patient was discharged home and continued breast-feeding with no further symptoms.
She was reevaluated by the Allergy Division because she suffered these reactions despite the recommended pretreatment. Skin tests to the patient’s breast milk and oxytocin were negative. Prolactin was not available for skin testing. In addition to prophylactic treatment with steroids and antihistamines, she was advised to avoid all nonsteroidal antiinflammatory medicines if she is to have another pregnancy.

**COMMENT**

The first report of a case of anaphylaxis associated with breast-feeding was in *Lancet* in 1991 and describes a 29-year-old woman with generalized urticaria and upper airway angioedema with each breast-feeding over 3 days after the birth of her first child. She was taking aspirin at the time, and the episodes resolved even with continuation of breast-feeding once the aspirin was discontinued. One month later she had another anaphylactic episode within a few minutes of breast-feeding while taking paracetamol (acetaminophen). After the birth of her second child 5 years later, she suffered similar episodes after breast-feeding despite not taking any aspirin or acetaminophen. Suppression of lactation was ultimately required for both postpartum periods. The authors suggested that the anaphylactic episodes were triggered by breast-feeding, milk let-down, and aspirin use and that progesterone may be a factor.

In the *Journal of Human Lactation* in 1998, a second case describes a 30-year-old woman with hives, throat edema, and wheezing after breast-feeding on postpartum day 3. She had breast-fed uneventfully for the first 48 hours after birth and was able to continue to breast-feed without subsequent reactions beginning on postpartum day 4. She was taking ibuprofen for pain control. The authors suggest that breast-feeding triggered the anaphylactic reactions in this woman and that nonsteroidal antiinflammatory medicines were probably a contributing factor.

The most recent report (European Annals of Allergy and Clinical Immunology 2007) describes a 31-year-old woman with a generalized rash, airway angioedema, wheezing, hypotension, and loss of consciousness 72 hours after the delivery of her first child. These symptoms occurred again with her second child in a similar manner. The episodes were temporally associated with breast-feeding and subsided when breast-feeding was discontinued or lactation suppressed. The authors suggest that the symptoms could be due to the actions of oxytocin and corticotropin-releasing hormone on mast cells, facilitated by the absence of the stabilizing role of progesterone, resulting in degranulation release of histamine and other mediators.

Lactation anaphylaxis remains a rare occurrence, and the actual pathogenesis of the reaction remains unclear. Prior case reports suggest a relationship to the hormone shifts related to the end of gestation and the beginning of lactation. The rapid decrease in progesterone after the delivery of the placenta in the presence of a high level of prolactin allows for the process of lactogenesis. This process typically occurs around postpartum days 2 to 3, which relates well to the appearance of symptoms in this patient as well as two of the three patients in the previous case reports. The use of nonsteroidal antiinflammatory medications is also cited as a contributing factor. These agents are known to exacerbate urticaria and anaphylaxis.

Recent studies have shown that during pregnancy, increased numbers of mast cells are found in the mammary gland and uterus. It has also been shown that progesterone has a stabilizing effect on the mast cell membrane, whereas estrogen increases mast cell degranulation and histamine release. The abrupt withdrawal of progesterone after delivery may facilitate the release of histamine. Steroid levels also peak with labor and delivery and then quickly decline. The removal of corticosteroid suppression of mast cells may also predispose these women to anaphylactic reactions. There may be many other mechanisms related to breast-feeding in these particular patients that have not yet been discovered because of the rarity of such events. For those patients with a previous history of anaphylaxis while breast-feeding, a prophylactic regimen with corticosteroids and antihistamines begun immediately after delivery and avoidance of all nonsteroidal antiinflammatory medications may offer the best protection.

**REFERENCES**

Postpartum hemorrhage is one of the most common causes of maternal mortality and morbidity, and when encountered, one must react rapidly to save a life. The most common cause of postpartum hemorrhage is uterine atony, but excessive bleeding may result from other causes and occasionally occurs because of coagulation defects. When a persistent or refractory hemorrhage is present despite adequate treatment, coagulation defects must be considered. Acquired inhibitors of coagulation factor VIII as a cause of postpartum hemorrhage are extremely rare. This extreme phenomenon is associated with significant morbidity and potential death. Diagnosis is based on a high index of suspicion followed by coagulation screening. Early treatment of this extreme phenomenon is crucial and can be life saving. We report a case of pregnancy-acquired factor VIII inhibitors with successful treatment using rituximab, an anti-CD-20 monoclonal antibody.

**CASE**

A 40-year-old woman at 36 weeks of twin gestation was admitted to our hospital due to elevated blood pressure. The pregnancy was induced by in vitro fertilization (IVF) due to male factor infertility. Investigation revealed mild preeclampsia and necessitated delivery at term. The patient chose cesarean as the mode of delivery. The operation was uneventful. Immediately postpartum, the patient developed severe preeclampsia and was treated accordingly. During the initial postpartum period, continuous bleeding through the abdominal scar was observed, which was unresponsive to local pressure efforts. A diagnostic laparotomy carried out a few hours later demonstrated clots in the subcutaneous area and a small amount of intraperitoneal blood (approximately 100 mL). Activated partial thromboplastin time (PTT) was prolonged (53 seconds), hemoglobin level dropped to 6.8 g/dL, and blood transfusion was required. Investigation of possible coagulation pathology was initiated because of an unusual lack of response to the massive administration of clotting factors. On postpartum day 2, a second laparotomy was required because of continuous intraabdominal bleeding. The laparotomy revealed generalized tissue oozing requiring abdominal packing and admission to the intensive care unit. On postpartum day 4, packing was removed. Bleeding was partially reduced, probably by the tamponade effect of a hematoma observed on an imaging study. Activated factor VII treatment was considered at this point; however, bleeding seemed to be under control, and this treatment was delayed. Despite infusion of numerous blood products (26 units of packed cells, 30 units of fresh frozen plasma, and 35 units of cryoprecipitate), the PTT was further prolonged (up to 149 seconds), and factor VIII activity was found to be less than 1%. The diagnosis of acquired hemophilia and the presence of specific inhibitors was soon established (postpartum day 5), using the Bethesda assay (up to 150 Bethesda units/mL). Steroid (methylprednisolone 120 mg bid) and immunoglobulins (150 g of human normal immunoglobulin G [Omr-IgG-am, Omrix, Tel Aviv, Israel]) only partially corrected factor VIII activity. Solely upon administration of rituximab was full bleeding control achieved. A total of four doses of rituximab were given at a dosage of 375 mg/m² once per week. No adverse effects were observed with the administration of rituximab. The patient was discharged on postpartum day 19. The inhibitor disappeared 1 month postpartum (18 days after the initial dose), whereas factor VIII activity normalized 2 months postpartum (Fig. 1).
follow-up visit 3 months postpartum, the patient’s activated PTT remained normal, and no additional therapy was required.

**COMMENT**

Acquired hemophilia, in which inhibitors to factor VIII are produced, is extremely rare, with an annual incidence of 0.2–1 per million.\(^1,2\) Factor VIII inhibitors are autoantibodies directed against specific domains of the factor VIII molecule, leading to low factor VIII activity.\(^4\) Although the majority of patients are labeled idiopathic, possible association was suggested to autoimmune illnesses, cancer, drugs, infection, and pregnancy.\(^5\)

Although only up to 11% of acquired hemophilia occurs postpartum, the mortality rate may reach 22%.\(^1,2\) Bleeding from acquired hemophilia becomes apparent in the postpartum period, usually within 3 months of delivery, but rarely, it can be detected antenatally or during delivery.\(^1,2\) Most cases experience a spontaneous remission of these autoantibodies, usually within a few months, but this occurrence is unpredictable.\(^1,3\) The prolongation of activated PTT, not corrected by multiple blood product transfusions, with normal prothrombin time is the hallmark of the laboratory diagnosis. Diagnosis can be confirmed when specific inhibitors are demonstrated using the Bethesda assay. Hemorrhage with low titer inhibitor (titer less than 5 Bethesda units) can be treated with factor VIII infusion, whereas eradication of factor VIII inhibitors with steroids, immunoglobulin, or immunosuppressive drugs is also beneficial. Severe hemorrhage associated with high-titer inhibitor is treated initially with immediate hemostatic treatment, including inhibitor bypassing agents, such as activated prothrombin complex concentrates or recombinant activated factor VII (Fig. 2).

Rituximab, an anti CD-20 monoclonal antibody, leads to a deep depletion of B lymphocytes and is a useful emerging treatment in postpartum acquired hemophilia, when initial therapies fail. Our patient received rituximab after the high inhibitor titer was resistant to initial therapy and only partial hemostasis was achieved. Three cases of postpartum acquired hemophilia treated with rituximab have previously been published.\(^3\) Unlike these previously published case reports with delayed presentations, our patient presented with an immediate and severe progressive postpartum hemorrhage. Furthermore, this is the only case accompanied with preeclampsia and twin gestation as a possible explanation of the patient’s rapidly progressive course, although no relationship between preeclampsia or twin gestation and acquired hemophilia is known. Two cases of acquired hemophilia in IVF pregnancies complicated by ovarian hyperstimulation syndrome were previously published.\(^6\) Our patient conceived with IVF but did not suffer from ovarian hyperstimulation syndrome. Although the risk of developing acquired hemophilia is greatest in young primigravidas, our patient was elderly and in

Fig. 1. Patient postpartum course, treatment modalities and final resolution. 
her second pregnancy. In our case, a slight decrease of the inhibitor titer was observed before rituximab treatment, a process which was intensified after the initial rituximab infusion. According to published data, most responses are observed within the first 2 weeks of therapy and complete normalization of factor VIII and activated PTT may take up to 1 year. Similarly, in immune thrombocytopenia, the median time to response after administration of the first dose of rituximab is 2 weeks. Transplacental transmission of factor VIII inhibitor was implicated in a case of severe neonatal intracranial hemorrhage, although in our case, the neonates had no known neonatal sequelae.

It is possible that the diagnosis of acquired hemophilia is becoming even less common in the past few years due to the introduction of activated factor VII given to patients with massive postpartum hemorrhage. However, this treatment was not administered in our case. In conclusion, this case illustrates the importance of maintaining a high index of suspicion and considering rare causes when a refractory postpartum hemorrhage event is encountered.

REFERENCES

Listeriosis in Pregnancy Complicated by Postpartum Heart Block

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BACKGROUND: Listeria monocytogenes is a food-borne pathogen that primarily affects pregnant women. Cardiac involvement is an uncommon complication of infection. We present a case of a gravida with Listeria bacteremia at 36 weeks of gestation.

CASE: Two of a patient’s blood cultures grew L monocytogenes after she experienced chills, headache, myalgia, and diarrhea. The patient was treated with antibiotics for 48 hours, and then labor was induced, resulting in a normal delivery with a healthy neonate. On day 5 postpartum, the patient developed progressive heart block, resulting in a third-degree block, which required a pacemaker. An electrocardiogram done 30 days after hospital discharge demonstrated an atrial-sensed, ventricularly paced rhythm, which indicated that the heart block had not resolved.

CONCLUSION: Heart block is a rarely reported and possibly overlooked complication of listeriosis. Mothers with listerial infection should be screened for cardiac complications to avoid unexpected decompensation.

Listeria monocytogenes is a β-hemolytic gram-positive rod. Cases of listeriosis are rare in the United States, with an overall annual incidence of 0.7 per 100,000 in the general population and 12 per 100,000 in pregnant women. The disease primarily affects pregnant women, newborns, the elderly, and patients who are immunocompromised. Infection generally results from oral ingestion of contaminated foods including those made from unpasteurized milk (soft cheese), ready-to-eat delicatessen meats, and meat patés.

Listeriosis in pregnancy usually presents as a flu-like illness with prodromal symptoms of fever, malaise, headache, and myalgia. Infection can less-commonly result in febrile gastroenteritis with diarrhea, nausea and vomiting, or bacterial meningitis. In the first trimester, infection typically leads to spontaneous abortion. Infection in the third trimester can cause chorioamnionitis, intrauterine fetal demise, stillbirth, and neonatal listeriosis. Almost all untreated pregnant women with documented maternal listerial bacteremia will have affected fetuses, with only 3–10% of fetuses being unaffected.

Cardiac involvement is an uncommon complication of listeriosis in pregnant and nonpregnant patients. Many reports describe listerial septicemia resulting in endocarditis in both prosthetic and normal heart valves. Myocarditis and myocardial infarction have also been reported in nonpregnant immunocompetent patients. There is a single report of fatal pericarditis in a pregnant patient. One series reports Listeria-associated atrioventricular block in children. To our knowledge, this is the first report of listeriosis in pregnancy complicated by heart block.

CASE

A 36-year-old Hispanic multigravida (gravida 5 para 4) at 35 5/7 weeks of gestation presented to labor and delivery triage with a 3-day history of chills, headache, and myalgia and a 1-day history of diarrhea. The patient was febrile to 38.9°C and tachycardic to 130–139 beats per minute (bpm). Her physical examination was otherwise unremarkable for infection. Fetal heart monitoring showed fetal tachycardia in the range of 200–209 bpm but was otherwise reassuring.

The patient emigrated from Mexico 2 years ago and had no other recent travel. Her prenatal course was otherwise unremarkable. Her obstetric history consisted of four normal spontaneous vaginal deliveries at term. She had no other relevant medical or surgical history.

Laboratory investigations showed a normal white blood cell count and urinalysis results. Blood and urine cultures were ordered. The patient was admitted for observation and treated with antipyretics. Early the next morning, the patient was afebrile, and maternal and fetal tachycardia were resolved. She was discharged home.

Three days later, two of two blood cultures grew mono-
cytogenes, and the patient was asked to return to labor and delivery. Now at 36 1/7 weeks gestation, her prior symptoms had resolved except for occasional headache. Her temperature was 38.5°C, heart rate 64 bpm, blood pressure 118/65 mm Hg, and O2 saturation 97%. The fetal heart tracing showed tachycardia in the range of 170–179 bpm but was otherwise reassuring. She had no abdominal pain...
or fundal tenderness. Routine investigations demonstrated elevated liver function tests, with an aspartate transaminase of 105 units/L, alanine transaminase of 72 units/L, and an alkaline phosphatase of 591 units/L. A viral hepatitis panel was negative. The patient, when specifically questioned, confirmed eating unpasteurized soft Mexican cheese (queso fresco) before her symptoms began.

The patient was admitted and treated with intravenous ampicillin and gentamicin. After 48 hours of treatment, the patient was no longer febrile and remained asymptomatic. Labor was then induced with oxytocin. Thirteen hours later, the patient had a normal spontaneous vaginal delivery of a healthy 2,548-g newborn male with Apgar scores 9 and 9 at 5 and 10 minutes. The newborn showed no signs of infection. He was admitted to neonatal intensive care for surveillance and empiric antibiotic therapy with 14 days of ampicillin and 4 days of gentamicin. The placental pathology confirmed acute villitis and intervillositis with abscesses. Placental culture, however, grew only a resistant Escherichia coli in the broth.

Ampicillin and gentamicin were continued postpartum. On postpartum day 1, the patient had two episodes of loss of consciousness that were not witnessed by a medical provider. Upon immediate evaluation, her vital signs and her examination were unremarkable. A computed tomography and magnetic resonance imaging of the brain demonstrated no lesions and no meningeal enhancement. A lumbar puncture was normal.

On postpartum days 3 and 4, the patient was noted to have an asymptomatic heart rate in the range of 50–59 bpm. An electrocardiogram (EKG) on postpartum day 5 revealed sinus bradycardia (47 bpm) and a first-degree atrioventricular block of 293 ms with a prolonged QTc of 495 ms. Serum potassium, magnesium, and thyroid-stimulating hormone levels were normal. Telemetry revealed type I and type II second-degree atrioventricular block. On postpartum day 6, her heart rate was 30–49 bpm, and she had a complete (third-degree) atrioventricular block. She was admitted to the cardiac care unit for closer management. Transthoracic and transesophageal echocardiograms were done, and they showed normal left ventricular size and function. There were no valvular vegetations and no wall motion abnormality. A troponin T on day 7 was 0.05 ng/mL, higher than the 99 percentile for this test (0.01 ng/mL).

In the cardiac care unit, an intravenous isoproterenol drip was started and titrated for a heart rate goal of greater than 45 bpm. Despite the addition of oral pseudoephedrine and theophylline, a heart rate over 50 bpm could not be maintained without isoproterenol.

A subcutaneous permanent dual chamber (DDD) pacemaker was placed on postpartum day 14 without complication. The patient received a total of 16 days of ampicillin and 14 days of gentamicin. Blood culture results from day 1 and 7 of treatment were negative. Surveillance blood cultures done 20 and 30 days after hospital discharge also had negative results. An EKG done 30 days after hospital discharge demonstrated an atrial-sensed, ventricularly paced rhythm, which indicated that the heart block had not resolved.

COMMENT

We believe this is the first report of listeriosis in pregnancy complicated by heart block after comprehensive searches of MEDLINE via PubMed, Web of Science, Popline, CINAL, the Cochrane Controlled Trials Registry, LILACS, and Google Scholar were completed with the help of a professional librarian. MEDLINE was searched, from 1950 through November 7, 2008 for the following MeSH and key word terms: “Listeria,” “pregnancy,” “heart diseases,” “heart block,” “postpartum period,” and “case reports.” These terms were similarly searched in the additional bibliographic databases listed above.

Food-borne infection with *L monocytogenes* is a rare complication in the pregnant patient. Clinical symptoms usually mimic a febrile viral illness, and diagnosis can easily be missed if blood cultures are not obtained. Undiagnosed infection frequently results in fetal loss, chorioamnionitis, and sepsis, threatening the life of both mother and fetus. For these reasons, blood cultures are recommended in any febrile pregnant patient with no obvious source of infection.1

Listeriosis in pregnancy is treated with antibiotics. In the case of bacteremia, antibiotic therapy with ampicillin with or without gentamicin is recommended for 10–14 days or until cultures are negative.12 Controversy exists regarding timing of delivery. Unlike typical chorioamnionitis, listerial chorioamnionitis may be successfully treated with maternal intravenous antibiotics without delivery. A number of reports demonstrate that maternal intravenous antibiotic treatment in the setting of listerial infection at previable or very-preterm gestations can result in healthy term or late preterm deliveries.3,8 Thus, maternal antibiotic therapy may be adequate to treat fetal infection and, therefore, may prevent complications of prematurity and neonatal listerial sepsis. It is, therefore, reasonable in the setting of a previable or very-preterm pregnancy to treat with antibiotics and delay delivery with close maternal and fetal surveillance. Delivery would be logical in cases of fetal distress or when the condition of the mother is unstable.

In the term or late preterm pregnancy, it is unclear if delay of delivery with antibiotic treatment is beneficial. The theoretic benefit would be to treat a potentially septic fetus in utero and deliver a healthy neonate, thus avoiding intensive care challenges of managing a septic neonate. Theoretic concerns of in utero treatment include unknown efficacy of fetal treatment and unknown time course between mater-
nal and fetal infection. Therefore, expeditious delivery at term may provide more efficacious (or at least more predictable) antibiotic treatment to the neonate and/or prevent the transmission of infection from the mother to the fetus. Furthermore, expeditious delivery may benefit the mother by evacuating a reservoir of infection. No studies currently exist that indicate which approach is more efficacious to prevent maternal and neonatal long-term sequelae.

Despite antibiotic therapy, negative culture results, and a normal delivery, our patient developed progressive atrioventricular heart block necessitating pacemaker placement. We believe that the heart block was a likely consequence of listeriosis. This assumption is supported by 1) biologic plausibility, especially in the setting of an elevated troponin, 2) prior reports linking *Listeria* with heart block, and 3) lack of a more likely clinical explanation. *Listeria* could have caused atrioventricular node dysfunction either by direct infection or an immune phenomenon. It is possible that this patient had pre-existing heart block that was coincidentally diagnosed during her hospitalization. This explanation is unlikely, however, since she did not originally present with a bradyarrhythmia.

Although many cases of endocarditis are treated for 4–6 weeks, there is no known appropriate duration of antibiotic therapy in patients with cardiac complications of *Listeria*. Given our patient was clinically well after 16 days of antibiotics, she was discharged home with a plan for surveillance cultures.

As a previously unreported complication of listeriosis in the immunocompetent pregnant patient, we feel that this case is an important addition to the existing literature. It may be that heart conduction abnormalities in these patients generally go undiagnosed. However, increased awareness of this possible complication with EKG screening may help avoid unexpected rapid cardiac decompensation.

**REFERENCES**


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**Recurrent Ovarian Torsion in a Premenarchal Adolescent Girl**

**Contemporary Surgical Management**

Nanette Rollene, MD, Melissa Nunn, DO, Timothy Wilson, MD, and Charles Coddington, MD

**BACKGROUND:** Recurrent ovarian torsion in a premenarchal adolescent girl is a rare event. Several methods of prevention using surgical plication have been proposed, which require varying degrees of technical expertise and can result in altered reproductive anatomy.

**CASE:** A premenarchal adolescent girl presented with a history of salpingo-oophorectomy for torsion and recurrence treated by detorsion. She was evaluated for preventive strategies and underwent a laparoscopic oophoropexy, performed using transvaginal ultrasound guidance, to facilitate access should oocyte retrieval be indicated for future fertility.

**CONCLUSION:** Recurrent ovarian torsion is an uncommon event, but given the possibility of permanent sterility, oophoropexy should be discussed. As assisted reproductive technology procedures become more common, oophoropexy designed to aid ovarian access should be considered before surgical intervention.

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can be treated using an ovarian-sparing procedure. Several risk factors have been proposed, such as ovarian cysts, tumors, impeded venous return causing adnexal congestion, or excess mobility of the adnexa, but given its rarity, the risk for recurrence remains unknown. Adnexal fixation procedures have been advocated as potential preventive measures. There are many ways to accomplish this surgically, but these may render the ovary inaccessible for future assisted reproduction. Given the advances in success rate and availability of assisted reproductive technology, we report the case of a laparoscopic oophoropexy performed with transvaginal ultrasound guidance to confirm position and optimize ovarian access should it be warranted for future fertility.

**CASE**

A 13-year-old premenarchal girl presented for consultation regarding a prophylactic right oophoropexy. Her history was significant for torsion of the left ovary at age 10 years, which was treated by a left salpingo-oophorectomy. Pathology revealed a 5-cm follicular ovarian cyst. Three years later, she presented to the emergency room at her local hospital with right lower quadrant pain, nausea, and vomiting. The ultrasonogram showed a 7-cm by 8-cm by 5-cm right ovary with good arterial and venous flow, but because of the concern for intermittent torsion, she underwent a laparoscopic evaluation. She was diagnosed with a right ovarian torsion, with the ovary noted to be twisted upon itself three times. Because of timely action and collaborative effort, this event was conservatively treated by detorsion, with return of normal color and restoration of the anatomic relationship.

Several months later, she presented for preventive strategy and surgery. Ultrasound evaluation revealed a multifollicular right ovary with good Doppler flow and without a dominant cyst. Given her history of recurrent ovarian torsion, with only one remaining ovary, she was counseled regarding undergoing a prophylactic ovarian plication procedure, and both the patient and her mother consented to proceeding. In the interim, she was started on the oral contraceptive pill to mitigate risk of future cyst development. Her height at the time was 65 inches, weight was 128 pounds, she had Tanner stage IV breast development, and Tanner stage V pubic hair.

The surgery consisted of a small infraumbilical incision and insufflation with the Veress needle. A 5-mm umbilical port was placed, followed by a 5-mm left lower quadrant and a 10-mm right lower quadrant port. She subsequently underwent the right-sided oophoropexy, during which a 1-cm incision was made in the ovary using needlepoint cautery. Three 10-mm Horizon titanium surgical clips (Teleflex, Research Triangle Park, NC) were used to plicate the ovary to the pelvic sidewall peritoneum with close attention to the location of the ureter and iliac vessels (Fig. 1). This was performed with transvaginal ultrasound probe placement and guidance to facilitate ovarian access, should the patient attempt natural conception or ovulation induction without success and require in vitro fertilization in the future (Fig. 2). Eleven months later, she was doing well without recurrence.
Ovarian torsion is an uncommon event that can present a diagnostic quandary for emergency room physicians, pediatric surgeons, and gynecologists alike. Presenting symptoms may include acute onset of lower abdominal pain, nausea, and vomiting. A low-grade fever and leukocytosis may also be present, and girls are commonly suspected to have appendicitis, especially because the right adnexa is more frequently involved than the left. In the early evaluation, one clinical difference between appendicitis and torsion that may be helpful is that patients with torsion have pain that is very abrupt in onset, and they often recount similar episodes in the past.

This particular patient presented for a routine consultation regarding her preventive options. Given her history of ovarian cysts and multifollicular ovary found during evaluation, we discussed the option of pharmacologic management with the oral contraceptive pill. This therapy has been shown to decrease ovarian cysts in the postmenarchal population, but its ability to prevent cysts in younger girls has not been studied. Our patient had documented bone growth consistent with her stated age, was several years past the point of greatest linear growth, and had Tanner stage IV breast development. Thus, our concern about hormone therapy affecting height and breast maturation was minimized.

The option of prophylactic surgical intervention was also discussed. In the past, this patient might have been offered exploratory laparotomy, but the field of pediatric and adolescent laparoscopy has expanded rapidly in recent years. Given the patient’s body habitus, she was similar to many of our adult patients and deemed a good candidate for laparoscopic intervention.

Multiple laparoscopic approaches have been described in the literature. When a patient is noted to have an elongated uteroovarian ligament, plication may be accomplished by suturing the proximal and distal ends of the uteroovarian ligament. Another option would be to shorten the ligament with placement of an Endoloop (Ethicon, Somerville, NJ). Often the uteroovarian ligament is normal in appearance, and in such cases use of oophoropexy has been described. One such technique is to fix the ovary to the back of the uterus using permanent suture. Another technique involves using permanent suture to fix the mesovarium to the pelvic sidewall at the level of the pelvic brim, which is similar to but less extensive than one that might be used for patients undergoing pelvic irradiation.

Each of these procedures presents its own set of technical challenges. Most oophoropexies require intracorporeal or extracorporeal knot tying. Such equipment and surgical expertise may not be immediately available. A concern regarding use of an Endoloop is tissue necrosis. It may be challenging to position the loop tight enough so it does not slip, but not too tight so as to cause necrosis and potential ovarian damage. An alternative procedure which does not involve laparoscopic knot tying or loops is the use of clips.

We chose to plicate the ovary to the sidewall with surgical clips, and this decision was based on experience and technical efficiency. Clips are easier to work with, especially if you have a small open surface such as from an ovarian cystectomy. In our case, a 1-cm opening was created in the ovarian capsule using needlepoint cautery. This allowed us to hook the free edge with the clip and readily grasp peritoneum at the same time.

The exact location of clip positioning was determined by placing a transvaginal ultrasound probe for guidance. This allowed the surgeon to choose a site for oophoropexy that was away from the ureter and vascular structures yet would permit transvaginal ovarian access should the patient attempt natural conception or ovulation induction without success and require in vitro fertilization. As assisted reproductive technology procedures become more common, oophoropexy designed to aid ovarian access should be considered before surgical intervention.

REFERENCES

Endometriosis Mimicking Ovarian Cancer in the Setting of Acquired Immune Deficiency Syndrome

Sina Haeri, MD, MHSA, and Jonathan A. Cosin, MD

BACKGROUND: With rising rates of human immunodeficiency virus (HIV) among women and resultant immunosuppression, clinicians face varying presentations of gynecologic pathologies. We report a case of endometriosis in a patient with acquired immunodeficiency syndrome (AIDS) presenting with a Sister Mary Joseph’s nodule and mimicking carcinomatosis.

CASE: A woman with AIDS and 2-month history of abdominal pain, distention, and weight loss was found to have periumbilical and pelvic masses, ascites, lymphadenopathy, and an elevated CA 125 level. Operative findings included chocolate-colored ascites and peritoneal seeding involving the ovaries, uterus, appendix, bowel, umbilicus, and omentum. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and resection of all gross disease. Pathologic diagnosis was endometriosis and AIDS-associated adenopathy.

COMMENT: Immunodeficiency from AIDS can affect the progression of endometriosis to the point of mimicking ovarian malignancy.

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Endometriosis is one of the most common gynecologic disorders affecting reproductive-aged women. It is characterized by the presence and growth of endometrial tissue in ectopic sites, usually in the pelvis. The most widely accepted theory of the cause of endometriosis is that retrograde menstruation and peritoneal spillage of endometrial endothelial cells leads to the adhesion and persistence of ectopic endometrial cells. A critical component of the pathology of endometriosis is immune dysfunction. This includes increased inflammatory activity and impaired immune recognition and clearance of endometrial cells. More specifically, endometriosis has been associated with an increase in resident macrophages in the peritoneum, increased secretion of cytokines that suppress cell-mediated immunity, and a decrease in effective natural killer cells that would normally clear endometrial cells from the peritoneal cavity. Given the importance of the immune system in the development of as those present in patients with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) may critically influence the course of endometriosis.

Acquired immunodeficiency syndrome is currently classified based upon CD4+ T cell count as well as presence or absence of AIDS defining conditions or diseases with AIDS defined as CD4+ T cell count less than 200/microliter at any time or the presence of a category C illness. Immune cell abnormalities associated with AIDS include CD4+ T cell depletion and dysfunction, loss of cytolytic activity and depletion of CD8+ T cells, aberrant activation of B cells, abnormal monocyte function and cytokine secretion, and decreased immunosurveillance by NK cells. This severe immunocompromise may profoundly affect the progression of endometriosis in patients with AIDS.

CASE
A 34-year-old gravida 2, para 2, woman with AIDS was evaluated with a 2-month history of noncyclic abdominal pain and worsening distention. Review of systems was also significant for an 8-pound weight loss in 2 months and increased fatigue but was otherwise negative. Her medical history included anemia of chronic disease, and her only previous surgery was a myomectomy for symptomatic uterine leiomyomas. She had subcategory A3 AIDS with a CD4+ count of 97/microliter at presentation but no history of an opportunistic infection or AIDS defining illness. Family history was negative for malignancy.

Physical examination was significant for a distended abdomen with a large periumbilical mass, along with a large and nodular pelvic mass palpated on rectovaginal examination. Imaging studies, including computed tomography and magnetic resonance imaging demonstrated a large lobulated pelvic mass (12.1×15.9×9.0 cm) suspicious for an adnexal neoplasm or myomatous uterus, a right ovarian complex cyst (4.4×3.2×3.9 cm), massive ascites, and retroperitoneal lymphadenopathy. There was an elevated in CA 125 at 172 units/mL (normal 0–35 units/mL). Our preoperative differential diagnosis, based on the above findings, included carcinomatosis secondary to a gynecologic (ovarian, fallopian tube, or uterine primary), gastrointestinal, or other nongynecologic sources (breast, lymphoma), and infectious causes such as disseminated tuberculosis.

Surgical evaluation demonstrated 6.8 liters of chocolate-colored ascites. There was a 3.5×7-cm omental nodule...
haeri and cosin

endometriosis mimicking ovarian cancer

the sister mary joseph’s nodule is metastatic carcinoma to the umbilicus. it was first described by dr. william mayo in 1928 and subsequently named after sister mary joseph, his long time assistant.6 although umbilical involvement of endometriosis is well described in the literature, its coexistence with ascites and peritoneal implants mimicking carcinomatosis and a sister mary joseph’s nodule is not.

previous publications have reported varying degrees of endometriosis mimicking ovarian cancer in its presentation.7,8 such presentations underscore the need to be aware of altered disease presentations in the setting of severe immunosuppression. of special concern is the mimicking of malignancy. failure to recognize this can lead to unnecessary interventions and treatments such as chemotherapy.8

endometriosis should be considered in the differential diagnosis of patients with hiv/aids who present with ascites, peritoneal seeding, and/or an umbilical nodule. this recognition would allow for a more comprehensive presurgical discussion with the patient regarding the possibility for more conservative, fertility-sparing surgical options for such nonmalignant conditions that would otherwise be inappropriate if the diagnosis were advanced malignancy and carcinomatosis.

comment

endometriosis is a common gynecologic disorder affecting reproductive-aged women and is characterized by ectopic endometrial tissue. although usually confined to the pelvis, it can be found in other sites in the body. a component of its pathology is immune dysfunction. acquired immunodeficiency syndrome is the state of hiv-induced severe immune depression. in this case, although we do not believe that the development of endometriosis was related to the patient’s aids, we do postulate that the resultant immunodeficiency accelerated the progression of the endometriosis to the point of mimicking advanced-stage ovarian malignancy. with rising rates of hiv among reproductive-aged women as well as the improved life span for patients with hiv/aids resulting in a more prolonged, chronic immunosuppressed state, clinicians will undoubtedly face altered presentations of common gynecologic pathologies, including endometriosis. cases such as the one presented here should alert providers to entertain a larger differential diagnosis when evaluating such patients.

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Lipodystrophy

An Unusual Diagnosis in a Case of Oligomenorrhea and Hirsutism

Jennifer Keller, MD, Lalitha Subramanyam, MD, Vinaya Simha, MD, Robert Gustofson, MD, Debra Minjarez, MD, and Abhimanyu Garg, MD

BACKGROUND: Familial partial lipodystrophy, Dunnigan variety, is a rare autosomal dominant disorder caused by missense mutations in LMNA gene. Individuals are predisposed to insulin resistance and its complications, including features of polycystic ovary syndrome.

CASE: A 27-year-old Hispanic woman presented with oligomenorrhea and hirsutism. Examination revealed cushingoid facies, significant hirsutism, acanthosis nigricans, and a lean body habitus. Metabolic testing identified diabetes mellitus, dyslipidemia, and steatohepatitis. A diagnosis of familial partial lipodystrophy, Dunnigan variety, was confirmed by the detection of a heterozygous p.Arg482Trp (c.1444C>T) missense mutation in the lamin A/C (LMNA) gene. Subsequently, seven female relatives were diagnosed with familial partial lipodystrophy, Dunnigan variety, four of whom had menstrual irregularities.

CONCLUSION: Familial partial lipodystrophy, Dunnigan variety, can present with features similar to polycystic ovary syndrome. Diagnosis is critical because the metabolic complications of the disorder have significant morbidity.

(Obstet Gynecol 2009;114:427–31)

Lipodystrophies are a heterogeneous group of acquired and inherited disorders characterized by selective loss of adipose tissue. Although genetic lipodystrophies are rare, acquired lipodystrophy due to antiretroviral therapy in human immunodeficiency virus–infected patients is increasingly recognized. The extent of fat loss in the different lipodystrophy syndromes varies and may be either generalized or restricted to certain regions. Familial partial lipodystrophy, Dunnigan variety, is a rare autosomal dominant disorder, first described by Dunnigan et al in 1974, with more than 300 subsequent patients being reported. It is caused by heterozygous missense mutations in the lamin A/C (LMNA) gene, but the molecular basis of fat loss due to LMNA mutations is not clear.

Patients with familial partial lipodystrophy, Dunnigan variety, have normal fat distribution during childhood but, after puberty, demonstrate progressive loss of adipose tissue from the extremities, variable loss from the body corpus, and, often, excess fat deposition in the face, neck, and intraabdominal regions. Fat loss leads to a characteristic muscular appearance, and other notable features include acanthosis nigricans and hepatomegaly. Metabolic abnormalities related to insulin resistance such as diabetes mellitus, hypertriglyceridemia, and hepatic steatosis are noted commonly, especially in affected women. Not only is the diagnosis more apparent in women because of the unusual muscular prominence, but also the metabolic complications are more severe. Further, oligomenorrhea and hirsutism have been reported in female patients, and thus it is important to consider the diagnosis of familial partial lipodystrophy, Dunnigan variety, in lean, muscular women who have polycystic ovary syndrome (PCOS). We report a patient with typical features of PCOS who subsequently was diagnosed to have familial partial lipodystrophy, Dunnigan variety.

CASE

A 27-year-old gravida 0 Hispanic woman was referred to a gynecology clinic at a teaching institution for oligomenorrhea, hirsutism, and infertility. Gynecologic history revealed menarche at age 12 followed by regular cycles for 5 years. Thelarche was not identifiable because the patient described lack of breast development, and she could not recall time of pubarche. The patient described the onset of oligomenorrhea at approximately age 17, which ensued for 9 years, after which she became amenorrheic. The patient also described a 12-year history of progressively worsening hirsutism, leading to a full beard that she shaved daily, and significant hair growth over her chest, abdomen, and back. The irregular, anovulatory cycles together with hirsutism had resulted in the patient’s previously receiving a diagnosis of PCOS. In addition to these complaints, the patient also was concerned about her physical appearance, specifically her “double chin” and small breasts. Her sister, mother, and maternal grandmother also had similar body habitus, with the latter two also having diabetes.
Fig. 1. (A and B) Anterior and lateral views of the index patient showing marked loss of subcutaneous fat from the extremities, hips, and anterior abdomen, with excess fat deposition around the face and in the submental and dorsocervical regions. Also note the presence of acanthosis nigricans over the neck, poor breast development, and increased vulvar fat. (C) Familial partial lipodystrophy, Dunnigan variety, pedigree with patient numbers corresponding to data in Table 1. Affected individuals are shown as filled black symbols, unaffected individuals as unfilled symbols, and deceased individuals are indicated by a diagonal line. Squares represent males, and circles represent females. Arrow indicates the index patient. RR indicates a person with the normal LMNA genotype (arginine in position 482 for both alleles), and RW indicates patients with the heterozygous missense LMNA mutation (arginine and tryptophan in position 482). (D) Sequence electropherogram of LMNA exon 8, with arrow showing the site of heterozygous missense mutation, c.1444C>T, resulting in substitution of one of the normal alleles, arginine by tryptophan at position 482. The colors denote nucleic acids: blue, cytosine (C); green, adenine (A); red, thymine (T); black, guanine (G). N, possible missense mutation.

Physical examination revealed a weight of 144 lb and a height of 5’3” (body mass index 25.5 [body mass index is calculated as weight (kg)/[height (m)]²]). The patient had marked loss of subcutaneous fat from the extremities, leading to prominence of muscular contours and veins, with excess fat around the face, submental, and dorsocervical region giving her a cushingoid appearance (Fig. 1A and B). Breast tissue was nearly absent, giving the appearance of Tanner stage 1 breasts with hirsute nipples. A male-pattern hair distribution was observed, with complete but light coverage of terminal hair on the abdomen, chest, back, upper arms, thighs, and buttocks (Ferriman-Gallwey score 39/48). She had extensive acanthosis nigricans of the neck, axilla, groin, and midline of chest, abdomen, and back, and also was found to have nontender hepatomegaly.

Vulvar examination revealed excess fat deposition. Ultrasonographic findings included a normal-appearing uterus and enlarged ovaries, with a total of more than 30 small follicles (measuring 2–9 mm in diameter), and ovarian volumes of 16.6 mL and 10.7 mL.

Initial laboratory evaluation revealed slightly increased total serum testosterone of 100 ng/dL (normal values, 11–59 ng/dL) but normal levels of serum thyroid-stimulating hormone, prolactin, dehydroepiandrosterone sulfate, basal and ACTH-stimulated 17-hydroxy progesterone, and 24-hour urinary cortisol levels. The patient’s fasting and postprandial plasma glucose levels after an oral glucose load were diagnostic of diabetes mellitus (151 mg/dL and 298 mg/dL, respectively). She also had hypertriglyceridemia (158 mg/dL) and low levels of high density lipoprotein cholesterol (32 mg/dL).

Fig. 2. T1-weighted magnetic resonance images of the head and neck, abdomen, and thigh of the index patient (A, C, and E, respectively) and a healthy 25-year-old woman (B, D, and F, respectively). Compared with the healthy woman, the patient has increased fat in the dorsocervical, submental, and intraabdominal regions (as shown by arrows) but marked paucity of subcutaneous fat in the thigh and anterior abdomen.

Liver function tests were abnormal, with twofold to threefold elevation of serum alanine aminotransferase and aspartate aminotransferase (174 units/L and 110 units/L, respectively), and right upper quadrant ultrasound examination revealed diffuse fatty infiltration of the liver.

In view of the patient’s characteristic physical appearance, history of similar affliction in other members of the family, and evidence of metabolic abnormalities related to insulin resistance, it was felt that her PCOS could be secondary to familial partial lipodystrophy, Dunnigan variety. She underwent further evaluation at the University of Texas Southwestern Medical Center at Dallas along with other family members. Written informed consent was obtained. The protocol had been approved by the institutional review board at the University of Texas Southwestern Medical Center. Measurement of skin-fold thickness and whole body magnetic resonance imaging confirmed loss of adipose tissue from the extremities with excess accumulation in the dorsocervical and intermuscular regions (Fig. 2). The patient’s fasting leptin level was low at 2.3 ng/dL (less than the 10th percentile of age- and sex-matched healthy participants). Sequencing of the LMNA gene revealed a heterozygous missense mutation (c.1444C>T) leading to substitution of arginine by tryptophan at position 482 (R482W), confirming the diagnosis of familial partial lipodystrophy, Dunnigan variety (Fig. 1D). The same mutation was identified in other family members, including the patient’s mother, sister, maternal aunt, cousin, and three nieces (Fig. 1C). They had similar body-fat distribution but variable metabolic and menstrual irregularities as indicated in Table 1.

**COMMENT**

The association of PCOS with obesity and insulin resistance is well known. However, not all women with PCOS are obese, and it is important to consider the diagnosis of lipodystrophy in lean PCOS patients. The reported case highlights the importance of careful evaluation of body-fat distribution by a thorough physical examination, which can offer important clues to the diagnosis of this rare disorder. Recognition of these disorders of adipose-tissue distribution is critical for the subsequent diagnosis of more serious metabolic abnormalities in patients and their family members. Only about 300 cases of familial partial lipodystrophy, Dunnigan variety, have been described in the literature. To date, all pedigrees described have been of European origin, and this is the first case report of a Hispanic pedigree with the R482W missense mutation in the LMNA gene.

Approximately 20–33% of patients with familial partial lipodystrophy, Dunnigan variety, develop hirsutism, menstrual abnormalities, and polycystic-appearing ovaries. These signs of androgen excess likely result from both the decrease in sex-hormone binding globulin production from the liver caused by hyperinsulinemia and the direct effect of insulin on theca cells leading to androgen production. Additionally, it can be hypothesized that a greater reduction in sex-hormone binding globulin and a higher production of testosterone occurs with an increase in visceral fat deposition as has been observed in patients with central obesity. The exact etiology of insulin resistance and hyperinsulinemia leading to these abnormalities in familial partial lipodystrophy, Dunnigan variety, is not clear but is likely the consequence of ectopic fat accumulation in nonadipose tissues. Owing to the limitation in subcutaneous fat storage depots, dietary fat is redirected to nonadipose tissue stores, such as the liver and muscle, leading to lipo-

<table>
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<th>Patient</th>
<th>Current Age (y)</th>
<th>Gravidity/Parity Infertility</th>
<th>Menstrual Function</th>
<th>Age at Menarche (y)</th>
<th>Total* Testosterone (ng/dL)</th>
<th>Ferriman-Gallwey Score</th>
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<td>2§</td>
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<td>100</td>
<td>39/48</td>
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<td>24</td>
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<td>54</td>
<td>18/48</td>
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<tr>
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<td>0/48</td>
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<tr>
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<td>13</td>
<td>42</td>
<td>5/48</td>
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<tr>
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<td>ND</td>
<td>0/48</td>
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<tr>
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<td>12</td>
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</tr>
<tr>
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<td>12</td>
<td>0/0 NA</td>
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<td>ND</td>
<td>0/48</td>
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</tbody>
</table>

GTT, glucose tolerance test; HDL, fasting high density lipoprotein; TG, fasting triglycerides; DM, diabetes mellitus; NGT, normal glucose tolerance; IGT, impaired glucose tolerance based on 2-hour glucose value (140–199 mg/dL); NA, not applicable; ND, not done.

* Normal range 11–59 ng/dL.
† Normal range 3.9–30.0 ng/dL.
‡ Normal range 3–13 microunits/mL.
§ Index case.

*Menstrual cyclicity during late reproductive years.
toxicity from steatosis. However, it is also not clear why some patients with familial partial lipodystrophy, Dunnigan variety, develop the PCOS phenotype and others do not. Potential causative factors include the regional differences in fat deposition, the quantity of excess intraabdominal fat, and the severity of insulin resistance, leading to hyperandrogenemia. Undoubtedly, as in patients with other causes for PCOS, multiple factors play a role in the development of metabolic and endocrine dysfunction, including variable expressivity of the genetic mutation, age, and lifestyle.

The cornerstone of treatment of patients with familial partial lipodystrophy, Dunnigan variety, is the prevention of excess fat accumulation in nonadipose tissues. Lifestyle factors including a low-fat diet and regular exercise are vital. In patients affected by the PCOS phenotype, improvements in insulin sensitivity lead to decreases in circulating androgens and resumption of menses. Traditional pharmacologic therapy for diabetes and dyslipidemia is also often necessary, but optimal control is generally difficult to achieve owing to marked insulin resistance. Replacement therapy with human recombinant leptin offers much promise in the treatment of patients with generalized lipodystrophy, Dunnigan variety, remains to be defined. A recent open-label trial involving six patients with familial partial lipodystrophy, Dunnigan variety, demonstrated a significant improvement in triglycerides, fasting glucose, and insulin sensitivity after replacement with recombinant leptin, but larger, controlled studies are needed.

Awareness of familial partial lipodystrophy, Dunnigan variety, is important for the gynecologist because female patients may present initially with features similar to lean PCOS. Accurate diagnosis is critical to both treatment and counseling. More detailed studies on the risk factors for PCOS in familial partial lipodystrophy, Dunnigan variety, cohorts are likely to shed much information on the relationship between fat deposition, insulin resistance, and hyperandrogenemia.

REFERENCES
Cyclic vomiting syndrome is a disease of unknown cause that consists of recurrent episodes of nausea and vomiting that occur within periods of normal health. Patients have no apparent organic cause of vomiting, thus it is diagnosed after negative laboratory, radiologic, and endoscopic findings. The nausea and vomiting episodes are stereotypical, having the same time of onset, symptoms, and duration. The intervals of normal health may vary in length, and the vomiting episodes may last from hours to weeks. Once thought of as a pediatric disorder, it is now well-defined in the adult population. There are no data regarding cyclic vomiting syndrome and pregnancy.

CASE

A primigravida in her early 20s presented to the emergency department at 8 weeks of gestation with a chief complaint of persistent, prolonged nausea and vomiting with severe abdominal pain. She reported an acute onset of 20 episodes of vomiting over the past 24 hours. Her medical history was significant for cyclic vomiting syndrome, diagnosed 2 years earlier after an extensive workup, including radiologic and endoscopic abdominal studies and neurologic imaging. She reported numerous hospitalizations for intravenous fluid therapy, antiemetics, and analgesia. Her past surgical history was significant for a laparoscopic cholecystectomy (performed for her cyclic episodes of vomiting). Her medications included nortriptyline and promethazine for use as needed for cyclic vomiting syndrome exacerbations. The physical examination was significant only for abdominal tenderness to palpation without signs of an acute abdomen. The complete blood count and serum chemistry analysis, including thyroid function tests, liver function tests, and pancreatic enzymes, were unremarkable. The urinalysis was significant for a specific gravity of 1.050 and positive ketones. The urine drug screen was negative. A pelvic ultrasound examination confirmed a singleton intrauterine pregnancy at 8 weeks of gestation. The results of an abdominal ultrasound examination were normal. The patient was admitted and given intravenous fluid therapy and antiemetics (promethazine and ondansetron). The patient’s condition failed to improve after 48 hours of this therapy, so a gastroenterology consultation was obtained. A repeat laboratory evaluation was performed, with normal findings. After 8 days without any food by mouth and numerous attempts at pharmacologic management, the patient was started on total parenteral nutrition. Given her persistent symptoms, she was transferred to a tertiary care facility on hospital day 17.

At the tertiary care facility, the patient again underwent an extensive laboratory and radiologic evaluation to include magnetic resonance imaging of the abdomen and an upper gastrointestinal endoscopy, which were both negative for pathology. A psychiatric evaluation was negative for mental illness. Her symptoms eventually abated, so total parenteral nutrition was discontinued and she was discharged from the tertiary care facility after 7 days. She was placed on an outpatient regimen of promethazine and ondansetron.

The patient represented to our facility at 19 weeks of gestation, again for persistent vomiting and abdominal pain. She was again admitted for intravenous fluid therapy, antiemetics, and analgesics. An obstetric ultrasound examination revealed normal fetal anatomy and growth (326 g, 41st percentile). Her symptoms improved after 7 days, and she was discharged to home. At 26 weeks of gestation, the patient again presented with similar complaints. The fundal height measurement was significantly smaller than expected, so an ultrasound examination was performed that revealed appropriate for gestational age fetal growth (850 g, 42nd percentile) and normal amniotic fluid volume. The
patient was noted to have minimal weight gain (2 kg) since her initial presentation.

Given the concern for her nutritional status, biweekly antepartum testing with nonstress tests and amniotic fluid index measurements was initiated. Outpatient therapy consisted of promethazine, ondansetron, and ranitidine. The patient’s lack of appropriate weight gain and lagging fundal height were of continued concern. An obstetric ultrasound examination at 29 weeks of gestation revealed an estimated fetal weight of 1,090 g (21st percentile).

At 32 weeks of gestation, during the patient’s eighth admission in the pregnancy, an ultrasound examination showed likely fetal growth restriction (1,480 g, 9th percentile), with an amniotic fluid index measurement of 4 cm. The nonstress test was nonreactive. Umbilical artery Doppler studies were within normal limits (systolic to diastolic ratio 2.35) for gestational age.

The patient was given betamethasone, and 48 hours later labor induction was performed with a transcervical Foley catheter and oxytocin. The patient delivered a viable female neonate with a 5-minute Apgar score of 9 and a weight of 1,590 g (7th percentile). The neonate spent 21 days in the neonatal intensive care unit for ventilatory and nutritional support and was discharged to home in stable condition.

**COMMENT**

Cyclic vomiting syndrome first was described in the 19th century in a series of children with “fitful or recurrent vomiting.” Until the 1980s, cyclic vomiting syndrome was thought to be exclusive to children, but it is now apparent that this disabling disease affects all ages. Scobie, in 1983, published the first series of adults with cyclic vomiting syndrome. The largest case series in adults involved 41 participants, and the authors report that the symptoms are similar between children and adults. Usually underrecognized, it often is misdiagnosed as either acute viral gastroenteritis or food poisoning. Episodes may be triggered by infection, stress, or excitement. A PubMed search, limited to English and humans (1966–December 2008), was performed using the search terms “cyclic vomiting” and “pregnancy.” It failed to identify any cases reported in pregnancy.

The Rome III diagnostic criteria for cyclic vomiting syndrome in adults must include all of the following: 1) stereotypical episodes of vomiting regarding onset (acute) and duration (less than 1 week), 2) three or more discrete episodes in the previous year, and 3) absence of nausea and vomiting between episodes. All criteria must be fulfilled for the previous 3 months with symptom onset at least 6 months before diagnosis. There can be no apparent cause of vomiting (negative laboratory, radiologic, and endoscopic findings).

The differential diagnosis for cyclic vomiting syndrome during pregnancy should be considered carefully because hyperemesis gravidarum and nausea and vomiting of pregnancy are certainly more prevalent. These two conditions present by 9 weeks of gestation in virtually all women. The onset of symptoms after 9 weeks of gestation should prompt the consideration for other conditions. Other known causes of vomiting in pregnancy are gastrointestinal disorders (gastroenteritis, gastroparesis, hepatitis), genitourinary disorders (pyelonephritis, ovarian torsion, kidney stones), metabolic disorders (diabetic ketoacidosis, hyperthyroidism), and pregnancy-specific disorders (preeclampsia, acute fatty liver of pregnancy). Our patient’s cyclic vomiting syndrome episodes occurred every 3 months before pregnancy and became more frequent (approximately once per month) during pregnancy. Her initial episode during pregnancy was significantly longer than later episodes. This is perhaps due to concomitant nausea and vomiting of pregnancy (“morning sickness”) that is experienced by the majority of gravidas. The patient was without symptoms during interepisodic “well phases.”

Initial treatment for a vomiting episode is aimed at intravenous fluid and electrolyte replacement. Patients may need to be admitted because of concerns for dehydration or metabolic derangements, which may be exacerbated by pregnancy. The medical treatment of cyclic vomiting syndrome is empirical and may be directed at prophylaxis or abortive pharmacotherapy.

Establishing an initial diagnosis of cyclic vomiting syndrome during pregnancy would be very difficult because nausea and vomiting of pregnancy and hyperemesis gravidarum can cause frequent vomiting episodes, thus the diagnosis should be made in the nonpregnant state. The treatments during pregnancy, however, are very similar. Initial management with intravenous fluid and electrolyte replacement should be employed early during an episode. Antiemetic agents and analgesic agents can aid with the symptoms, but most episodes resolve spontaneously. As with other gastrointestinal disorders that potentially lead to poor maternal weight gain and malnutrition, cyclic vomiting syndrome may be a risk factor for fetal growth restriction and oligohydramnios, as was the case with our patient. We recommend that pregnancies complicated by cyclic vomiting syndrome be managed with increased fetal surveillance and periodic assessments of fetal growth and amniotic fluid status.
REFERENCES

Postpartum Vertigo and Superior Semicircular Canal Dehiscence Syndrome

Jacqueline Ogutha, MD, Nathan C. Page, MD, and Timothy E. Hullar, MD, FACS

BACKGROUND: Superior semicircular canal dehiscence is a recently described cause of imbalance, hearing loss, and tinnitus. Symptoms may begin after abrupt changes in intracranial or middle ear pressure.

CASE: This patient presented with a 6-year history of imbalance, hearing loss, and pulsatile tinnitus beginning when she was pushing during labor. A temporal-bone computed tomography scan showed a dehiscence of the superior semicircular canal. Surgical repair of the dehiscence through the middle cranial fossa resulted in immediate resolution of the patient’s symptoms, and she returned to full activity within 3 weeks.

CONCLUSION: Superior semicircular canal dehiscence is recognized increasingly as a cause of multiple otologic symptoms. Obstetricians and gynecologists with patients complaining about postpartum vertigo should inquire about symptom onset and focus their questions around events during the second stage of labor. Patients with symptoms of dehiscence should be referred to a neuro-otologist for treatment, including possible surgical repair.

(Obstet Gynecol 2009;114:434–6)

Imbalance is a common complaint, including among obstetrics and gynecology patients. Dehiscence of the superior semicircular canal increasingly has been recognized as a cause of episodic or chronic imbalance, hearing loss, autophony (an abnormally loud perception of one’s own voice), or a combination of these symptoms. We present a case of superior semicircular canal dehiscence syndrome presenting with acute vertigo during labor (see Box 1).

BOX 1. SYMPTOMS AND SIGNS OF SUPERIOR SEMICIRCULAR CANAL DEHISCENCE

Vertigo in response to loud sounds
Vertigo in response to abrupt pressure changes (such as sneezing or performing a Valsalva maneuver)
Conductive hearing loss
Hypersensitivity to bone-conducted sounds (hearing one’s own heartbeat, breathing, eyeballs moving, or feet striking the ground while walking)
Autophony (hearing one’s own voice)
Chronic imbalance

CASE

A 43-year-old G5P2 patient was referred for neurotologic care with a 6-year history of imbalance, tinnitus, and hearing loss on the right side. Her symptoms began with an “explosion” in her right ear as she was pushing during labor with her eldest child. This was accompanied by a sudden onset of pain, pulsatile tinnitus, and autophony in the right ear. After delivery, she noted new symptoms of dizziness...
that she described as feeling like she was “being pushed or knocked over by a wave,” which worsened with exposure to loud sounds. She also reported a newly heightened sensitivity to motion that made it impossible for her to enjoy amusement park rides and forced her to walk next to walls to steady her gait. Her previous history was remarkable only for a slight high-frequency sensorineural hearing loss on the left side related to noise exposure at work as a firefighter and paramedic and occasional headaches that had been evaluated previously with normal magnetic resonance imaging studies.

On physical examination, the patient appeared well, with normal findings on otoscopy and an unremarkable general neurologic examination. Valsalva with glottis open blowing against a pinched nose elicited combined vertical-torsional eye movements and caused subjective imbalance. She had a positive Hennebert sign (abnormal eye movements with pressure in the external auditory canal) on the right side. She heard a tuning fork placed on her forehead louder in her right ear than in her left, indicating a right conductive or left sensorineural hearing loss.

Pure-tone audiometry of the right ear confirmed a mild conductive hearing loss and demonstrated an abnormal hypersensitivity to bone-conducted sounds transmitted directly through the skull to the inner ear. Pure tones of 500, 1,000, and 2,000 Hz presented at 120 dB HL provoked symptoms of imbalance when presented in the right ear but not in the left. Vestibular testing with caloric (warm and cool water irrigations of the external auditory canals) and with rotation in a chair about an earth-vertical axis were unremarkable. Vestibular-evoked myogenic potential testing indicated hypersensitivity of the vestibular system to sound in the right ear but not in the left. A high-resolution temporal-bone computed tomography (CT) scan showed a dehiscence of the bone normally separating the lumen of the superior semicircular canal and the middle cranial fossa on the right (Fig. 1). Surgical repair of the dehiscence through the middle cranial fossa resulted in immediate resolution of the patient’s symptoms, and she returned to full activity within 3 weeks.

**COMMENT**

Superior semicircular canal dehiscence syndrome relates a dehiscence of the bone normally overlying the superior semicircular canal to symptoms of vertigo and oscillopsia induced by loud sounds (Tullio’s phenomenon), changes in middle ear pressure, or changes in intracranial pressure. The syndrome is recognized increasingly as a cause of chronic disequilibrium and dizziness, tinnitus, and conductive hearing loss sometimes accompanied by enhanced bone-conducted hearing.

Dense labyrinthine bone surrounding the superior semicircular canal normally bulges into the middle cranial fossa, forming the arcuate eminence. This bone covering the canal is extremely thin in about 1.3% of all individuals and frankly dehiscent in approximately 0.7%. It is believed that a dehiscence may result from congenital underdevelopment of the temporal bone followed by an event later in life that breaks open the weak area. Precipitating events may involve high intracranial or middle ear pressures such as during weightlifting or pushing during labor as reported here, but most patients do not remember a specific time of onset of symptoms. The differential diagnosis includes perilymphatic fistula, which also can be caused by a rapid pressure change and manifest with symptoms of imbalance and hearing loss. This condition results from leakage of fluid from the inner ear into the middle ear, usually through the oval or round windows.

High-resolution noncontrast temporal bone CT is used to confirm the clinical diagnosis of semicircular canal dehiscence. Using patients with symptoms of superior semicircular canal dehiscence as a gold standard, the positive predictive value of axial and coronal CT scans is only about 50%. However, fine-cut (0.5 mm or finer) scans reformatted parallel to and orthogonal to the semicircular canals can achieve a positive predictive value for dehiscence of 93%. A convincing clinical history and a positive CT scan may be sufficient to make the diagnosis, but audiom-etry and vestibular assessment usually are used as
confirmatory tests. Patients often demonstrate a conductive hearing loss and supranormal bone conduction manifesting as an abnormal sensitivity to sounds normally generated by the body. An audiogram with these findings can be an important indicator of canal dehiscence in a patient with an appropriate clinical history and merits a referral to a neurootologist. This is particularly important in health care settings in which other tests are not available.

Standard vestibular tests including calorics and rotational examination are rarely informative, but recently developed techniques to quantify vestibular-evoked myogenic potentials can help determine the presence of a dehiscence. A vestibular-evoked myogenic potential is a normal reflex relaxation of the sternocleidomastoid muscle in response to loud sounds in the ipsilateral ear. In patients with semicircular canal dehiscence, the threshold for evoking a potential from the affected ear is often lower than normal, as in the patient reported here.6

Several conditions other than superior canal dehiscence and perilymphatic fistula are important to consider when evaluating gravid or postpartum patients with symptoms of imbalance. Meningiomas are known to be progesterone-sensitive and may grow rapidly during pregnancy. These can cause imbalance if they affect the vestibular nerve directly or central areas of the brainstem or cerebellum that govern balance function. Otosclerosis is also hormone-sensitive and is known to worsen during pregnancy. This disorder of bone homeostasis affecting the inner ear often presents with hearing loss and tinnitus, but imbalance is not uncommon.

The management of semicircular canal dehiscence ranges from reassurance for patients with mild symptoms to surgery for more severely affected patients. There is no medical therapy for semicircular canal dehiscence. The superior canal can be approached through either the mastoid or the middle cranial fossa, allowing the dehiscent area to be plugged with bone wax. In a series of 20 patients undergoing surgical repair, results were excellent, with a complete resolution in symptoms in 15.7 Hearing is theoretically at risk for any ear procedure, but no loss was reported in a large series of patients undergoing primary repair of a canal dehiscence.8

Disequilibrium is notoriously difficult to diagnose, and patients may go untreated for years. Obstetricians and gynecologists with patients complaining about new-onset postpartum vertigo should inquire about symptom onset and focus their questions around events during the second stage of labor. Patients with symptoms of semicircular canal dehiscence should be referred to a neurootologist.

REFERENCES
Insights Into Angiogenic Imbalances During Pregnancy

Jimmy Espinoza, MD, John E. Uckele, MD, Robert A. Starr, MD, Robert P. Lorenz, MD, Richard A. Bronsteen, MD, and Stanley M. Berry, MD

BACKGROUND: An excess of either angiogenic or anti-angiogenic factors may participate in the pathophysiology of life-threatening pregnancy complications.

CASES: We describe two patients with severe early onset preeclampsia associated with partial mole or sacrococcygeal teratoma who had an excess of circulating concentrations of the antiangiogenic factors soluble vascular endothelial growth factor receptor-1 and soluble endoglin. In contrast, a patient with severe ovarian hyperstimulation syndrome at 5 weeks of gestation had an excess of circulating free vascular endothelial growth factor, a key angiogenic factor.

CONCLUSION: Angiogenic imbalances may participate in the pathophysiology of early onset preeclampsia associated with partial mole or sacrococcygeal teratoma as well as in the pathophysiology of severe ovarian hyperstimulation syndrome during pregnancy. (Obstet Gynecol 2009;114:437–40)

Accumulating evidence indicates that an imbalance between angiogenic factors, such as vascular endothelial growth factor (VEGF) and placental growth factor, and antiangiogenic factors, such as soluble VEGF receptor-1 and the soluble form of endoglin, are involved in the pathophysiology of pregnancy complications. Indeed, an excess of antiangiogenic factors has been described in preeclampsia,1 small for gestational age, parvovirus infection,2 and mirror syndrome associated with immune and nonimmune hydrops.3 In contrast, an excess of circulating angiogenic factors, specifically VEGF, has been described in ovarian hyperstimulation syndrome,4 a life-threatening condition that complicates 2.4% of pregnancies after in vitro fertilization (IVF). We report that angiogenic imbalances may participate in the pathophysiology of ovarian hyperstimulation syndrome during pregnancy and of preeclampsia associated with partial mole or mirror syndrome with sacrococcygeal teratoma.

CASE 1

A patient, gravida 2 para 1, was referred to our unit at 18 weeks of gestation with the diagnosis of severe preeclampsia according to conventional criteria (severe hypertension and proteinuria). Ultrasound examination demonstrated the presence of a growth-restricted fetus with multiple anomalies and a large, cystic placenta suggestive of partial mole. After counseling, the patient was induced with vaginal misoprostol, delivering a stillborn fetus. After delivery, the patient’s blood pressure normalized and the proteinuria resolved. Pathologic examination of the placenta revealed molar changes in one population of chorionic villi and increased syncytial knots in the population of normal villi (Fig. 1). Furthermore, p57 antibody stain in the normal villous cytotrophoblast was positive, confirming the diagnosis of partial mole.5 The maternal serum concentration of free VEGF was below the limit of detection, whereas the maternal plasma concentration of soluble VEGF receptor-1 was 18,319 pg/mL and that of soluble endoglin was 51.2 ng/mL. Both values were above the 95th percentile of the maternal serum concentration of these antiangiogenic factors at 18 weeks of gestation (less than 1,100 pg/mL and less than 10 ng/mL, respectively).1,6

Fig. 1. Examination of the villi in a patient with partial mole revealed molar changes in one population of chorionic villi and increased syncytial knots in the population of normal villi. Hematoxylin-eosin stain; magnification 200X.


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CASE 2

A second patient, gravida 1 para 0, was referred to our unit at 26 weeks of gestation with a diagnosis of sacrococcygeal teratoma and severe preeclampsia. A two-dimensional ultrasound examination found a hydropic fetus with a large sacrococcygeal teratoma. The patient was diagnosed with mirror syndrome due to severe maternal edema and fetal hydrops. A cesarean delivery was performed for maternal indications. A female neonate was delivered with a birth weight of 2,520 g and Apgar scores of 2, 2, and 1 at 1, 5, and 10 minutes, respectively. The maternal serum concentration of free VEGF was below the detection limit, whereas the maternal plasma concentration of soluble VEGF receptor-1 was 18,033.3 pg/mL and of soluble endoglin was 70.1 ng/mL. Both values are above the 95th percentile of the maternal plasma concentration of soluble VEGF receptor-1 in the pregnant and nonpregnant state.7,6

CASE 3

A patient gravida 1 para 0 who underwent ovulation induction, IVF, and embryo transfer was referred to our unit at 5 weeks of gestation because of severe abdominal distension, shortness of breath, hyponatremia, and anasarca. The patient was admitted to the hospital with a diagnosis of severe ovarian hyperstimulation syndrome. During her hospital stay, the patient developed bilateral pleural effusions and severe ascites requiring several paracenteses. With supportive measures that included the administration of intravenous albumin, adequate hydration with fluid balance, thrombosis prophylaxis, and ascites drainage, the severe ovarian hyperstimulation syndrome resolved. The maternal serum concentration of free VEGF was 1,128.2 pg/mL, a concentration well above that described during normal pregnancies and pregnancies after IVF (less than 70 pg/mL),7 whereas the maternal plasma concentration of soluble VEGF receptor-1 was 118.9 pg/mL and of soluble endoglin was 3.0 ng/mL.

The collection and use of samples and the use of clinical data for research purposes was approved by the Human Investigation Committee of William Beaumont Hospital.

Maternal plasma concentrations of free VEGF (free VEGF 165 and VEGF 121), soluble VEGF receptor-1, and soluble endoglin were determined by specific and sensitive enzyme-linked immunoassays (R&D Systems Quantikine Human VEGF-R1, Endoglin, and VEGF Immunoassays, Minneapolis, MN). The minimum detectable concentrations of free VEGF, soluble endoglin, and soluble VEGF receptor-1 were 9.0 pg/mL, 0.007 ng/mL, and 3.5 pg/mL, respectively.

Comments

The human adult endothelium is the largest autocrine, paracrine, and endocrine organ, covering approximately 700 m² and weighing 1.5 kg.8 This organ regulates vessel tone, platelet activation, monocyte adhesion, thrombogenesis, inflammation, lipid metabolism, and vessel growth and remodeling.8 A fundamental property of vascular endothelial cells is the ability to proliferate and form a network of capillaries, a process known as angiogenesis. This process is regulated by three growth-factor families, including VEGF, angiopoietins, and ephrins. Other factors proposed to regulate angiogenesis include transforming growth factors α and β and their functional coreceptors (endoglin and soluble endoglin). However, VEGF signaling represents a critical rate-limiting step in physiological angiogenesis. Indeed, endothelial cell proliferation and survival require continuous low levels of VEGF.9 The bioavailability of this angiogenic factor is thought to be regulated by angiogenic factors including the soluble form of VEGF receptor 1 in the pregnant and nonpregnant state.

The most frequent placental lesions in patients with preeclampsia are thought to represent chronic placental hypoperfusion and include: 1) arteriolopathy of the decidual portion of the spiral arteries, 2) intervillous thrombi, 3) localized ischemic villous necrosis, 4) thrombotic occlusion of the fetal stem villous artery, 5) increased syncytiotrophoblastic knotting, and 6) decreased number of terminal villi.10 In contrast, the main histological feature of the placenta in hydropic fetuses, such as in mirror syndrome, is severe villous edema,10 whereas the placental villi in molar pregnancies are considered avascular.10 It is possible that these three different placental pathologies may be associated with chronic uteroplacental ischemia leading to angiogenic imbalances and to the clinical presentation of preeclampsia.

The onset of placental hypoperfusion due to uteroplacental ischemia may determine the timing of the clinical presentation of preeclampsia. Indeed, accumulating evidence indicates that chronic uteroplacental ischemia is more relevant in the pathogenesis of early onset preeclampsia than in term or postterm preeclampsia. To the extent that the vasculature is limited to villous capillary remnants,10 partial mole may represent one extreme in the spectrum of ischemic disease of the trophoblast. Hence, it should not be surprising that the clinical presentation of preeclampsia in patients with partial mole frequently occurs before 20 weeks.

Mirror syndrome, or Ballantine’s syndrome, refers to the association of fetal hydrops with placentomegaly.
and severe maternal edema. Mirror syndrome also has been called pseudotoxemia. However, the clinical presentation of preeclampsia has been reported in about 50% of cases. Mirror syndrome initially was reported in cases of rhesus isoimmunization; however, it also has been described in other pregnancy complications associated with fetal hydrops, including sacrococcygeal teratoma. Recent reports indicate that mirror syndrome associated with immune and nonimmune hydrops is linked to an excess of circulating antiangiogenic factors. This is consistent with our observation that mirror syndrome in the context of sacrococcygeal teratoma is associated with an excess of circulating soluble VEGF receptor-1 and soluble endoglin.

Preeclampsia occurs in 42% of pregnancies with partial mole. The clinical management of partial mole with preeclampsia is challenging and may require delivery before fetal viability if severe preeclampsia or hemolysis, elevated liver enzymes, low platelets syndrome develops. The observation that an angiogenic imbalance, characterized by high maternal serum concentrations of soluble VEGF receptor-1 and soluble endoglin and low circulating free VEGF, may participate in the pathophysiology of preeclampsia associated with partial mole warrants further investigation into the biology of preeclampsia in molar pregnancies.

Accumulating evidence indicates that hypoxia/ischemia may induce the placental overexpression and release of antiangiogenic factors during pregnancy. Evidence supporting this view includes the following:

1. In twin–twin transfusion syndrome, the VEGFR-1 mRNA expression is present only in villi with hypoxic/ischemic changes.
2. Cytrophoblasts cultured under hypoxic conditions upregulate the mRNA expression and production of soluble VEGF receptor-1 in the supernatant.
3. Among patients with preeclampsia, the higher the impedance to blood flow in the uterine arteries (a surrogate marker of chronic uteroplacental ischemia) the higher the maternal plasma of soluble VEGF receptor-1.

Thus, it is possible that villous edema in cases of mirror syndrome and avascular villi in some cases of partial mole may result in trophoblast hypoperfusion and subsequent placental overexpression of antiangiogenic factors (soluble VEGF receptor-1 and soluble endoglin among others).

Our observation that severe ovarian hyperstimulation syndrome during pregnancy is associated with high serum concentrations of free VEGF is consistent with previous reports indicating that an excess of ovarian-produced VEGF may participate in the pathophysiology of ovarian hyperstimulation syndrome in nonpregnant women. Evidence supporting this view includes the following:

1. Patients with ovarian hyperstimulation syndrome have high plasma concentrations of VEGF and an imbalance between VEGF and its soluble receptors.
2. The maternal plasma concentrations of free VEGF and soluble VEGF receptor-1 may determine the timing of ovarian hyperstimulation syndrome (early compared with late onset).
3. The administration of gonadotropins with hCG to pregnant rats increased ovarian mRNA expression of VEGF and increased vascular permeability.

Of note, these effects were prevented by VEGF-receptor blockade. These observations indicate that an excess of free VEGF may participate in the mechanism of disease in ovarian hyperstimulation syndrome and may contribute to increased vascular permeability, leading to severe edema, ascites, and pleural effusion in patients with severe ovarian hyperstimulation syndrome.

It has been proposed that VEGF is a potential candidate to modulate the angiogenic imbalance in severe preeclampsia. Recently, it has been reported that the administration of recombinant VEGF 121 to a rat model of preeclampsia, which was induced by administration of adenovirus expressing the soluble VEGF receptor-1 gene, attenuated the preeclamptic phenotype. The authors propose that VEGF 121 could be a potential therapeutic agent for preeclampsia in humans. However, the therapeutic range of VEGF in pregnant women should be determined before clinical studies to prevent the life-threatening complications observed in severe ovarian hyperstimulation syndrome.

Collectively, our observations indicate that an excess of antiangiogenic factors (soluble VEGF receptor-1 and soluble endoglin) may participate in the pathophysiology of preeclampsia associated with partial mole and mirror syndrome due to sacrococcygeal teratoma. In contrast, an excess of angiogenic factors (free VEGF) may participate in the mechanisms of disease in severe ovarian hyperstimulation syndrome during pregnancy.

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Bacterial Sacroiliitis and Gluteal Abscess After Dilation and Curettage for Incomplete Abortion

Cedric P. Yansouni, MD, Vincent Ponette, MD, and Danielle Rouleau, MD

BACKGROUND: Pyogenic infection with Streptococcus agalactiae is a potentially life-threatening disease associated with significant morbidity and mortality. This type of infection has seldom been reported as a complication of dilation and curettage after an incomplete abortion.

CASE: A young woman presented to the emergency department with rapidly progressive left-sided lower back pain, general malaise, and chills evolving over the previous 48-hours after dilation and curettage for incomplete abortion. Streptococcus agalactiae was isolated in the blood. The patient developed pelvic osteomyelitis despite aggressive medical therapy and required prolonged treatment before significant clinical improvement was noted.

CONCLUSION: Although very rare, serious pyogenic complications of dilation and curettage after incomplete abortion do occur and may present a diagnostic challenge.

Spontaneous abortions occur in approximately 8–20% of clinically recognized pregnancies in the United States. While expectant and medical management of early incomplete abortions often results in the evacuation of retained products of conception, surgical evacuation is a more successful primary therapy, especially for more advanced first-trimester losses. Postabortal infection rates are similar for all three approaches. Serious extraterine supplicative infections after dilation and curettage (D&C) are rare in the medical literature. We report the case of a pyogenic sacroiliitis and gluteal abscess complicating D&C after an incomplete abortion.

CASE

A 22-year-old primigravid woman of Haitian descent presented to the emergency department with rapidly progressive left-sided lower back pain, general malaise, and chills evolving over the previous 48-hours after D&C. Her medical and gynecologic history was unremarkable, and she took no medications aside from ibuprofen and acetaminophen for her pain. Six days earlier, she had an incomplete abortion at 12 weeks of gestation, signaled by sudden onset bloody vaginal discharge. There was no fever or back pain at that time. Two days before presentation to the emergency department, she underwent dilation and suction curettage at another hospital as part of her postabortion care, using intravenous sedation and a paracervical block for anesthesia. There were no reported complications during this intervention. She was well until approximately 20 hours after the procedure, when she began feeling vague left-
sided progressive lower back pain that became sharp upon any movement. She also described general malaise and occasional chills. Over the next 24 hours, her condition worsened to the point of being unable to ambulate at all because of exquisite pain on bearing weight or mobilization of the left lower limb. The pain was posterior, focused high in the left buttock, and did not radiate to the thigh.

On arrival to the emergency department, the patient’s oral temperature was 38.3°C with otherwise unremarkable vital signs. Her physical examination was notable for obesity and extreme left-sided lower back and buttock pain on any flexion or extension of the left hip. There was no pain on hip rotation and only mild pain on deep palpation of the abdomen. A neurologic examination showed no abnormalities. The gynecologic examination was unremarkable with no pain on bimanual pelvic examination and no foul vaginal discharge or pus seen at the cervical os. Blood cultures were drawn but, unfortunately, no cultures of vaginal secretions were taken by the initial attending physician. Laboratory testing revealed leukocytosis (16.9 G cells/L, with 84% neutrophils [13.3 G cells/L]), and an elevated erythrocyte sedimentation rate (110 mm/h) and C-reactive peptide (38.60 mg/L). Pelvic ultrasonography showed an unremarkable uterus with no evidence of retained products of conception, normal adnexae, and no free fluid. An abdominal computed tomography (CT) scan with contrast showed no abnormality. Magnetic resonance imaging of the pelvis was then performed and interpreted as being consistent with a septic process in the left sacroiliac joint with an associated 34×13 mm collection in the left gluteus maximus (Fig. 1). Blood cultures yielded S agalactiae, ß-hemolytic Streptococcus, Lancefield group B, sustained over 24 hours. After obtaining orthopedic and general surgery opinions, the decision was made to manage the patient conservatively with intravenous penicillin and gentamicin for 2 weeks, and penicillin alone for a duration tailored to her clinical evolution. After the 8-week follow-up on antibiotics, the patient was improved but not yet pain free, with repeat imaging showing near-complete resolution of her gluteal abscess. However, her left sacroiliac joint space was persistently enlarged, and there was evidence of a small bony sequestrum with early signs of remineralization in the adjacent pelvic bone, suggesting a healing osteomyelitis. Her erythrocyte sedimentation rate and C-reactive peptide at this time had decreased to 49 mm/h and 12.1 mg/L, respectively.

**COMMENT**

We searched MEDLINE for references from 1950 to 2008 using the MeSH and textword search terms “curettage,” “abortion,” “miscarriage,” “sacroiliac joint,” and “infection,” and found no reports of pyogenic sacroiliitis and gluteal abscess complicating D&C after an incomplete abortion. However, other uncommon pyogenic complications following D&C in this setting have been reported. Struthers and co-workers described the case of a previously healthy woman with septic arthritis of the right knee and an abscess in the right thigh after D&C. Scheepers and co-workers reported the case of a 34-year-old woman with a similar presentation to our patient’s who suffered a retroperitoneal abscess at the level of the right iliopectos muscle near the os ilium and the sacroiliac joint 10 days after an aspiration curettage for an incomplete spontaneous abortion at 11 weeks of gestation. The abscess in this case was visualized with a pelvic CT scan, and Staphylococcus aureus was isolated from the blood and abscess samples. Important differences with our case include the facts that this woman was found to have an intrauterine device in situ at the time of the curettage and that she had retained products of conception at the time of abscess presentation. It is notable that in our patient’s case, a contrast-enhanced pelvic CT did not reveal a specific diagnosis despite severe symptoms of nearly 48 hours’ duration. Pelvic magnetic resonance imaging without contrast performed on the same day clearly demonstrated acute inflammatory changes at the left sacro-
iliac joint and a left gluteal collection with diffuse inflammation in the surrounding soft-tissues (Fig. 1). This suggests that a high index of suspicion is required to diagnose early pyogenic soft-tissue infections in the pelvis and that serial CT scans may be necessary if magnetic resonance imaging is not available. Whether this case represents a complication of D&C or a missed septic abortion deserves comment. Although our patient did have an incomplete spontaneous abortion that could have been a source of infection, she had no fever or signs of sepsis before uterine evacuation, and pelvic ultrasonography on presentation to the emergency department did not suggest retained products of conception. Moreover, there was no evidence of endometritis. Thus, we do not consider this to be a case of septic abortion.

Most data regarding the complications of D&C pertain to induced abortions. Apart from pelvic inflammatory disease and/or endometritis, which complicates between 29% and 40% of induced abortions in women harboring *Neisseria gonorrhoeae* or *Chlamydia trachomatis* and approximately 3% of procedures in women who do not, serious infectious complications of D&C are rare. Of 497 Canadian women undergoing first-trimester suction curettage abortion without antimicrobial prophylaxis, 3% developed pelvic infection (defined as lower abdominal pain, adnexal or cervical motion tenderness, and either temperature higher than 38°C or leukocytosis greater than 10 G cells/L or an erythrocyte sedimentation rate more than 15 mm/h), and none of these involved pyogenic infections outside the uterus. In a much larger series of 170,000 first-trimester outpatient abortions in New York City from 1971 to 1987, sepsis requiring hospitalization (defined as a temperature of 40°C or higher for 2 or more days) was recorded in only 36 women (0.021%). The procedures were all performed in one of three clinics run by single organization, using a single protocol that did not use prophylactic antibiotics. No further details are given about these septic episodes.

Predictors of pyogenic infections after D&C are yet to be determined. As described above, several studies have evaluated the clinical significance of the genital microbial flora at vacuum aspiration after miscarriage. Knudsen and co-workers reported no significant relation between microorganisms other than *C trachomatis* and postabortal pelvic inflammatory disease, including the 7.5% of women that harbored *S agalactiae*, β-hemolytic *Streptococcus*, Lancefield group B. While many reports have identified risk factors for adverse events after D&C, the extremely low incidence of extraterine pyogenic infections makes it impossible to extrapolate conclusions about this type of complication. Possible mechanisms leading to such sequelae might include perioperative transient bacteremia or clinically unapparent uterine perforation. Advanced gestational age, multiparity, and performance of the procedure by a resident rather than by an attending physician have been shown to be risk factors for perforation. Use of laminaria for dilation and of ultrasound guidance during D&C may also be protective.

Similarly, the role of antimicrobial prophylaxis for the prevention of postprocedure pelvic inflammatory disease has been extensively discussed, but other pyogenic infections have not been specifically addressed. Regarding D&C performed for diagnostic purposes, there are no data supporting the routine use of prophylactic antibiotics, and subacute bacterial endocarditis prophylaxis is not recommended in current guidelines.

In conclusion, our report demonstrates that, although very rarely described, serious pyogenic complications of D&C after incomplete abortions do occur and may present a diagnostic challenge despite aggressive investigation. At present, it does not appear possible to predict which patients will have such complications. This ability might allow for targeted prophylactic interventions, such as preprocedure antibiotics, that are not justified in the general population undergoing this procedure.

REFERENCES

Atypical Graft Infection Presenting as a Remote Draining Sinus

Deborah Karp, MD, Costas Apostolis, MD, Roger Lefevre, MD, and G. Willy Davila, MD

BACKGROUND: Synthetic materials are being used increasingly in reconstructive pelvic surgery. Multifilament polypropylene mesh in particular has been associated with healing abnormalities and other postoperative complications. This article describes an atypical infection presenting as a draining sinus tract to the lower extremity after intravaginal slingplasty.

CASE: An otherwise healthy 75-year-old woman presented with recurrent leg cellulitis 18 months after posterior intravaginal slingplasty for vaginal vault prolapse. A 35-cm fistulous tract draining from the pelvis to the lower thigh was identified. The patient underwent surgical debridement and was treated with 12 weeks of intravenous antibiotics with complete healing and no recurrence of symptoms.

CONCLUSION: Complications associated with the multifilament mesh used in the intravaginal slingplasty tunnel device include pain, erosion, localized abscess, and genitourinary fistula.

(Obstet Gynecol 2009;114:443–5)

The use of graft materials for the correction of pelvic organ prolapse and urinary incontinence recently has been incorporated into vaginal reconstructive surgery. Among synthetic materials, polypropylene has emerged as the most widely used graft because of its high tensile strength and low erosion rate.

The intravaginal slingplasty procedure involves a transvaginally placed multifilament polypropylene tape that can be used for incontinence as a suburethral sling (anterior intravaginal slingplasty) and in prolapse for vaginal vault suspension (posterior intravaginal slingplasty). Although the intravaginal slingplasty procedure has demonstrated a short-term success rate of 88–95%, it has been associated with mesh complications.1–3

We describe a case of delayed graft infection after posterior intravaginal slingplasty vaginal vault suspension presenting 18 months postoperatively as a distant, draining fistulous tract to the lower extremity.

CASE

In 2004, an otherwise healthy 75-year-old woman (para 5) underwent an uncomplicated vaginal vault suspension by posterior intravaginal slingplasty technique, anterior and posterior repairs, and anterior intravaginal slingplasty suburethral sling for stage four prolapse and intrinsic sphincter deficiency with urethral hypermobility. She was treated with vaginal estrogen for 6 weeks preoperatively and beginning 6 weeks postoperatively.

After surgery, the patient had a full functional and anatomic recovery; 1 year after surgery, she began having pain in her right thigh. Initial examination performed by her primary care physician was consistent with cellulitis along the medial thigh approximately 4 cm above the knee. She was prescribed a 2-week course of oral levofloxacin.

One month later, the thigh cellulitis persisted and the patient presented to the urogynecology clinic with vaginal discharge and bleeding. Pelvic examination revealed a piece of exposed intravaginal slingplasty tape at the vaginal apex. In the office, the right portion of the intravaginal slingplasty tape was removed intact. The left portion could not be removed, and the tape was cut at the mucosal edge. The patient was continued on vaginal estrogen. Follow-up 1 month later showed the vaginal mucosa to be healed without erosion or inflammatory changes.

Eighteen months postoperatively, the patient was admitted to the hospital for intravenous antibiotics owing to the presence of a draining sinus at the site of the previous cellulitis (Fig. 1A). Pelvic imaging showed a 10-cm fluid collection contiguous with the inferior posterior margin of the right ischial tuberosity and an area of lytic destruction of
the inferior pubic ramus and ischial tuberosity. Fistulogram revealed a sinus tract measuring 35 cm in length extending from the right pelvis to the lower thigh (Fig. 1B).

The patient was taken to the operating room for incision and drainage of the abscess owing to a concern about the possibility of retained mesh as a source of infection. Examination under anesthesia was notable for mass effect on the right side of the rectum and levator plate with no draining tract to the genital area. A right vaginal–paravaginal incision was made with dissection along the right posterior vaginal wall into the right paravaginal and pararectal spaces. The abscess cavity was entered and copiously irrigated. No gross residual graft material was found within the abscess cavity, although a large amount of inflammatory tissue was débrided and removed. Cultures of the abscess grew methicillin-resistant Staphylococcus aureus.

The patient remained on intravenous ertapenem and vancomycin for a total of 12 weeks postoperatively. She recovered fully, without a decline in her functional status, recurrent prolapse, or reinfection on follow-up examinations over a 2-year period.

**COMMENT**

The posterior intravaginal slingplasty procedure uses a multifilament type 3 polypropylene tape to restore apical support and involves placement of an intravaginal slingplasty tunneler device and tape through the ischiorectal fossa to the level of the ischial spines bilaterally. Several authors have reported retrospectively an unusually high rate of graft erosion or infection or both ranging from 4–18% associated with use of the multifilament intravaginal slingplasty tape.2,4 Serious graft complications leading to retropubic abscess, vesicovaginal fistula, and cutaneous suprapubic fistula have been reported.5 This case is unique because the infection presented outside of the pelvis, thus not alerting us of its relationship to a previous implant.

It is not known whether it is the path of the device in close proximity to the anus, the composition of the synthetic material, or other additional unknown factors that predisposes patients to infectious complications. In 1999, the material in the intravaginal slingplasty was changed from a nylon mesh to a multifilament mesh after the original nylon material was associated with a 10% risk of tape rejection.

Macroporous synthetic materials allow for collagen deposition, neovascularization, and fibroblast invasion, which in theory lead to better tissue integration. However, the multifilament composition of the intravaginal slingplasty tape prevents macrophages and neutrophils from entering its interstices while allowing the smaller bacteria to accumulate. This construction predisposes to chronic infection and poor tissue ingrowth.5 Multifilament mesh also has a larger surface area, facilitating bacterial adherence and allowing bacteria to persist over time. In addition, this mesh construction allows deposition of a surface biofilm made by bacteria, further preventing its incorporation.7 Several authors describe being able to remove multifilament material “intact” with minimal traction and pulling force, demonstrating further this material’s difficulty in incorporating into the surrounding tissue.8

Fig. 1. A. Draining sinus seen along medial posterior aspect of the right thigh, originating from an infected posterior intravaginal slingplasty tape. The arrow indicates the site of the draining sinus tract along the patient’s posterior medial thigh. B. Fistulogram revealed a sinus tract measuring 35 cm in length extending from the right ischial tuberosity to the thigh. Figure courtesy of Robert Cravero. Copyright 2009, Cleveland Clinic Florida.

Other investigators have reported severe mesh complications with multifilament mesh. Baessler et al published a series of 19 women with complications after intravaginal slingplasty procedures. All 19 patients underwent mesh excision for reasons ranging from pain, dyspareunia, and intractable infection to persistent retropubic abscess and cutaneous fistula formation. Like with our patient, other authors have reported that excision of infected grafts does not necessarily result in prolapse recurrence in short-term follow-up studies.\(^2,3\)

Knowing the composition of synthetic implanted materials and their biologic behavior is essential for the appropriate selection of graft materials for incontinence and prolapse surgery and fundamental for the effective management of postoperative complications. This case report illustrates the importance of maintaining a high index of suspicion in patients with atypical infections in sites remote from the original operative site in those with either recent or remote reconstructive pelvic surgery using non–type I synthetic mesh materials.

**REFERENCES**


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**Sepsis After Bipolar Radiofrequency Endometrial Ablation**

**Kirsten Salmeen, MD, and Daniel Morgan, MD**

**BACKGROUND:** Endometrial ablation offers an alternative to hysterectomy for the treatment of menorrhagia. The literature suggests low rates of complications for this procedure.

**CASE:** A perimenopausal woman underwent an endometrial ablation using a bipolar radiofrequency device. She presented 36 hours postoperatively with sepsis. Her condition worsened despite 18 hours of intravenous antibiotics and aggressive fluid resuscitation, and she underwent exploratory laparotomy and hysterectomy. Blood cultures and uterine tissue cultures grew *Escherichia coli*. The patient improved quickly after hysterectomy.

**CONCLUSION:** This case demonstrates that life-threatening infection can occur after endometrial ablation. (Obstet Gynecol 2009;114:445–8)

Endometrial ablation has been used since the mid-1980s as an alternative to hysterectomy to treat women with menorrhagia. There are several U.S. Food and Drug Administration (FDA)-approved devices available in the United States, each of which has a different mechanism. All of the available ablation devices destroy the endometrium, rendering it inactive.\(^1\)

The newest device available is the NovaSure (Cytyc, Marlborough, MA) endometrial ablation system, which uses bipolar radiofrequency energy to desiccate the endometrium. This device is unique in that a cavity-integrity assessment is performed before it can be activated to ensure there are no perforations in the uterus.\(^2\)

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*Safemeen and Morgan  Sepsis After Endometrial Ablation 445*
Many studies about each of the available endometrial ablation devices have demonstrated low rates of complications. All devices have been associated with occasional uterine perforation and injuries to surrounding structures. Infectious complications are reported to occur in fewer than 1% of cases, and most are mild cases of endometritis that respond quickly to antibiotics.3

CASE

A generally healthy, perimenopausal woman underwent an uncomplicated, outpatient endometrial ablation with a bipolar radiofrequency device for the treatment of menorrhagia. The cavity-integrity assessment was passed on the first attempt, and the ablation cycle was unremarkable. Blood loss was minimal. No antibiotic prophylaxis was administered. The patient had a negative endometrial biopsy and Pap test performed 6 weeks before the procedure.

The patient presented to her local urgent care center 36 hours postoperatively with fever, chills, vomiting, diarrhea, and general malaise. Her temperature was 102.3, with blood pressures in the 80s/40s. Blood cultures were obtained, and the patient was given intravenous doses of clindamycin, gentamicin, and cefazolin in addition to intravenous fluids. Given the potential need for intensive care, the patient was transferred for further management.

In our emergency department, the patient’s blood pressure was 83/62, pulse was 102, and SaO2 was more than 92% on 3 L/min oxygen by nasal cannula. A computed tomography scan of the abdomen and pelvis revealed a small amount of gas and fluid contained within the endometrium, consistent with recent instrumentation. There was no myometrial gas, hematoma, abscess, or visceral perforation. Laboratory test results showed a white count of 10.3, hemoglobin 12.4, and platelets 81,000 (no history of thrombocytopenia). A comprehensive metabolic panel and cardiac enzymes were within normal limits.

On admission, clindamycin and gentamicin were continued and vancomycin was added. During the 10 hours after admission, 14 L of intravenous fluid was required to maintain blood pressures in the 80s–100s/50s–60s. By the next morning, the patient’s oxygen requirement increased to 10 L/min via 100% nonrebreather and she remained hypotensive. The white blood cell count increased to 14.6, and platelets fell to 59,000. Given the patient’s worsening clinical status despite intravenous antibiotics and fluid resuscitation, the decision was made to proceed to the operating room for exploratory laparotomy and hysterectomy.

At the time of laparotomy, the uterus was erythematous and boggy to palpation, but no other abnormalities were noted. There was no evidence of uterine perforation or bowel injury (Figs. 1 and 2). The patient remained hemodynamically stable throughout the procedure. She was transferred postoperatively to the intensive care unit, intubated and sedated.

Blood cultures were ultimately positive for \textit{Escherichia coli}, sensitive to the antibiotic regimen the patient had received. A uterine tissue culture was also positive for \textit{E. coli}. Final pathology revealed chronic cervicitis, thermal injury, acute myometritis, and acute salpingitis.

Postoperatively, the patient improved quickly. She required no pressors and only maintenance intravenous fluids. Because of signs of pulmonary edema, she remained intubated until postoperative day 2. She was discharged from intensive care on postoperative day 3 and discharged home on postoperative day 5 with a peripherally inserted central catheter line in place to complete a 14-day course of ertapenem, which was selected for its once-daily dosing regimen with appropriate bacterial coverage.

COMMENT

This case provides an example of a rare but potentially life-threatening infectious complication after bipolar radiofrequency endometrial ablation in a patient who improved after hysterectomy. This
does not appear to be a recognized complication with this device. There have been several studies of the bipolar radiofrequency endometrial ablation device that have shown overall low rates of infection and other complications. The study done to obtain FDA approval for the device included 175 women who underwent bipolar radiofrequency ablation without infectious complications. There was, however, one case of endometritis and one case of pelvic inflammatory disease in the control group of 90 women who underwent loop resection plus rollerball.4 Two additional studies, which together included 156 patients, reported only two mild cases of endometritis in the 2 weeks after the procedure.5,6

The available literature seems to suggest that severe infectious complications after bipolar radiofrequency endometrial ablations have not been observed. However, not every adverse event is reported in the literature, and clinical trials will not necessarily reveal rare complications. A 2003 study used the FDA’s Manufacturer and User Facility Device Experience (MAUDE) database to identify complications after global endometrial ablations that had not been reported in the literature. The MAUDE database is a government-sponsored Web site for voluntary reporting of adverse events associated with medical devices. In the 2003 study of global endometrial ablation devices, 11 complications in four patients who underwent bipolar radiofrequency ablation were identified—two cases of endometritis, and one case of sepsis.7

For this case report, the MAUDE database was searched for “NovaSure™” for the dates September 1, 2001, to October 31, 2008. This search yielded 351 reports. Of those, 35 reports were descriptions of infectious complications. The remainder included descriptions of device difficulties, uterine perforations, and bowel injuries. Of the 35 infectious complications, seven described performing hysterectomy, eight described sepsis, five mentioned intensive care unit admission, and one death was described. Although the MAUDE database has many limitations, including that it is a self-reporting site with no mechanism for verification or further investigation, it does seem to suggest that there have been significant postprocedural complications noted after bipolar radiofrequency endometrial ablations that are not well represented in the published literature.

It is unclear why this type of infection occurs in certain patients. For this case, the patient had no evidence of underlying chronic endometritis or cervicitis, was immunocompetent, and had a vaginal preparation with Betadine immediately before the procedure; there was no evidence of contamination of the device. Antibiotic prophylaxis is not recommended for hysteroscopic procedures based on existing evidence, although a recent Cochrane Database review of prophylactic antibiotics for transcervical intrauterine procedures failed to identify any appropriate randomized controlled trials investigating the effect of antibiotic prophylaxis for women undergoing hysteroscopic procedures.8 It does not appear as though there is evidence to support the use of prophylactic antibiotics before endometrial ablation; however, there does appear to be a need for more investigation in this area.

The bipolar radiofrequency endometrial ablation device is easy to use and enables many women to avoid hysterectomy. Studies of several hundred patients suggest low infection rates. However, life-threatening infections after bipolar radiofrequency ablation can occur. For patients presenting with symptoms consistent with postablation endometritis, sepsis should remain in the differential diagnosis and management with aggressive fluid hydration, intravenous

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**Fig. 2.** Opened uterus. Bivalved uterus with evidence of char from prior endometrial ablation (arrow). There was no evidence of uterine perforation.


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antibiotics, and expeditious surgical intervention with intensive care support may be life-saving.

REFERENCES

Severe Lead Poisoning Caused by Use of Health Supplements Presenting as Acute Abdominal Pain During Pregnancy

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BACKGROUND: The public and some health care providers regard complementary and alternative medications as gentle and safe. There is no scientific basis for that belief, but there is evidence of poor quality control and toxicity of some remedies. Complementary and alternative medications may contain levels of toxic compounds high enough to cause poisoning. Lead poisoning due to the use of traditional health supplements among Asian Indians (known as Ayurvedic medicines) living in the United States has been reported.

It is estimated that as many as 0.4% of women of childbearing age may have elevated blood levels (higher than 10 micrograms/dL). Severe lead poisoning (blood level higher than 45 micrograms/dL) is rare in pregnancy, and only 15 such cases have been reported in the English literature. Lead crosses the placenta, putting the fetus at risk for lead poisoning. We report a case of acute abdominal pain in a white woman during pregnancy due to severe lead poisoning from ingestion of Ayurvedic medications meant specifically for use in pregnancy. This case provides a chance to review sources of lead poisoning, the confusing presentation of lead poisoning, and the difficulty in establishing appropriate treatment in pregnancy.

CASE
A parous white woman presented at the end of the second trimester with diffuse, acute abdominal pain. Her history was significant for a cesarean delivery. Her family and social history were noncontributory. The rest of her family...
was in good health. She was a vegetarian and had no known exposure to industrial toxins. She had had some loss of appetite and diarrhea 4 days earlier. On examination, she had moderate abdominal tenderness without rebound. Laboratory studies were significant for a white blood cell count of 8.1 k/mm³, hemoglobin of 9.3 g/dL, mean corpuscular volume of 80 fl, and platelets of 119 k/mm³. Her amylase and lipase levels were normal. She was discharged with a diagnosis of gastroenteritis.

The patient presented twice during the next 5 days with similar and then worsening complaints and no relief with Tylenol 3 (McNeil-PPC, Inc., Fort Washington, PA). The pain was in the lower abdomen and back and was described as tenderness, cramping, and pressure-like, with a tightening sensation. She'd had no bowel movement despite a bowel regimen and no urinary symptoms. Aspartate transaminase and alanine transaminase levels were elevated to 74 and 54 units/L, respectively, with normal bilirubin. Diagnoses considered but deemed unlikely included appendicitis, chorioamnionitis, round-ligament pain and pain due to adhesions/scar tissue, and constipation. An amniocentesis showed no chorioamnionitis. She had negative tests for hepatitis A, B, and C. She had no evidence of antiphospholipid antibody syndrome.

During 9 days of hospitalization, the patient’s aspartate transaminase and alanine transaminase levels increased to as high as 178 and 144 units/L, respectively. During this time, she also had a normal right upper quadrant ultrasound examination and an abdominal computed tomography examination. Surgical and gastrointestinal consultations were noncontributory. During the hospitalization, she admitted to using several “herbal” preparations that she had obtained from India. Persistent abdominal pain led to testing for porphyria, which revealed a negative urine porphobilinogen. However, a 24-hour urine collection revealed a markedly elevated aminolevulinic acid (ALA) level (87.0 mg/24 hours; normal range less than 6.4). The differential diagnosis for the combination of an elevated ALA level in the absence of urinary porphobilinogen includes the exceedingly rare ALA dehydratase porphyria or lead poisoning. Therefore, a lead level was obtained and found to be markedly elevated at 102 micrograms/dL. The health supplements were now thought to be the source of the lead poisoning. The patient was told to discontinue these supplements. A lead level 10 days later was 79.4 micrograms/dL. Testing showed that one of the herbal products, Garbhpal ras, contained extremely high levels of lead (3,000 micrograms/dL). She was started on a 2-week course of meso-2, 3-dimercaptosuccinic acid (succimer) 500 mg twice-daily chelation therapy. At term, she delivered an average-weight male neonate. Other than hypospadias, he did not have any physical abnormalities. At delivery, lead levels were: maternal 35 micrograms/dL, cord blood 54.5 micrograms/dL, neonatal blood 59.8 micrograms/dL, and amniotic fluid less than 1.0 micrograms/dL. Beginning on day 2 of life, the neonate was treated with succimer 25 mg orally three times daily for 5 days, then 25 mg orally twice daily for 14 days. He was followed for 6 months and had normal developmental milestones. The mother received three more courses of oral succimer in the first 6 months postpartum.

**COMMENT**

We present a patient with abdominal pain of unclear etiology, microcytic anemia, and elevated transaminases. This case raises several important issues, including the difficulty in diagnosing lead poisoning, potential unusual sources of lead poisoning, effects of maternal lead poisoning on the fetus/neonate, and treatment options.

The differential diagnosis of abdominal pain during pregnancy in a patient with previous surgery is large. Although elevated lead levels are thought to be fairly common in the pregnant population, levels high enough to lead to abdominal pain would be much more rare. It is not unusual that these patients undergo extensive evaluation before the diagnosis is made. Although the majority of cases of lead poisoning in adults result from occupational exposure, use of complementary and alternative medications also can cause lead poisoning. Table 1 contains a list of some health supplements reported to contain high lead concentrations.

To determine the source of the lead exposure, we took an in-depth medical history including living and work environments. The patient eventually admitted taking several Ayurvedic medicines, which she had received from a friend outside of the United States. One of them, Garbhpal ras, contained very high levels of lead. Garbhpal ras meaning, “protector of fetus,” is a medicine made from various bhasmas (metallic oxides and used for pregnant women to cure gastrointestinal problems associated with pregnancy.

There is no firm evidence that exposure to low levels of lead produces major malformations in the human fetus. Controversy exists regarding intrauterine lead exposure and minor malformations. In a case series of severe lead poisoning during pregnancy (initial maternal blood lead level 72 ± 27 micrograms/dL), chelation was conducted in accordance with current guidelines, placing maternal health as the treatment priority. No neonate had an identified birth defect. However, among reported cases, neonates had skeletal problems including delayed maturation and distal long bone sclerosis. In our case, the infant had hypospadias. There were no obstetrical complications in our case, nor have they been reported in the majority of studies.
Perhaps the most feared consequence of lead exposure is neurotoxicity. Many prospective studies evaluated low-dose lead exposure prenatally and postnatally with mixed results regarding developmental deficits. Effects of chelation therapy on the fetus are unclear. Human data on chelating agents (dimercaprol, succimer, ethylenediaminetetraacetate, and D-penicillamine) are severely limited. Chelation therapy potentially carries the added risk of mobilizing maternal lead stores so that lead transmission to the fetus increases. Thus, current recommendations are that chelation during pregnancy be reserved for severe, symptomatic lead poisoning.8

Use of complementary and alternative medications is relatively common in the United States. As this case shows, use of traditional medicines may extend beyond the ethnic group in which the treatment originated. When symptoms warrant, physicians should consider lead or other heavy metal poisoning as the cause of disease, even if the patient has no apparent history of exposure. Treatment of the pregnant patient with elevated lead levels continues to be controversial. In our case, severe maternal symptoms necessitated treatment. The benefits of treatment in the absence of maternal symptoms are less clear.

REFERENCES

Irinotecan Use During Pregnancy

Justin Taylor, Adanna Amanze, MD, Elaine Di Federico, MD, and Claire Verschraegen, MD

BACKGROUND: Ovarian tumors during pregnancy are rare. There is sparse clinical evidence about the safety of chemotherapy in this situation.

CASE: A 34-year-old woman was diagnosed by ultrasonography at 15 1/2 weeks of pregnancy with a Krukenberg tumor. She was treated with surgical removal and 10 courses of the combination of 5-fluorouracil, folinic acid, and irinotecan every 2 weeks until the 36th week of her pregnancy. The neonate was born without complications, and at age 4 months, showed normal development and no teratogenic effects.

CONCLUSION: In this case, irinotecan started at the second trimester and was safely used at full adjuvant dose.

The incidence of cancer during pregnancy is between 0.02% and 0.1% but is expected to increase as the age of child bearing also extends. This relatively rare occurrence has limited human studies of treatment safety, and most available data come from experimental and animal trials. This case report details the use of irinotecan in pregnancy, but no known reports of the use of 5-fluorouracil, but no known reports of the use of irinotecan in pregnancy.

This 34-year-old woman first presented with symptoms of bowel obstruction and was diagnosed with colon cancer by colonoscopy shortly after her 33rd birthday. She underwent surgical resection and was diagnosed with a stage III colon cancer metastasized to the ovary (Krukenberg tumor) during the second and third trimesters of an otherwise uncomplicated pregnancy. There are many reports of the use of 5-fluorouracil, but no known reports of the use of irinotecan in pregnancy.

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respectively. The patient had normal blood loss and recovered well. She was breast-feeding her newborn and was discharged after 48 hours. The patient followed up a month after the birth of her infant and was doing well at that time. She was to resume adjuvant chemotherapy for another 6 months and then have a hysterectomy with full intraabdominal staging. She will transition the infant from breast-feeding to bottle before beginning treatment.

**COMMENT**

Ovarian tumors during pregnancy are very rare. An estimated 1 in 16,000 pregnancies is complicated with a malignant adnexal mass. The most common tumors are germ cell tumors and borderline epithelial tumors, then metastatic malignancies. In the United States, ovarian metastases originate most commonly from colon or breast primary sites. Treatment of these tumors during pregnancy is usually individualized based on histologic type, gestational week, and patient’s wishes. In this case, the histologic cell type and immunohistochemical staining were consistent with metastatic adenocarcinoma of the colon. Cytokeratin 20 is a well-known positive marker in tumor cells of colonic origin, whereas CDX2 is a newer marker with greater specificity for detecting a gastroenteric origin. Cytokeratin 7 is a marker that is positive in tumors from gastroenteric organs located above the duodenum, but is also present in epithelial ovarian cancers. This tumor profile of cytokeratin 20 and CDX2 positivity but cytokeratin 7 negativity, with the history of colon cancer, helped diagnose metastatic colon cancer rather than a primary ovarian tumor or metastasis of another origin. This is further supported by positive nuclear staining for mismatch repair enzymes and negative staining for hormone receptors. The patient presented in the second trimester, which is a safe time to initiate chemotherapy. Her prognosis, the option of pregnancy termination, the benefits and risks of chemotherapy for her and the fetus, and the timing of chemotherapy were extensively discussed in multidisciplinary conferences and with the patient. Because there is no evidence that pregnancy has adverse effects on cancer outcomes, she was inclined to continue the pregnancy. However, because her 5-year survival prognosis is approximately 5%, with or without pregnancy, she decided to receive treatment.

The U.S. Food and Drug Administration approved irinotecan as part of a first-line treatment regimen containing 5-FU and leucovorin for metastatic colorectal cancer in April 2000. In the first-line treatment of metastatic colorectal cancer, irinotecan in combination with 5-FU and leucovorin resulted in significant improvements in objective tumor response rates, time to tumor progression, and survival when compared with 5-FU and leucovorin alone. Irinotecan is a watersoluble derivative of camptothecin, a cytotoxic alkaloid isolated from the flowering Chinese tree Camptotheca acuminata. The activity of irinotecan is due to the parent compound and the active metabolite 7-ethyl-10-hydroxycamptothecin, which is approximately 1,000 times as potent as irinotecan. Irinotecan has not been reported to have been used in pregnant women and is an U.S. Food and Drug Administration pregnancy class D drug, meaning that human data show risk but potential benefit may outweigh risk. Radiolabeling studies have shown that 14C-irinotecan crosses the placenta of rats after intravenous administration. Administration of irinotecan to rats during the period of organogenesis is embryotoxic as characterized by increased postimplantation loss and decreased numbers of live fetuses. Teratogenic effects included a variety of external, visceral, and skeletal abnormalities. Irinotecan administered to pregnant rats for the period after organogenesis through weaning caused decreased learning ability and decreased female body weights in the offspring. There is one report of the use of a related compound, topotecan, in pregnant rats without adverse outcomes (Camptostr [irinotecan] [package insert]. Kalamazoo [MI]: Pharmacia and Upjohn Company; 2006). Irinotecan is excreted into breast milk and breast-feeding is not recommended during therapy. The mean terminal elimination half-life for its longest-acting active metabolite, 7-ethyl-10-hydroxycamptothecin, is 10–20 hours, meaning that breast-feeding should be safe after at least 1 week off treatment.

**REFERENCES**

Appendicitis is the most common surgical problem in pregnancy occurring in approximately 1 in 1,500 pregnancies. The natural history of appendicitis is a progression from simple appendicitis to perforation with subsequent complications including peritonitis, sepsis, and abscess formation. Recent advances in imaging have improved diagnostic accuracy for appendicitis. The diagnosis remains challenging particularly because pregnancy-related symptoms and physiologic changes in the gravid state can overlap with appendicitis. Increased cardiac output, leukocytosis, and tachycardia, in addition to compression of the intraabdominal viscera by the enlarged uterus, can make the diagnosis of appendicitis more difficult in a pregnant woman. Despite rapid and accurate diagnosis, a subset of patients will present with ruptured appendicitis.

When uncomplicated appendicitis is suspected in pregnant patients, prompt surgical treatment is recommended to avoid perforation and its subsequent complications. The role for surgery is less clear in pregnant patients with evidence of a ruptured appendicitis upon presentation. Substantial increases in maternal and fetal morbidity and mortality occur with perforated appendicitis. Studies in the nonobstetric population support medical treatment of a ruptured appendicitis to avoid surgical morbidity. The best treatment for pregnant patients with a ruptured appendicitis is unclear.

In this report, we present two pregnant patients with ruptured appendicitis treated nonsurgically with antibiotics, bowel rest, and intravenous fluids. Both patients and their newborns had favorable outcomes. We also review the literature on nonsurgical management of nonobstetric patients with a ruptured appendix. Nonsurgical management of ruptured appendicitis may be a treatment option for the pregnant population.

CASE 1
A gravida 1 para 0 woman at 32 4/7 weeks of gestation presented with fever and right lower quadrant pain. The patient reported 1 week of intermittent diarrhea and cramping before her presentation. Physical examination findings were significant for right lower quadrant tenderness with rebound and a white blood cell (WBC) count of 22×10⁹/L. A pelvic ultrasound examination was nonrevealing. Magnetic resonance imaging (MRI) confirmed a ruptured appendix with phlegmon measuring 7 cm in greatest dimension (Fig. 1). After consultation between general surgery and maternal–fetal medicine, a strategy of medical management was elected.

The patient was treated with intravenous ampicillin, gentamicin, and clindamycin. Her WBC count peaked on hospital day 2 to 33×10⁹/L with 9% bands. Laboratory results were followed twice daily. The patient had evidence of peritoneal inflammation on examination and developed an ileus but otherwise remained clinically stable. She developed preterm contractions; tocolysis and steroids were not administered due to concerns for possible intraamniotic infection. An amniocentesis was not performed given concern of seeding an intraamniotic infection by passing the needle through infected material. The antibiotics were continued, and the patient’s clinical examination and laboratory studies improved over the course of 2–3 days; her preterm contractions and ileus resolved. Fetal heart tracings were reassuring, and biophysical profiles improved.

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were performed daily. A repeat MRI on hospital day 5 showed no change in the phlegmon, and there was no drainable collection. She was transitioned to oral antibiotics on hospital day 9 and was discharged on hospital day 11 in stable condition with a normal WBC count.

The patient had weekly obstetric follow-up with reassuring testing. The patient presented in spontaneous labor at 38 5/7 weeks of gestation and had an uncomplicated vaginal delivery of a female neonate with Apgar scores of 8 and 9 and a weight of 3,544 grams. The neonate and patient had an uncomplicated postpartum course. Two months after delivery, the patient underwent interval laparoscopic appendectomy. The pathology returned as xanthogranulomatous appendicitis with partial obstruction of the appendiceal lumen.

**CASE 2**

A gravida 2 para 0 woman presented at 26 6/7 weeks of gestation with 8 days of right upper and right lower quadrant pain. Her WBC count was elevated to 19×10⁹/L with a normal differential. A pelvic ultrasound examination demonstrated a noncompressible appendix with phlegmon measuring 1.4 cm. An MRI confirmed the diagnosis of ruptured appendicitis. After consultation with general surgery, medical management with ampicillin, gentamicin, and clindamycin, bowel rest, and intravenous fluids was elected. The patient remained afebrile, and her WBC count returned to normal. The patient was discharged to home on hospital day 9 with close follow-up.

The patient’s right lower quadrant pain recurred at 32 weeks of gestation. Repeat MRI imaging demonstrated no interval change in the appendix or phlegmon. The patient was again managed with intravenous antibiotics, bowel rest, and intravenous fluids. The patient developed preterm labor at 33 6/7 weeks of gestation; antenatal steroids and tocolytic agents were held. She underwent cesarean delivery via low transverse uterine incision for breech presentation. A liveborn male neonate was delivered with Apgar scores of 8 and 9 and a weight of 2,005 grams. The appendix was removed at the time of the cesarean delivery. The patient had an uncomplicated postoperative course. Appendiceal pathology noted acute and chronic appendicitis with a focal periappendiceal abscess. Placental pathology showed no evidence of chorioamnionitis. The newborn’s neonatal intensive care unit stay was uncomplicated.

**COMMENT**

The goal in treatment of appendicitis is prompt diagnosis and surgical management before appendiceal rupture and abscess formation. Accurate means of imaging is crucial in making a prompt diagnosis. Magnetic resonance imaging was used in both of these patient cases because it provides an accurate means for diagnosing appendicitis; in one study, MRI had 100% sensitivity, 94% accuracy, 100% negative predictive value, and 94% specificity.² In pregnancy, appendiceal rupture is of particular concern due to increased maternal and fetal morbidity, including peritonitis, sepsis, preterm labor, and fetal demise.¹,³–⁶ A subset of patients will present with a ruptured appendix. Studies in the nonpregnant population demonstrate the morbidity of surgical management of a ruptured appendix and favorable outcomes with nonsurgical management.⁷ There is a dearth of liter-

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**Fig. 1.** Coronal (A) and axial (B) T2-weighted image at 32 4/7 weeks of gestation with fetus in cephalic position shows an enlarged appendix with stranding of the adjacent fat (arrow) consistent with phlegmon.

ature regarding conservative management of ruptured appendicitis in the obstetric population. This report highlights two cases of ruptured appendix treated with medical management.

A perforated appendix is the leading surgical cause of fetal loss during pregnancy. The intraabdominal infection can lead to peritonitis, sepsis, preterm labor, and fetal loss. Ruptured appendicitis remains a major predictor of fetal loss; McGory et al found the rate of fetal loss was three times that with simple appendicitis. In their 1977 case review of 300 pregnant patients with appendicitis, Babaknia et al found that the rate of fetal loss with nonperforated appendicitis was 1.5% compared with the rate of fetal loss with perforated appendicitis of 35.7%.

Preterm labor and delivery is common in women with perforated appendicitis due to the intraabdominal inflammatory response. Infection stimulates inflammatory mediators and subsequently increases prostaglandin production that can cause contractions and cervical change. In the McGory et al case series, 11% of patients with ruptured appendicitis underwent early delivery compared with 4% of patients with simple appendicitis. Additionally, Tracey and Fletcher describe 17 patients with appendicitis in the second and third trimesters of pregnancy; of these patients, 5 developed preterm labor in the third trimester. All five patients were diagnosed with ruptured appendicitis.

Preterm labor developed in both of our patients. We did not tocolyze the patients’ preterm labor due to the concern that intrauterine infection may be causing the contractions. Given imaging studies consistent with ruptured appendix and the concern of seeding an intraamniotic infection by passing the needle through infected material, an amniocentesis was not performed. In case 1, the patient’s preterm labor resolved with expectant management. Tocolysis was not necessary. In case 2, preterm labor developed at 34 weeks of gestation, and a recurrence of the patient’s appendicitis was diagnosed. Antenatal steroids were deferred in both cases due to concerns over suppressing clinical manifestations of worsening infection. Due to the risk of fetal and maternal complications from this type of intraabdominal infection, a management strategy that minimizes further risk to the patient and her fetus is crucial.

Medical management is the preferred treatment of ruptured appendicitis in the nonpregnant population. Medical management of ruptured appendicitis is associated with higher success rates and lower rates of complications compared with operative management. A meta-analysis of 61 retrospective and prospective studies found an overall success rate of 93% with nonoperative management of ruptured appendix. Nonoperative management of ruptured appendix includes bowel rest, intravenous antibiotics, and serial exams. Patients undergoing immediate surgery for a ruptured appendix had a statistically significant increased rate of infectious complications, intestinal fistulae, and small bowel obstruction compared with patients managed nonoperatively. Intense tissue inflammation from a ruptured appendix may lead to a right-sided hemicolectomy or difficulties closing the appendiceal stump during appendectomy. Additionally, immediate surgical management may expose the fetus directly to the intraabdominal phlegmon, increasing infectious morbidity. Although patients with ruptured appendicitis treated nonoperatively had a significantly decreased complication rate in this meta-analysis, the patients had a statistically significant longer hospital stay of 3 days compared with the operative group.

Given the morbidity to both the mother and fetus from a ruptured appendix, immediate surgical management of these two patients with ruptured appendicitis was deemed to be higher risk than medical management. We opted to medically treat the patients’ infection, hypothesizing that the perinatal condition would improve with improvement of the patient’s condition. These two cases resulted in good outcomes for both the patients and the infants with delivery at or close to term without any known fetal infectious morbidity.

While preferable to diagnose and surgically treat appendicitis before rupture, it is uncertain what the best treatment plan is for pregnant women who already have a ruptured appendix. Our experiences in these two patient cases suggest that nonsurgical management of ruptured appendicitis in pregnancy is possible and warrants further study to fully elucidate the risks and outcomes to the patient and her fetus. The short-term and long-term fetal effects of possible prolonged exposure to inflammatory mediators from the intraabdominal infection are unknown. Even in the era of potent antibiotics and improved imaging, ruptured appendicitis in pregnancy can cause significant morbidity to both the patient and her fetus.

REFERENCES
Pregnancy Outcomes After Laminaria Placement and Second-Trimester Removal

Matthew Siedhoff, MD, and Miriam L. Cremer, MD, MPH

BACKGROUND: Even after comprehensive counseling, patients change their mind about the decision to terminate a pregnancy. There are few data about the effect of laminaria placement and removal on subsequent pregnancy outcome.

CASE: We describe four cases of laminaria removal at 12–17 weeks of gestation with varying outcomes. Two of the four cases developed cervical dilation and delivered early with documented acute chorioamnionitis.

CONCLUSION: Patients should be counseled that pregnancy termination begins with laminaria placement and that their removal could result in premature delivery.

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OUTCOMES AFTER LAMINARIA PLACEMENT/REMOVAL


CASES

Case 1 was a 27-year-old gravida 5, para 4, who presented for pregnancy termination at 18 weeks of gestation. Eleven laminaria tents were placed over 2 days; however, she opted to continue the pregnancy on the scheduled day of her procedure. The dilators were removed and she was given 7 days of doxycycline, 100 mg twice daily. Although she had three documented episodes of sexually transmitted cervicitis outside this pregnancy, gonorrhea and Chlamydia screens were negative immediately before her laminaria placement. The internal os was 2 cm dilated at the time of removal, but she subsequently was found to have a closed cervix when seen for follow-up obstetric care. At 22 3/7 weeks, she developed active preterm labor and delivered a 390-g neonate 6 hours after presentation. The neonate was provided with comfort measures and died approximately 30 minutes after delivery. Repeat screens for gonorrhea and Chlamydia as well as placental cultures were negative, but histologic examination of fetal membranes revealed acute chorioamnionitis.

Case 2 was a 26-year-old gravida 6, para 1, who presented at 23 3/7 weeks of gestation with 2 days of bleeding per vagina and cramping, increasing in intensity in the several hours before presentation. At this time, her cervix was closed on digital examination but significantly shortened on transvaginal ultrasonography. Attempts at tocolysis were unsuccessful, and, within 24 hours after presentation, she delivered a breech neonate with an intact fetus enveloped in the amniotic sac weighing 530 g. The newborn died on day-of-life 11 with multiorgan system failure. Fetal membranes showed evidence of acute chorioamnionitis. Placental cultures and gonorrhea and Chlamydia screens were negative at the time of delivery.
Review of her obstetric history revealed a term spontaneous vaginal delivery, two first-trimester elective terminations, a ruptured ectopic pregnancy, and a preterm delivery in January 2000, where five laminaria were inserted at 15 weeks, then removed the same day when she changed her mind. That pregnancy resulted in a delivery at 26 weeks, 5 days, after preterm premature rupture of membranes, active preterm labor, and gross evidence of chorioamnionitis at the time of cesarean delivery performed for nonreassuring fetal status. This neonate did well during its stay in the neonatal intensive care unit and is currently without physical or neurologic deficit at the time of this report. Her laminaria placement occurred at another institution and it is unknown if she was given antibiotics when they were removed, but a gonorrhea and Chlamydia screen was positive when she presented to Bellevue in preterm labor, and she was treated with 1 g of azithromycin.

Case 3 was a 22-year-old gravida 2, para 0, who presented at 17 4/7 weeks of gestation for pregnancy termination. Six laminaria were placed, then removed 1 day later at the patient’s request. Gonorrhea and Chlamydia screens were negative the day before laminaria insertion. Doxycycline started at insertion was continued for 3 days, and she had an uncomplicated remaining antenatal course. At 38 2/7 weeks, she spontaneously delivered a healthy neonate weighing 3,290 g.

Case 4 was an 18-year-old gravida 1, para 0, who had three laminaria placed for pregnancy termination at 12 5/7 weeks. They were removed the next day. The cervix was long and 1 cm dilated internally initially, then closed on subsequent examinations. Two gonorrhea and Chlamydia screens sent in the 2 months preceding laminaria placement were negative. Three days of doxycycline were given after laminaria removal. She delivered a viable female neonate at 40 1/7 weeks of gestation weighing 3,600 g.

**COMMENT**

The first case demonstrates a very likely complication of laminaria placement and continued pregnancy. Given her history of four term deliveries it is logical to assume her second-trimester preterm delivery was associated with intentional cervical dilation. Even though her cervix was closed on bimanual examination after laminaria removal, she still went on to have a preterm delivery. A small study by Stubblefield et al in 1982 also showed that cervical dilatation returned quickly to normal after removal of laminaria. This case highlights the fact that cervical dilatation alone may not be a good surrogate for risk of preterm delivery.

Explaining the second patient’s recent delivery is more complicated, because she did not have laminaria placed in this pregnancy, but still developed preterm labor and experienced a poor outcome. Her fifth pregnancy, in 2000, however, was complicated by laminaria placement and removal and resulted in chorioamnionitis and 26-week premature delivery. It is unlikely that the laminaria placed and removed in 2000 would affect the subsequent 2008 pregnancy. It is also unlikely that this patient had innate cervical incompetence, given her history of a prior normal term delivery. The cause of either preterm delivery is unknown, but the first could very likely have been related to laminaria placement and removal. That this child was successfully treated by his neonatologists should not minimize the risk of delivery at this early gestational age, the cost of intensive care for such an infant, or that many other infants in similar situations are not as fortunate.

Although an causative organism was not identified in the two patients with a poor outcome, there was evidence of acute chorioamnionitis on postdelivery histologic examination, and these patients had risk factors for sexually transmitted genital infections (prior episodes of cervicitis, ectopic pregnancy). No data exist on the value of antibiotic prophylaxis in the setting of removed laminaria, but extrapolating from proven benefit for surgical termination, it seems logical. If pregnancy is to be continued, macrolides and nitroimidazoles are preferable to tetracyclines because they are associated with teratogenicity.

Although certainly some women, such as the third and fourth patients presented here, go on to deliver healthy term infants after removed laminaria, the excessive risks of premature delivery emphasize the importance of counseling before pregnancy termination. Providers of induced abortion services have an obligation to provide documented informed consent to patients receiving osmotic dilating devices, acknowledging their right to request and receive removal of these devices if they reverse their original intention to abort. The abortion provider also has a duty to make clinically and logistically appropriate obstetric referrals as part of ensuring continuity of care. With such limited available data, the exact risk of complications such as miscarriage, heavy bleeding, and infection are unknown. Their presence and significant consequence, however, mandates counseling patients that laminaria placement begins the termination process and should be viewed as irreversible.

**REFERENCES**

Coexistent Lithopedion and Live Abdominal Ectopic Pregnancy

Anthony Naju Massinde, MD, Richard Rumanyika, MD, MMED, and Hyunsoon Beatrice Im, MD

BACKGROUND: Abdominal pregnancy is a rare, life-threatening variant of ectopic pregnancy, and thus its diagnosis and management remain controversial.

CASE: A multigravida was admitted for complaints of abdominal swelling that had been occurring for 2 years and symptoms of pregnancy in the 3 months before admission. Radiologic studies revealed a live intraabdominal pregnancy at 15 weeks of gestation with a concurrent lithopedion of advanced gestation. The patient underwent laparotomy, removing both fetuses; the placenta was left in situ. She was discharged 1 week later in good condition.

CONCLUSION: The case of a concurrent lithopedion of advanced gestation and a live intraabdominal ectopic pregnancy was successfully managed.

A bdominal pregnancy is a rare, life-threatening variant of ectopic pregnancy. Approximately 1% of all pregnancies are extrauterine, and up to 1.4% of these may have peritoneal implantations.1 On rare occasions, an extrauterine pregnancy is not identified and resolves spontaneously, even when the gestation is quite advanced. An extrauterine pregnancy that has become calcified over time is known as a lithopedion. Approximately 300 cases of lithopedion have been reported in the literature.2 Here we report the management of a concurrent lithopedion and live abdominal pregnancy.

CASE

A 40-year-old gravida 7, para 6 Tanzanian woman presented to our institution in November 2007 with complaints of unremitting lower abdominal pain for 3 months associated with gradual abdominal swelling over a 2-year period. The abdominal swelling began shortly after the delivery of her last child in 2005 and was associated with amenorrhea that had lasted for 1 year. Normal menses resumed, but, in August 2007, the patient noticed abnormal vaginal bleeding, for which a dilation and curettage was performed at another institution. She then had remained amenorrheic until the time of admission to our institution and had developed symptoms of nausea and vomiting in addition to lower abdominal pain of increasing severity. The patient had no other prior medical or surgical history. She had had six uncomplicated term vaginal deliveries. She denied any history of pelvic infection and had never used any form of contraception. She was monogamous and denied the use of any substances or medications and had no drug allergies.

The physical examination was remarkable for an abdominal pregnancy was distended by a fixed mass of approximately 28 weeks size of mixed consistency. A speculum examination revealed a closed external cervical os with no bleeding. On bimanual palpation, the posterior fornix of the vagina was bulging and the uterus could not be differenti-
ated from the mass. The patient had a positive urine pregnancy test and a hemoglobin level of 6.0 g/dL. Pregnancy with concurrent ovarian mass was suspected clinically, and an ultrasound examination was performed. The ultrasound examination revealed an empty uterus but showed a single, live fetus at a gestational age of 15 2/7 weeks posterior to the uterus with a posterior placental attachment (Fig. 1). A solid mass on the right side appeared to contain a calcified fetal spine, suggesting the presence of a larger, nonviable fetus. An abdominal X-ray was performed to confirm the ultrasound findings (Fig. 2). A concurrent live abdominal pregnancy and lithopedion of advanced gestation was diagnosed.

The patient was taken for an exploratory laparotomy. Intraoperatively, she was found to have a right-sided lithopedion and a large, left-sided cystic mass containing dark fluid likely to be old blood. These masses were removed first to access the second pregnancy. The placenta appeared to have implanted in the posterior cul-de-sac toward the right pelvic side wall and possibly onto a portion of bowel. Visualization of the fallopian tubes was very limited owing to distortion of the pelvic anatomy. A small window of membrane was visualized between the posterior aspect of the right broad ligament and an area of raw placental edge that had been exposed incidentally during the blood clot removal, through which an immature male fetus weighing 70 g was extracted. The umbilical cord was ligated with a 0-gauge polyglactin suture. The raw placental edge began to bleed briskly at this point and persisted despite applying pressure. The abdomen then was packed with abdominal packs and closed with nylon tension sutures. The estimated blood loss was 2 L, and four units total of whole blood were transfused. The patient was observed in the intensive care unit. The packing was removed 24 hours later without event, and the patient was sent back to the intensive care unit for 24 hours of close observation. She was discharged on the 8th postoperative day in good condition to continue her follow-up care through the outpatient clinic. Unfortunately, the patient never returned to the clinic and was lost to follow-up.

**COMMENT**

Lithopedion is derived from the Greek words *lithos*, meaning stone, and *paidion*, meaning child. This rare event requires the presence of a medically undetected extrauterine fetal demise of usually greater than 3 months with continued asepsis of the products of conception.3 A history of recurrent abdominal discomfort, fetal movement beneath the abdominal wall, and presence of fetal movement high in the upper abdomen should alert the clinician to the possibility of an abdominal implantation.4 Ultrasonography continues to be the gold standard for diagnosing extraterine pregnancy. However, the ultrasonographic diagnosis of abdominal pregnancy may be missed in up to half of all cases,5 and other means must be used to confirm uncertain or unusual ultrasonographic findings. In our case, an abdominal X-ray was performed to confirm the presence of the lithopedion.

With regard to the timing of laparotomy, some of the literature suggests that, in select cases, surgery may be delayed until fetal viability has been achieved.6 In this case, however, it was our judgment that expectant management could lead to life-threatening hemorrhage. After removal of the fetus, the placenta may be left in situ.7 Even when the placenta is not removed, it still may bleed if disrupted. In places where the latest hemostatic agents are unavailable and blood for transfusion is often in limited supply, packing the abdomen for 24–48 hours can achieve life-saving hemostasis,7 as it did in our patient.
In our setting, prenatal care is often inconsistent, and unresolved abdominal swelling in a reproductive-aged woman with a history of pregnancy stigmata should alert the physician to the possibility of a past or current abdominal ectopic pregnancy. Both intraabdominal pregnancy and lithopedion formation are rare but can occur in the same patient. PubMed and Medline searches of the English literature from 1958 until September 2008 for the terms “lithopedion and abdominal pregnancy,” “lithopedion, ectopic pregnancy,” “lithopedion, abdominal ectopic,” “lithopedion,” and “lithopedion” did not identify any previous reports of this concurrence. Ours appears to be the first reported case in the English literature of the treatment of a patient with a coexisting live intraabdominal ectopic pregnancy and a lithopedion of advanced gestation.

Ectopic Breast Fibroadenoma of the Vulva

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BACKGROUND: Ectopic breast (extramammary) fibroadenomas of the vulva are rare, cosmetically disfiguring, and very difficult to distinguish from other labial masses on physical examination. Extramammary tissue is susceptible to similar benign and malignant changes seen in the breast. Some patients with ectopic breast lesions may harbor an underlying urinary tract anomaly.

CASE: We report a case of a young woman who presented with an unknown progressively enlarging mass in the vulva. The mass was excised completely in a cosmetic manner and histology demonstrated an ectopic breast fibroadenoma.

CONCLUSION: Clinicians should include extramammary lesions in their preoperative differential diagnosis of vulvar masses since some may become neoplastic. Treatment is complete excision and renal imaging should be considered after a confirmed histopathologic diagnosis. (Obstet Gynecol 2009;114:460–2)

Ectopic breast (extramammary) lesions of the vulva, like fibroadenomas, are rare and difficult to distinguish from other labial masses on physical examination, but they have been documented in the literature as far back as 1872. For a long time, supernumerary mammary glands derived from rudiments of the embryonic milk lines in the vulva were considered the possible etiology of these unusual tumors. Recently, there has been more focus on mammary-like anogenital glands as a possible source. The clinical significance of extramammary breast lesions in the vulva, apart from their cosmetic disfigurement, is their vulnerability to the same pathologic changes that plague the normal breast. In addition, patients who are diagnosed with ectopic breast lesions may also harbor congenital urinary tract anomalies.

We recently encountered a case of a young woman who presented with a progressively enlarging mass in her vulva. Excision was accomplished by a mucocutaneous approach using 20% vasopressin, bipolar cautery, and meticulous sharp dissection. This resulted in minimal blood loss and a favorable cosmetic outcome. Histology demonstrated an ectopic breast fibroadenoma.

CASE

A young, healthy, Hispanic nulligravida presented to our clinic with a 1.5-year history of progressive enlargement of her right vulva. The patient described the mass as “pea size” in

REFERENCES

late 2007 and increasing to “golf ball size” at the time of her presentation in December 2008. Occasionally, she admitted to some discomfort when sitting but otherwise the mass was painless. She reported no cyclic changes. She denied drainage, redness, or dyspareunia. She had no exposure to hormonal medications. The patient confided that the mass disfigured her sexually, and she was very self-conscious of her partner or anyone visualizing her genitals. The rest of her gynecologic and medical history was unremarkable. Her family history, however, was significant for stage II breast cancer treatment in her mother in 2005.

On physical examination, she presented with normal stature and a normal female phenotype. Her breasts were symmetric and free of any palpable masses or axillary nodes. There were no signs of polythelia or polymastia in the thorax, abdomen, or groin. She had a normal hair pattern in the pubic area with no clitoromegaly. The right labia majora was distinctly expanded with a 5-cm firm, movable, well-circumscribed mass. There was no tenderness or discharge elicited from the mass. The opposite vulva, perineum, anus, and inguinal areas were completely normal.

The preoperative differential diagnosis included Bartholin cyst, labial sebaceous cyst, lipoma, and liposarcoma. The notion of an ectopic breast lesion was never considered.

The procedure was performed under general anesthesia in a hospital surgical suite. The mass was excised with clear margins using a small vertical incision along the mucocutaneous aspect of the labia minora. Meticulous dissection and repair was used to preserve cosmesis. The specimen was a round, well-circumscribed, encapsulated mass with a pale-yellow hue that measured $3.7 \times 2.8 \times 2.3$ cm (Fig. 1). The postoperative course was uneventful. The final histology revealed an ectopic breast fibroadenoma of the vulva. This finding prompted a renal ultrasound study that was reported as normal.

**COMMENT**

Historically, awareness of polymastia has been present for centuries in the form of cultural folklore such as the mythical fertility deities Artemus of Ephesus and the Phoenician goddess Astarte who were studded with numerous breasts. As early as 1872, the scientific literature cited the rare phenomena of ectopic breast tissue in the vulva.

Since 1954, when Burger and Marcuse reported their two cases of ectopic breast fibroadenoma of the vulva, more than 20 similar cases have been reported in the literature worldwide in the last 5 decades.

Two hypotheses have evolved to explain the embryogenesis of ectopic breast tissue in the vulva. There is the traditional long-held theory based on the embryonic milk lines. The milk lines are ectodermal thickenings or ridges that arise between the upper and lower limb buds during the sixth week of gestation (equivalent to a line extending from the axillary-pectoral region to the groin). Somehow there is regression and displacement of the milk line giving rise to this anomaly. The second and more recent hypothesis subscribes to the notion that mammary-like anogenital glands are a normal constituent of the vulva. These anogenital glands in turn have the potential to evolve into benign lesions like the fibroadenoma or neoplastic lesions like extramammary Paget’s and invasive adenocarcinoma.

Recent observations on human embryos have failed to show migration of primordial mammary gland cells extending beyond the axillary-pectoral region. This theory would also better explain the rare occurrence of perianal fibroadenomas.

When clinicians are confronted with a vulvar mass, it is imperative that they consider ectopic breast lesions in their differential diagnosis. Like normal breast, this tissue is hormonally sensitive and can hypertrophy during pregnancy or with exogenous hormone usage.

loma, hidradenoma papilliferum, sclerosing adenosis, hyperplasia, fibroadenoma, Phyllodes tumor, extramammary Paget's, and invasive adenocarcinoma.2

These lesions therefore present the surgeon with a twofold goal: excise with clear margins, while not compromising the cosmetic restoration of the labia that is vital to the patient’s self-esteem. If clear margins are not achieved, re-excision should be considered because occult breast tissue in the vulva is vulnerable to the same pathologic changes seen in the normal breast. Tumors with a biphasic histology, such as fibroadenomas, can sometimes reoccur.

Several investigators have reported a higher incidence of urinary tract anomalies, such as hydronephrosis, polycystic kidneys, ureteric stenosis, and supernumerary kidneys, in patients with ectopic breast lesions.3,4,8 The patient in the report underwent a renal ultrasound examination but no anomalies were revealed.

Fortunately, as in this patient, an ectopic breast fibroadenoma of the vulva usually represents only a painless, cosmetic, and psychological inconvenience. By using a mucocutaneous approach aided by 20% vasopressin, bipolar cautery, and careful sharp dissection, the excision is fairly bloodless. This technique restored vulvar symmetry with a good cosmetic result.

REFERENCES

Choriocarcinoma in a Postmenopausal Woman

Bradley Chittenden, MBChB, MRCOG, Eliyaz Ahamed, MBBS, MRCPI, PhD, and Abha Maheshwari, MBBS, MRCOG

BACKGROUND: Choriocarcinoma typically occurs within 12 months of pregnancy but rarely may present many years after an antecedent pregnancy. This report describes choriocarcinoma in a postmenopausal woman.

CASE: A 62-year-old woman presented with dyspnea, a history of postmenopausal vaginal spotting, and metastatic disease on chest X-ray. A transvaginal ultrasound revealed a thickened endometrium. Endometrial biopsy and an elevated β-hCG confirmed the diagnosis of metastatic choriocarcinoma. Multagent chemotherapy was initiated, and the patient developed fatal toxic epidermal necrolysis.

CONCLUSION: This case reminds practitioners that choriocarcinoma can occur in postmenopausal women, and although cure rates are high, deaths occasionally occur because of toxicity associated with treatment.

Gestational trophoblastic neoplasia refers to a group of uncommon malignant conditions arising from placental trophoblastic cells, which include invasive mole, choriocarcinoma, and placental site tumor. Gestational trophoblastic neoplasia is a rapidly invasive and widely metastasizing neoplasm. Macroscopically, it appears as a soft, purple hemorrhagic...
mass. Microscopic evaluation shows cores of cytotrophoblast surrounded by syncytiotrophoblast with a lack of chorionic villi. The disease stimulates hyper-vascularity of the surrounding tissues but not connective tissue support, and this is probably what allows for its highly metastatic and hemorrhagic behavior.

Gestational trophoblastic neoplasia usually arises from within the uterine cavity and is typically associated with a current or recent pregnancy, usually within a year of a preceding pregnancy. In the premenopausal group of patients, gestational trophoblastic neoplasia follows hydatidiform mole in 60% of cases, miscarriage or abortion in 30%, or normal pregnancy or ectopic pregnancy in 10%. The majority of gestational trophoblastic neoplasias present with abnormal vaginal bleeding, abdominal pain, or a pelvic mass, but up to a third of all gestational trophoblastic neoplasias present with symptoms from distant metastases. Gestational trophoblastic neoplasia is rare in whites but far more common in women of Southeast Asian origin.

Gestational trophoblastic neoplasia is exquisitely chemosensitive, and since the first description of cure of choriocarcinoma with single-agent methotrexate by Hertz, significant progress has been made in treatment regimens. Cure rates of almost 100% in the low-risk group and nearly 90% in the high-risk group are possible with current chemotherapy regimens.

Gestational trophoblastic neoplasia affecting postmenopausal women is exceedingly rare, and there are few reported cases in the literature. We describe the case of a postmenopausal women diagnosed with metastatic gestational trophoblastic neoplasia presenting with dyspnea.

**CASE**

A 62-year-old woman, gravida 2 para 2, was admitted to the medical department of our local hospital in 2007 with a 2-month history of weight loss, fatigue, and increasing dyspnea. She had had three discrete episodes of per vaginal spotting in the preceding 2 months of her admission. She was a smoker with a 20-pack-year history spanning 30 years. She had a medical history of mild chronic obstructive airway disease that was controlled with beclomethasone and salbutamol inhalers.

Her gynecologic history was unremarkable. She had a normal menstrual history and went through menopause at the age of 48 years. She used a continuous oral preparation hormone replacement therapy for 8 years but stopped this in 2004. She had had a single episode of postmenopausal bleeding at the age of 60 years that was investigated with a transvaginal scan. This confirmed an endometrial thickness of less than 3 mm. She was reassured and discharged.

She had had two vaginal deliveries. Her last delivery was in the year 1970. These were uncomplicated term pregnancies, and there were no postpartum complications. There was no history of molar pregnancy or persistent gestational trophoblastic disease.

On examination, she was apyrexial, pale, and tachypneic with a nonproductive cough. On auscultation, she had widespread crepitations through both lung fields. There was no palpable lymphadenopathy, and no abdominal masses could be demonstrated.

Blood investigations confirmed that she was anemic, with a hemoglobin of 9.8 g/dL. Her platelets were raised at 620×10^9. She had a raised white blood cell count (15×10^9) and raised C-reactive protein (330 mg/L). She was hypokalemic (2.6 mmol/L) and hyponatremic (134 mmol/L) and had mildly deranged liver function tests.

A chest X-ray showed multiple pulmonary metastatic deposits of varying sizes in both lungs suggestive of metastatic disease. In search of a primary lesion, she had an ultrasound examination of the abdomen and pelvis. Normal abdominal anatomy was demonstrated, but the endometrial lining was thickened at 32 mm. Specialist opinion was sought from the gynecology department. On pelvic examination, she had a normal-appearing cervix and a 14-week bulky mobile uterus with no palpable adnexal masses. A biopsy sample of the endometrium was obtained by pipelle. Histologic examination reported the sample as being predominantly blood clot but with elements of neoplastic tissue resembling malignant trophoblast. Syncytiotrophoblast, cytotrophoblast, and yolk sac was identified. Immunohistochemistry demonstrated a strong reaction with β-hCG. A serum β-hCG was dramatically raised at 226,668. Her CA 125 was normal. The tumor was considered to be metastatic gestational trophoblastic neoplasia based on the clinical findings, histologic appearance, and raised serum β-hCG.

The patient was transferred to a specialist center for further management. Further investigations were performed. A Doppler pelvic ultrasonogram showed a bulky uterus with a volume of 450 mL, with a heterogeneous vascular mass on the anterior fundal wall. The mass measured 6×5.8×5.2 cm and distorted the endometrial cavity posteriorly. Both ovaries were of normal size and there was no free fluid demonstrated. A computed tomography scan of the chest, abdomen, and pelvis showed multiple pulmonary metastases and an enlarged uterus measuring 13.5×9×8.5 cm. A hypervascular mass was confirmed arising from the posterior wall of the uterus. An magnetic resonance imaging scan of the brain was unremarkable. An assessment of the β-hCG contained in the cerebrospinal fluid measured 700 international units. The paired serum β-hCG was 180,000 international units. This suggested that there was no central nervous system involvement, because a cerebrospinal fluid β-hCG of more than 1/60th of the paired serum human chorionic gonadotropin is suggestive of central nervous system involvement. The investigative findings were consistent with a International Federation of Gynecology and Obstetrics.
Obstetrics (FIGO) stage IV classification of the disease. She scored 17 on the modified World Health Organization (WHO) prognostic scoring system. This placed her in the high-risk disease category requiring combination chemotherapy.

In view of her severity of chest symptoms and impending risk of respiratory failure, she was initially treated with a 2-day etoposide and cisplatin regimen (etoposide 100 mg/m² and cisplatin 20 mg/m² on days 1 and 2). She tolerated this well, and a week later she was commenced on the standard treatment for gestational trophoblastic neoplasia: etoposide, methotrexate, and actinomycin alternating weekly with cyclophosphamide and vincristine (Oncovin, Eli Lilly and Co., Indianapolis, IN). Four days after receiving her first dose of etoposide, methotrexate, and actinomycin, she developed acute renal failure (urea 15.5 mmol/L; creatinine 397 micromol/L) and neutropenic sepsis. The acute renal failure was thought to be caused by a combination of neutropenic sepsis and tumor lysis. She was commenced on intravenous fluids, broad spectrum intravenous antibiotics, and granulocyte colony stimulating factor.

Her condition was further complicated by severe mucositis. This was followed by the development of erythema of her palms and elbows. This progressed into extensive desquamation of the skin of her arms, abdomen, buttocks, and perineal region, with a total of 10–20% of the skin surface being affected. A skin biopsy confirmed a diagnosis of toxic epidermal necrolysis. She scored 6 on the SCORTEN prognostic scale for toxic epidermal necrolysis. The patient was transferred to intensive care, where she received intravenous immunoglobulin and supportive management for toxic epidermal necrolysis. Her condition was further complicated by neutropenia. Her condition deteriorated further until she eventually required intubation. She died 6 days later.

COMMENT

The above case is unusual in a number of ways. First, the patients’ advanced age was unusual for the development of gestational trophoblastic neoplasia. In the above case, disease occurred 14 years after the presumed menopause. Second, the tumor developed a considerable length of time after her antecedent pregnancy. Last, the management of the disease was complicated by toxic epidermal necrolysis that was thought to be because of an extremely rare adverse effect of chemotherapy.

Gestational trophoblastic neoplasia is rare in the white race. It is also rare for gestational trophoblastic neoplasia to develop in a postmenopausal woman without an antecedent molar pregnancy. In the case described above, the interval between the last pregnancy and the development of the tumor was 37 years. The overwhelming majority of trophoblastic disease occurs in premenopausal women between the ages of 13 years and 49 years. The risk of a hydatidiform mole increases significantly with increasing maternal age. Stone et al⁵ estimated that the risk to a pregnant woman aged older than 49 years developing a hydatidiform mole is about 800 times that for a pregnant woman between the ages of 15 years and 19 years. This trend is confirmed by a study by Stanton et al.⁶

It is rare for trophoblastic disease to present in a postmenopausal woman. There are very few cases reported in the literature. However, if it does occur, then it is far more likely to be of malignant nature. Jequier et al⁷ reported that 27% of women aged older than 50 years with trophoblastic disease developed gestational trophoblastic neoplasia. This is in contrast to the findings of gestational trophoblastic neoplasia in younger women, where the incidence is on the order of 5% of trophoblastic disease.

The treatment of gestational trophoblastic neoplasia is guided by the modified WHO scoring system and FIGO staging. Those patients who are assigned a low risk score (6 or below) or FIGO stage I, II, or III are assigned single-agent chemotherapy. Methotrexate is the drug of choice, and a dose of 1.0 mg/kg intramuscularly is given on alternate days for four doses. Patients who have a modified WHO score of 7 or more or who are assigned FIGO stage IV are treated with combination chemotherapy. Combination chemotherapy with etoposide, methotrexate, and actinomycin given weekly alternating with cyclophosphamide and vincristine, has become the standard of care in the management of high-risk disease.

Response is monitored by β-hCG levels, and treatment is continued for three courses after normalization of human chorionic gonadotropin levels. Gestational trophoblastic neoplasia is exquisitely chemosensitive, and up to 85% of patients treated with etoposide, methotrexate, and actinomycin plus cyclophosphamide and vincristine combination chemotherapy can be cured.

Treatment in our patient was modified because of the clinical picture, volume of disease in her lungs, and the perceived risk of respiratory failure. The β-hCG level before initiation of therapy was 226,668 international units/mL. Three weeks after the first dose of chemotherapy, the β-hCG level had dropped to less than 4,000 international units. The patient thus demonstrated a good response to treatment as is evident by the drop in her serum β-hCG levels.

Toxic epidermal necrolysis is a life-threatening skin disorder that is commonly drug-induced. The mucocutaneous reaction is characterized by widespread erythema, necrosis, and bullous detachment of the epidermis and mucous membranes resulting in
Placental site trophoblastic tumor is a rare type of gestational trophoblastic disease that is a malignant proliferation of intermediate trophoblastic cells. It usually presents with local symptoms, most commonly vaginal bleeding. It has been reported to present distantly from the most recent antecedent pregnancy, up to 18 years after the gestational event. In previously described cases, positron emission tomography (PET) was used as a diagnostic method, suggesting that metastatic placental site trophoblastic tumor acts as a hypermetabolic neoplasia. Because this is a relatively rare disease entity that would benefit from further characterization of optimal diagnostic approaches, we present the case of stage 3 placental site trophoblastic tumor in a 47-year-old woman with 1 year of amenorrhea who presented with cough.

CASE
A 47-year-old gravida 2, para 2 presented with a history of persistent cough for 1 year, and a 1-year history of amenorrhea. The patient had a past medical history significant only for gastroesophageal reflux disease and rhinitis; her surgical history included a bilateral tubal ligation in 1998. Her most recent antecedent pregnancy (full term normal spontaneous vaginal delivery) was 12 years earlier. She had no history of known molar pregnancies or miscarriages.

Upon physical examination, the patient was visibly short of breath, with a slight inspiratory crackle of the right lower lobe. Initial chest radiographs demonstrated ill-defined bilateral nodular lung opacities. The patient had a CT scan of her chest, which revealed multiple cystic and nodular lesions in the lungs. Subsequent transbronchial biopsy showed nonspecific findings; the patient underwent a video-assisted thorascopic surgery.
wedge biopsy of the left lung. Pathologic analysis demonstrated multiple neoplastic nodules scattered throughout the lung parenchyma. Invasion of blood vessels was present (Fig. 1). Immunohistochemical staining was positive for pan-keratin, cytokeratin-7, and inhibin; focally positive for human chorionic gonadotropin, human placental lactogen (HPL), and cytokine-20 (Fig. 2). Based on this pathologic analysis, the initial histologic differential diagnosis included metastatic germ cell tumor, choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and high-grade carcinoma with choriocarcinomatous differentiation.

Laboratory analyses revealed a positive urine pregnancy test, with a serum $\beta$-hCG of 190. Lactate dehydrogenase was mildly elevated at 247. Serum HPL was less than 0.1. The rest of her blood work, including a complete blood count, chemistries, and liver function tests, were within normal limits.

Magnetic resonance imaging and CT scan with PET of the head, chest, abdomen, and pelvis were done, which showed no lymphadenopathy or metastatic disease of the head and neck. There were innumerable pulmonary nodules superimposed on cystic lung disease, areas of cystic bronchiectasis, subcarinal lymphadenopathy and a borderline right hilar lymph node (1×1.5 cm), none of which were metabolically active on the PET scan. There was also prominence of the cervix and lower uterine segment, without a discrete mass, but no evidence of hypermetabolic activity (Fig. 3).
An endometrial biopsy was inadequate, so a dilation and curettage was then performed with ultrasound guidance, revealing atypical multinucleated epithelioid cells consistent with trophoblastic tumor. The overall histologic interpretation suggested either epithelioid trophoblastic tumor or placental site trophoblastic tumor, with immunohistochemistry favoring the latter as a final diagnosis for this patient.

**COMMENT**

The hallmark of gestational trophoblastic disease is abnormal cellular growth that arises from trophoblastic tissue after some type of gestational event, and includes cytotrophoblasts, syncytiotrophoblasts, and intermediate trophoblasts. Although the relatively more common invasive mole and choriocarcinoma are composed of sheets of an alternating pattern of cytotrophoblasts and syncytiotrophoblasts, epithelioid trophoblastic tumor and placental site trophoblastic tumor are both composed of the intermediate trophoblast, which shares characteristics of both cytotrophoblasts and syncytiotrophoblasts.

Placental site trophoblastic tumor was first described in 1976 by Kurman et al who referred to 12 cases of “trophoblastic pseudotumor,” which was then redescribed as “placental site trophoblastic tumor” in 1981. Placental site trophoblastic tumor comprises about 1–2% of all gestational trophoblastic disease; there have been approximately 150 reported cases in the literature since 1976.

Placental site trophoblastic tumor is usually seen in women in the reproductive age group. The most common presentations are local symptoms, usually abnormal vaginal bleeding (79%), which may or may not be preceded by amenorrhea. It is associated with a gestational event and more commonly develops in the uterus as an abnormal proliferation of the cells that form the placental bed. It can present as a primary uterine malignancy or with extraterine metastases, most commonly in the lungs and vagina. Metastases have also been described in the lymph nodes, brain, liver, kidney, stomach, and spleen. Approximately 10 previous case reports have documented placental site trophoblastic tumor developing in a postmenopausal woman.

Aiding in the diagnosis of placental site trophoblastic tumors from other variants of gestational trophoblastic disease and other germ cell tumors is the characteristic production of high levels of HPL and relatively lower levels of β-hCG. Placental site trophoblastic tumors share this biochemical profile with epithelioid trophoblastic tumors; both stand in contrast to choriocarcinomas, which have higher levels of β-hCG. With immunohistochemistry, placental site trophoblastic tumor will stain strongly for HPL and less so for β-hCG, as opposed to choriocarcinoma, which stains strongly for β-hCG. Placental site trophoblastic tumors are also immunoreactive for cytokeratin (AE1/AE3, cytokeratin-18), inhibin-α HPL, and Mel-CAM (CD146). They are rarely positive for placental alkaline phosphatase.

Our case is typical of placental site trophoblastic tumor with respect to clinical presentation, site of metastasis, serum biochemical profile, and immunohistochemistry. It is unique because of the lack of hypermetabolic activity on the PET scan. Three other reported cases comment on their use of PET in the evaluation of placental site trophoblastic tumor; one case from Brody School of Medicine of East Carolina University in Greenville, North Carolina described PET scan–detected pulmonary metastases that were...
treated surgically. A second case from Vanderbilt University Medical Center in Nashville, Tennessee reported persistence of existing pulmonary nodules and several new nodules shown on PET-CT in a patient with placental site trophoblastic tumor. In 2005, a case report from Taiwan described the case of a patient in whom exclusion of placental site trophoblastic tumor lung metastases was accomplished with PET. In that case, the patient had a history of tuberculosis, and her lung lesions seen on imaging before the PET were diagnosed as residual granulations, rather than metastatic nodules. The authors’ conclusions were that PET may play a critical role in the evaluation of patients with suspected metastatic placental site trophoblastic tumor because the treatment of these patients may vary dependent upon the presence of metastases. Our case may contradict this conclusion, because our patient has histologically confirmed metastases, which did not show hypermetabolic activity on PET. The generalizability of this observation is unknown because there are so few reported cases in the literature. The relatively slow growth rate of placental site trophoblastic tumor may explain the lack of PET findings in our case.

REFERENCES

Impaction After Partial Expulsion of a Neglected Pessary
Judith Berger, MD, Thierry Van den Bosch, MD, PhD, and Jan Deprest, MD, PhD

BACKGROUND: Vaginal pessaries are effective for treating pelvic organ prolapse, and severe complications are rare. We describe an exceptional case of pessary impaction with partial expulsion.

CASE: An elderly woman had mild discomfort from a pessary protruding through the perineal skin. The pessary was cut, removed, and the perineum healed uneventfully.

CONCLUSION: Negligence of vaginal pessaries may result in migration to the bladder or to the rectum. This case of perineal expulsion was eventually easily treated. Although no evidence-based guidelines for pessary care exist, this rare manifestation suggests the need for follow-up on a regular basis.

(Obstet Gynecol 2009;114:468–70)

Vaginal pessaries are often used in pelvic organ prolapse, especially in elderly women who are unfit to undergo surgical pelvic floor repair, but also in women who wish to avoid surgical intervention, in pregnant women or in women planning to have children in the future, and in patients waiting for surgery.1,2

Our case presents an exceptional example of impaction with partial expulsion of a pessary because of extreme neglect. Complications with pessaries are rare, but if they occur, extensive surgical intervention may be necessary. Although the presentation in our patient was egregious, a simple procedure was performed to remove the pessary.

CASE
We were consulted about an 81-year-old woman who had a pessary inserted at the age of 53 years for symptomatic prolapse. She had no follow-up until age 70 years, when she was seen for vaginal spotting. At that time only 1 cm of

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the pessary was visible within the vagina, and the rest seemed to be covered by vaginal mucosa. Removal of what seemed to be uncomplicated vaginal impaction was advised, but she never returned. At the age of 81 years, she was admitted for unrelated reasons, and a gynecologic consultation was requested.

On examination, the pessary was found to be half visible, protruding through a midline skin defect under the introitus and one more posterior and lateral (Fig. 1). Rectovaginal examination did not indicate involvement of the vagina or rectal mucosa. Remarkably, the pessary could easily be rotated. Using an orthopedic “heavy cutter,” the visible part of the pessary was removed, after which the perineal part was rotated out of the perineum (Fig. 2). On inspection, an epithelialized subcutaneous tract was suspected. To exclude any communication with pelvic viscera, the fistula trajectory was injected with povidone iodine and air instillation to visualize it on perineal ultrasonography (Fig. 3). No communication with the vagina could be demonstrated. In the first month after removal, the fistula was daily flushed with povidone iodine. At 4 months, the patient had no complaints besides persistent urinary incon-
COMMENT

Our case illustrates one of the risks of extreme pessary neglect. The pessary was first impacted underneath the posterior vaginal mucosa, migrated toward the skin of the perineum, and moved more caudally, where it reappeared at the surface without fistulization to the rectum or the bladder.

The most common adverse effects of pessaries are vaginal irritation, allergic reactions, leukorrhea, and bleeding. If neglected, serious complications may occur. Erosion leading to impaction of the pessary has been described, as has been fistula formation to the bladder or to the rectum and even intravesical migration. These complications may necessitate extensive surgical intervention.

To prevent complications, proper fitting, local estrogen application, and careful follow-up are important. There is little consensus about the management of patients with a pessary, especially on the need for regular cleaning and replacement of the pessary. Wu et al performed a prospective study in which a regimen of three monthly visits for the first year and thereafter every 6 months had proven to be safe. It is important to instruct the patient to present for clinical evaluation in case of pain or vaginal bleeding. Local estrogen application or acid douches are used in case of vaginal erosion or impaction. Although careful follow-up may reduce complications, fistula formation is an exception that occurs even in well-managed cases.

Although there is no consensus on the optimal management after pessary insertion, the case presented here strongly suggests that some form of clinical follow-up is indicated in all women with a vaginal pessary, to enable the early detection of complications.

REFERENCES

Methicillin-Resistant *Staphylococcus aureus* Bacteremia and Chorioamnionitis After Recurrent Marsupialization of a Bartholin Abscess

David M. Sherer, MD, Mudar Dalloul, MD, Ghadir Salameh, MD, and Ovadia Abulafia, MD

**BACKGROUND:** Methicillin-resistant *Staphylococcus aureus* (MRSA) is an extremely rare etiology of chorioamnionitis.

**CASE:** A young primigravida, with sickle cell (Hb SS) disease and β thalassemia presented at 37 weeks of gestation with fever, chills, and lower abdominal pain in the presence of intact fetal membranes, 10 days after recurrent marsupialization of a Bartholin abscess. Overt clinical chorioamnionitis was diagnosed. The patient received intravenous triple antibiotics and delivered by immediate cesarean. Maternal blood, uterine, placental and neonatal nares, external auditory canal, and umbilical cord stump cultures all yielded MRSA. Both the mother and infant received intravenous vancomycin and did well.

**CONCLUSION:** Our case and the literature suggest that it may be prudent to consider MRSA when contemplating the possibility of chorioamnionitis in the presence of intact fetal membranes, especially in gravidas with recurrent admissions or minor surgical procedures or who are hospital staff.

(Obstet Gynecol 2009;114:471–2)

Genital tract colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) affects 3.5% of pregnant women and has been associated with colonization by group B *Streptococcus*, but is not considered to predispose to a high risk of early-onset neonatal MRSA infection.1,2 Laibl et al3 noted that comorbid conditions of patients with community-acquired MRSA in pregnancy include immunodeficiency virus, acquired immunodeficiency syndrome (AIDS), asthma, and diabetes. Of note in this study, 18% of cases occurred in the postpartum period. Skin and soft tissue infections accounted for 96% of cases. The most common sites for a lesion were the extremities (44%), followed by the buttocks (25%) and breast (mastitis) (23%). Fifty-eight percent of the patients had recurrent episodes.3 Accordingly, these authors recommended that recurrent skin abscesses during pregnancy should raise prompt investigation for MRSA.3

We present an unusual case in which a pregnant patient with sickle cell disease (Hb SS) and β thalassemia who required recurrent marsupialization of a Bartholin abscess presented at 37 weeks of gestation with overt clinical chorioamnionitis, delivered immediately, and was later proven to have MRSA bacteremia and culture-proven MRSA chorioamnionitis.

**CASE**

A 19 year-old gravida 1 was followed during her pregnancy at the State University of New York, Downstate Medical Center (New York, NY). Her medical history was significant for sickle cell disease (Hb SS) and β thalassemia. Her blood type was O Rh(+), and she was antibody negative, rapid plasma reagin nonreactive, and rubella immune and negative for human immunodeficiency virus (HIV), chlamydia, gonorrhea, and group B *Streptococcus*. She denied previous Bartholin or any other perineal abscess or surgery and was not involved in the health care field. Her hemoglobin throughout gestation was 7 g/dl, hematocrit 20.2%, white blood cell count 11.3×10⁹/L. Serum creatinine, blood urea nitrogen, and electrolyte levels were normal. Second-trimester quadruple screen for fetal aneuploidy was negative (calculated risk for trisomy 21; 1 in 7,742, and trisomy 18; 1 in 250,000). Ultrasonography at 21 weeks of gestation disclosed a singleton fetus with normal anatomy, normal amniotic fluid volume, and appropriate-for-gestational-age biometry. Her pregnancy was uneventful other than an upper respiratory infection at 19 weeks of gestation, for which she was hospitalized briefly and received intravenous antibiotics. At 30 and later at 35 weeks of gestation, the patient underwent marsupialization of a Bartholin abscess. Although cultures obtained at both marsupializations were negative for growth, during and after each of these procedures, the patient received intravenous antibiotics consisting of nafcillin 1 g every 6 hours, and metronidazole 500 mg every 12 hours, for 5 days.

At 37 weeks of gestation, 10 days after the repeat marsupialization, the patient presented with generalized weakness, chills, and lower abdominal pain. On physical examination on admission, she appeared acutely ill, her temperature was 39.4°C, blood pressure 111/76 mm Hg, heart rate 150 beats per minute, respiratory rate 20 breaths per minute, and oxygen saturation on room air 99%. Both lungs were clear to auscultation, and heart sounds were normal. Fundal height was...
appropriate, yet the patient’s abdomen was tender with notable uterine contractions. The cervix was 3-cm dilated and 50% effaced with the presenting vertex at maternal ischial spine station -3. Fetal heart rate was 185 beats per minute with decreased variability. The maternal hemoglobin was 7 g/dL, hematocrit 20.3%, and white blood cell count 30.2×10^9/L. Shortly after her admission, spontaneous rupture of membranes occurred, which was confirmed at sterile speculum examination. With the diagnosis of acute chorioamnionitis, the patient received intravenous triple antibiotics consisting of ampicillin, gentamycin and clindamycin. Cesarean delivery was performed through a transverse lower uterine incision because of the patient’s clinical status, the early stage of labor (considered remote from delivery), and the presence of fetal tachycardia with decreased variability. Concurrent with the delivery, the patient received 1 unit of packed red blood cells. The newborn weighed 2,890 g with Apgar scores of 5 and 8 at 1 and 5 minutes, respectively. Umbilical artery pH was 7.28, and base excess was -2.7.

Subsequently, maternal blood obtained before delivery, uterine and placental cultures obtained at delivery, and neonatal nares, external auditory canal cultures, and umbilical cord stump cultures all yielded MRSA. The patient was not cultured for MRSA (nares, throat, skin, or rectum). Neonatal blood and cerebrospinal fluid cultures were negative. Histopathology of the placenta demonstrated suppurative chorioamnionitis, suppurative stem vessel vasculitis, gram-positive cocci, and edema of the umbilical cord. After consultation with Infectious Disease, both mother and neonate were treated with intravenous vancomycin (1 g every 12 hours and 10 mg/kg every 6 hours, respectively) and were discharged in good health on postpartum day 10. At the patient’s 6-week postpartum follow-up, nares, vaginal, and perineal cultures for MRSA were negative.

**COMMENT**

Recently reported severe adverse postpartum complications attributed to MRSA include a patient with a wound abscess, sepsis, septic thrombophlebitis, and septic pulmonary embolism, and another patient with an infected episiotomy site manifested necrotizing pneumonia and pelvic thrombophlebitis.

To our knowledge, only two previous reports have described chorioamnionitis due to MRSA. Interestingly, both previous reports involved patients who were hospital staff. One of these, like ours, involved a patient who developed MRSA chorioamnionitis despite the presence of intact membranes. Similarly, in our case, the histological appearance of the placenta depicting extensive suppurative infection in conjunction with overt clinical chorioamnionitis and maternal bacteremia in the presence of intact membranes on admission supports transplacental, rather than ascending, infection. It therefore may appear to be prudent to consider MRSA when contemplating the possibility of chorioamnionitis with intact fetal membranes, especially among hospital staff or patients with recurrent admissions or minor surgical procedures, such as our patient.

A recent retrospective study involving 162 women, noted that MRSA was the most common organism isolated from vulvar abscesses, at a prevalence of 64% (85 of 133). Notwithstanding, a systematic English literature search (PubMed, MEDLINE) between 1966 and 2009 using the search terms “pregnancy,” “chorioamnionitis,” “Bartholin’s abscess,” “vulvar abscess,” “marsupialization,” and “methicillin-resistant *Staphylococcus aureus*” reveals that this is the first report of MRSA bacteremia and acute chorioamnionitis after marsupialization of a Bartholin abscess.

This case reiterates the recommendation of Laibl et al that that recurrent skin (including perineal) abscesses during pregnancy should raise prompt investigation for MRSA. Finally, this case supports that, given the increase in the incidence of infection with MRSA, close surveillance should be conducted when encountering pregnant patients manifesting febrile morbidity after hospitalization or otherwise minor surgical procedures, including marsupialization of Bartholin abscess.

**REFERENCES**

Severe Separation of the Pubic Symphysis and Prompt Orthopedic Surgical Intervention

Gena C. Dunivan, MD, Ashley M. Hickman, MD, and AnnaMarie Connolly, MD

BACKGROUND: The incidence of pubic symphysis separation during delivery is 1 in 300 to 1 in 30,000 pregnancies, and it can cause a variety of problems such as pain, bladder dysfunction, and difficulty ambulating. There is no consensus on how to treat pregnancy-related pubic symphysial separation.

CASE: A patient, gravida 1 para 1, who underwent vacuum-assisted vaginal delivery was found to have a severe vaginal sidewall laceration and a 6.2-cm symphyseal disruption. The patient was treated with external fixation of an open book pelvis and physical therapy. She was discharged to home on postpartum day 4, voiding spontaneously and ambulatory with a walker.

CONCLUSION: Aggressive treatment of severe pubic symphysis separation with external fixation resulted in early ability to ambulate, void, and care for self and baby. (Obstet Gynecol 2009;114:473–5)

S
eparation of the pubic symphysis during delivery is fairly uncommon. The reported incidence of spontaneous symphyseal rupture or intrapartum separation ranges from 1 in 300 to 1 in 30,000 pregnancies.1 This can lead to a variety of problems, such as pain, bladder dysfunction, and difficulty ambulating. Currently, there is no consensus in the literature on the treatment of pregnancy-related pubic symphysis separation. We present a case of severe pubic symphysis separation and the associated early surgical intervention.

CASE

A healthy gravida 1 para 1 patient had undergone vacuum-assisted vaginal delivery at a referring hospital and delivered a female newborn weighing less than 8 lb. After delivery, a large left vaginal side wall laceration and pubic symphysis separation were noted; given the referring physician’s concern for a possible bladder injury, a Foley catheter and vaginal packing were placed, and the patient was transferred to the university hospital with a running epidural in stable condition.

Upon arrival, the patient was examined, pelvic X-rays were obtained, and the orthopedic team was consulted. The X-rays confirmed 6.2 cm of diastases at the pubic symphysis with no fractures of the pelvis seen. (Fig. 1) The patient was taken to the operating room, and an examination under anesthesia revealed a large, 7-cm laceration of the left anterolateral vaginal mucosa. Exploration revealed exposed retropubic space, visible symphyseal bone on the left, and the bladder, which appeared to be intact. (Fig. 2) A cystourethroscopy was performed revealing no lacerations of the urethra or bladder and bilateral ureteral efflux. The vaginal mucosa was reapproximated incorporating the endopelvic fascia using interrupted 2-0 Vicryl (Ethicon, Inc., Somerville, NJ).

The orthopedic team then performed an external fixation of an open book pelvis. Upon completion, fluoroscopic images demonstrated marked improvement from 6.2 cm to approximately 2 cm of diastasis (Fig. 3).

The epidural was continued for pain control until postpartum day 1. As recommended by the orthopedic team, physical therapy was started on postoperative day 2, and the patient was able to ambulate with a walker with touchdown weight bearing on the left lower extremity and weight bearing as tolerated on the right lower extremity. Once the patient was ambulatory on postoperative day 2, the Foley catheter was removed, and successful voiding was noted. The patient was discharged to home on postoperative day 4, ambulating with a walker, voiding spontaneously, and requiring only ibuprofen and oxycodone with acetaminophen for pain.

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Fig. 1. Anteroposterior pelvic radiographic view of the pelvis demonstrating the 6.2 cm of diastasis of the pubic symphysis (arrows), with no fractures of the pelvis.

At the 6-week postpartum visit, the vaginal wall lacerations were well healed, and no voiding dysfunction complaints were elicited. At the 6-week postoperative visit with orthopedics, the patient was ambulatory with mild discomfort at the left pin sites only. Pelvic X-rays revealed stable pubic symphyseal diastasis of 1.5 cm. (Fig. 4) The external fixator was removed at this visit with plans for increased independent weight bearing as tolerated, and she was released from Orthopedic care.

**COMMENT**

Relaxation of the joints and ligaments can occur during pregnancy beginning around the 10th week of gestation and persist up to 12 weeks postpartum.² The posterior sacroiliac complex provides the majority of pelvic ring stability, whereas anterior structures, including the pubic symphysis, provide approximately 40% of pelvic stability. In obstetrics, when a patient has a disruption of the pubic symphysis, the posterior stabilizers can remain intact and maintain partial stability.³ Pubic symphyseal diastasis can result from a variety of etiologies including multiparity, fetal macrosomia, precipitous labor, difficult deliveries, cephalopelvic disproportion, and/or previous pelvic pathology or trauma.¹² Patients may report stinging pelvic pain radiating to the groin or thighs, pain with stair climbing, walking, standing or carrying heavy objects, bladder dysfunction, difficulty ambulating, and a “duck-like gait.”²⁵

Debate exists regarding the treatment of intrapartum pubic symphyseal separation. Conservative therapy has been recommended in patients with symphyseal separation of 4 cm or less with surgical fixation reserved for separation of greater than 4 cm.⁵ The patient presented here demonstrated a wide separation of 6.2 cm and had the concomitant morbidity of a significant...
vaginal sidewall laceration with exposure of the pubic symphysis bone. Given the large separation and exposed bone, surgical intervention was deemed appropriate. Culligan et al.\(^6\) reported on a patient with a 5-cm rupture of the symphysis pubis who was managed with a pelvic binder, remained hospitalized for 18 days, was immobile in the supine position, and was unable to move her lower extremities for 10 days postpartum secondary to pain. She started physical therapy on postpartum day 14 and was unable to walk without crutches until 6 months postpartum.\(^6\) In contrast, the patient presented in this case was treated at the time of presentation with external fixation of her symphysis separation and had an epidural through postoperative day 1. The patient was ambulatory on postoperative day 2, voiding spontaneously, and discharged with a walker on postoperative day 4. At the 6-week visit, the patient was transitioning to completely independent walking. The markedly shorter hospital stay, rapid return to ambulation and independence, and decreased potential morbidities such as blood clot, pressure ulcers, and interrupted mother–infant bonding provide strong support for the prompt orthopedic operative intervention at the time of initial presentation.

Thus, in a patient with a greater than 4-cm separation of the pubic symphysis, prompt orthopedic surgical correction with external fixation could be considered, as it may result in shorter hospitalization, decreased prolonged pain, no adverse effect on voiding, and a more rapid return to ambulation and independent care for the patient and infant.

REFERENCES

Cecal Volvulus in a Multiple-Gestation Pregnancy

Daniel M. Chase, MD, Dorothy A. Sparks, MD, Murtaza Y. Dawood, MD, and Earnest Perry, MD

BACKGROUND: Intestinal obstruction during pregnancy is rare, with volvulus being responsible for about 25% of cases.

CASE: We present a case in which a woman in the 12th week of a twin gestation presented with abdominal pain and distension. She was initially diagnosed with an ileus, and radiological studies at the time were deferred. The patient’s symptoms worsened, and eventually she was taken to surgery for a diagnostic laparoscopy, which revealed a cecal volvulus with ischemic changes. A right hemicolectomy with primary anastomosis was performed.

CONCLUSION: Volvulus in pregnancy carries a high mortality rate, often because diagnosis is delayed due to avoidance of radiography and because of similarity of symptoms to other clinical entities. A high index of suspicion for volvulus must be maintained when a pregnant patient presents with obstructive symptoms. Abdominal radiographs may be justified in aiding the diagnosis, and diagnostic laparoscopy is a viable alternative when the patient has an acute abdomen.

(Obstet Gynecol 2009;114:475–7)
CASE

A 33-year-old woman in her 12th week of a twin pregnancy presented to the emergency department with abdominal pain, nausea, and emesis. Physical examination revealed a distended abdomen with mild tenderness in the right lower quadrant and a midline mass just above the pubis, consistent with a gravid uterus. She was admitted for observation by her obstetrician.

Ultrasound examination revealed a small amount of free fluid in the right lower abdomen. The appendix and adnexa were not easily visualized. Laboratory studies revealed a leukocytosis of 11,800/mL with a normal differential. A general surgery consult was obtained for suspected appendicitis. Because of the patient’s lack of peritoneal signs at the time, the consultant made a diagnosis of ileus. She was observed, but after 24 hours, her clinical condition worsened and she began to display signs of peritonitis, with severe pain, diffuse rebound tenderness, and involuntary guarding. She was taken emergently to the operating room for a diagnostic laparoscopy. Further imaging was considered but was not done because it was felt that any results would not alter the decision to operate.

Laparoscopy revealed a cecal volvulus with ischemic changes and normal adnexa. A lower-midline laparotomy incision was made and the abdomen explored. There was no perforation and no fecal spillage. The cecum volvulus was visualized with a maximum diameter of 14 cm, and it appeared gangrenous. A right hemicolectomy was performed to remove the volvulized segment, and an ileocolic anastomosis was fashioned. The abdomen was thoroughly irrigated and closed. The patient tolerated the procedure well and had an unremarkable postoperative course with return of normal bowel function in 2 days. She was discharged to home with antenatal follow-up in her obstetrician’s high-risk clinic. At 25 weeks of gestation, the patient had premature rupture of membranes and preterm labor. Viable twin neonates were delivered, one vaginally and one via cesarean delivery due to breech position.

COMMENT

Bowel obstruction is rare in pregnancy. The literature suggests an incidence of between 1 in 1,500 and 1 in 66,431. Variation in this wide range might be attributable to patient demographics unique to the individual studies, such as age, previous surgeries, or the presence of hernias. Volvulus accounts for about one quarter of these bowel obstructions, as opposed to 3% to 5% of obstructions in the nonpregnant population. Volvulus is most likely to occur at times of rapid change in the size of the uterus: between 16 and 20 weeks of gestation when the uterus becomes intraabdominal, between 32 and 36 weeks of gestation as the fetus enters the pelvis, and immediately after delivery.

Cecal volvulus accounts for 25–44% of volvulus cases in pregnancy. A cecal volvulus involves an axial twisting of the colon on the mesentery, resulting in an obstruction. For this to happen, there must be a lack or laxity of fixation of the cecum, and a fixed point around which the twist occurs.

The importance of early diagnosis of volvulus in pregnancy is paramount. Maternal mortality from intestinal obstruction in pregnancy is reported at about 6%, but fetal mortality is higher at up to 25%. The mortality in patients with gangrenous bowel is reported at between 30% and 50%. However, volvulus in pregnancy continues to be a difficult diagnosis to make in a timely manner. According to one literature review, the average time from onset of symptoms to diagnosis of volvulus is 48 hours. This delay is attributable to two factors. The first is due to a similarity between the signs and symptoms of other entities associated with the gravid condition. Second, practitioners are reluctant to order diagnostic X-rays in pregnancy.

The most common symptoms of cecal volvulus are crampy abdominal pain and distension, although nausea, vomiting, and constipation are often present as well. A mass may be palpable in the hypogastria. Ischemic bowel will result in peritoneal signs. Cecal volvulus can be mistaken for placental abruption, a ruptured uterus, hyperemesis, ovarian torsion, choledolithiasis, appendicitis, and urinary tract infections, as well as other differential diagnoses. The diagnosis is also made more difficult by the fact that the symptoms of nausea and abdominal pain are common in normal pregnancies.

Plain abdominal X-ray has a sensitivity of 95% in diagnosis of cecal volvulus. A characteristic “coffee bean” shape directed to the left upper quadrant is made by the distended cecal volvulus on X-ray. Clinicians are often hesitant to use X-rays in pregnant patients because of fear of harmful effects on the fetus. Patients also frequently decline diagnostic X-rays, as in our case. However, the benefit of plain abdominal X-ray in aiding the diagnosis of intestinal obstruction probably outweighs the risks to the fetus. The approximate fetal dose from an abdominal X-ray is 1.4 mGy. The deleterious cumulative effects of radiation on the fetus have a threshold of 100 milligray or higher, much more than the doses given during abdominal X-rays. Although there was a very small but statistically significant increase in childhood malignancy (one additional cancer death per 1,700 exposures), a recent literature review found that there was no statistically significant increase in intrauterine death or teratogenicity at this level of radiation exposure.
Laparoscopic surgery during pregnancy is becoming increasingly more accepted. Studies have shown no difference in abortion rates, mean gestational age or weight, and fetal anomalies between laparoscopy and laparotomy during pregnancy. The advantages of laparoscopy in pregnancy are the same as in the general population: less incisional pain, less need for analgesics, rapid return of bowel function, and fewer atelectasis and thromboembolic events. The data available suggest laparoscopy in pregnancy is safe, and it may be equivalent or even preferable to laparotomy.8

Cecal volvulus is treated by untwisting and decompressing the bowel, removing compromised tissues, and preventing recurrence, of which the preferred method is bowel resection.2,4 Of course, necrotic bowel or perforation necessitates resection at the time of surgery. The abdomen should be copiously irrigated to decrease the risk of postoperative intraabdominal abscess formation due to translocation or contamination.

Cecal volvulus in pregnancy is uncommon and can be difficult to diagnose, but it should be considered in the differential diagnosis for any bowel obstruction presenting in the pregnant patient. A high index of suspicion is needed for early diagnosis, which is essential in reducing morbidity and mortality from volvulus. Early use of abdominal X-rays should be strongly considered in patients with abdominal pain, vomiting, and abdominal tenderness. Also, diagnostic laparoscopy should be considered an acceptable option in cases of a surgical abdomen.

REFERENCES

Endometrial Cancer in an Adolescent
A Possible Manifestation of Cowden Syndrome

Kathleen M. Schmeler, MD, Molly S. Daniels, MS, Amanda C. Brandt, MS, and Karen H. Lu, MD

BACKGROUND: Cowden syndrome is an autosomal dominant disorder characterized by the development of multiple intestinal hamartomas, distinctive mucocutaneous lesions, and an increased risk of endometrial, breast, and thyroid cancer.

CASE: An adolescent girl whose mother had a known germline PTEN mutation presented with abnormal vaginal bleeding and was diagnosed with a grade 2 endometrial adenocarcinoma. She underwent a robotic hysterectomy and was found to have no myometrial invasion or distant disease. Genetic testing revealed the patient to have the familial germline PTEN mutation.

CONCLUSION: The strikingly young age of onset of this patient’s endometrial cancer highlights the need for additional study to better understand Cowden syndrome and to determine what endometrial cancer screening and preventive strategies are needed.

PTEN hamartoma tumor syndrome is an autosomal dominant disorder characterized by the development of multiple gastrointestinal hamartomas, distinctive mucocutaneous lesions, and an increased risk of certain malignancies. PTEN hamartoma tumor syndrome comprises a family of disorders including Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, and Proteus syndrome.1–4 Cowden syndrome and Ban-

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nayan-Riley-Ruvalcaba syndrome, in particular, have overlapping phenotypic features.3

Cowden syndrome is caused by a germline mutation in the protein tyrosine phosphatase with homology to tensin (PTEN) gene on chromosome 10q22-23.3 PTEN encodes for a phosphatase that acts as a tumor suppressor, mediating cell cycle arrest and apoptosis. Somatic PTEN mutations have been noted in multiple sporadic tumors, including cancers of the thyroid, endometrium, prostate, and brain.6 The incidence of Cowden syndrome is approximately 1 in 200,000, although this is believed to be an underestimation owing to underdiagnosis from variable penetration and subtle clinical findings.2

The cardinal features of Cowden syndrome include facial trichilemmomas (hamartomas of the infundibulum of the hair follicle) and mucocutaneous papillomatous papules. Other common features include macrocephaly, thyroid abnormalities, and fibrocystic breast disease. Cowden syndrome also is associated with an increased risk of endometrial, breast, and thyroid cancer.1,2 Bannayan-Riley-Ruvalcaba syndrome is characterized by macrocephaly, hamartomatous intestinal polyposis, lipomas, developmental delay or autism or both, and pigmented macules of the glans penis. Individuals diagnosed with Bannayan-Riley-Ruvalcaba syndrome are thought to have the same increased risk of cancer as those with Cowden syndrome given the overlapping PTEN mutation spectrum of the two disorders.3

To date, little has been published on endometrial cancer associated with Cowden syndrome. This report describes a case of endometrial cancer diagnosed during adolescence in an individual with Cowden syndrome.

CASE

An adolescent, nulliparous, white girl presented to an outside institution with abnormal vaginal bleeding and pelvic pain. She underwent dilation and curettage as well as a diagnostic laparoscopy and drainage of an ovarian cyst. Final pathology showed a grade 1 endometrioid adenocarcinoma of the endometrium and benign ovarian cyst fluid. At the time of diagnosis, the patient’s weight was 125.7 lb, with a body mass index of 23 (body mass index is calculated as weight (kg)/[height (m)]²), and she had no known risk factors for endometrial cancer.

The patient was placed on high-dose megestrol for 4 months. Repeat endometrial sampling showed persistent grade 1 adenocarcinoma, and she was continued on megestrol for an additional 4 months. Her weight increased from 125.7 lb to 174.2 lb while on the megestrol. The patient then presented to our institution and underwent a repeat endometrial biopsy, which showed a grade 2 endometrioid adenocarcinoma. Magnetic resonance imaging of the abdomen and pelvis showed no evidence of myometrial invasion or lymphadenopathy and normal-appearing ovaries.

The patient has no significant family history of cancer. However, the patient’s mother had a history of multiple gastrointestinal hamartomas and ganglioneuromas as well as macrocephaly, facial trichilemmomas, papillomas of the tongue, and acral keratoses. The patient’s mother therefore underwent genetic testing and was found to have the c.370delT germline PTEN mutation. In addition, the patient reported that her brother had been diagnosed clinically with Bannayan-Riley-Ruvalcaba syndrome based on his history of autism and penile freckling and the family history of PTEN hamartoma tumor syndrome; he had not undergone genetic testing.

The patient underwent a robotic hysterectomy. Her ovaries were noted to be normal in appearance and were left in situ. There were no surgery-related complications, and the patient was discharged home on postoperative day 1. Final pathology showed multiple small foci of grade 1 and grade 2 endometrioid adenocarcinoma associated with complex atypical hyperplasia. There was no myometrial invasion, and the pelvic washings were negative. The patient is currently 6 months postsurgery and is without evidence of disease. Before surgery, she underwent single-site genetic testing for the known familial PTEN mutation. She tested positive, confirming that she has Cowden syndrome.

COMMENT

To date, little information is available on endometrial cancer in women with Cowden syndrome. Starink et al report on 21 individuals with Cowden syndrome and note no cases of endometrial cancer among the 18 women in the study. However, the authors combined their results with other reported cases of Cowden syndrome and noted endometrial cancer in 4 of 63 women (6%). Compared with the current case, the age at endometrial cancer diagnosis was significantly higher in these women (38, 58, and 59 years and unknown in one patient).

De Vivo and colleagues evaluated 103 women with more than one primary cancer among the 32,826 members of the prospective Nurses’ Health Study cohort. Endometrial cancer was noted in two of the five individuals found to have germline PTEN mutations. A subsequent study by Black et al noted no deleterious PTEN mutations in 240 consecutive patients with endometrial cancer. The authors concluded that, although their data do not preclude the possibility of an increased risk of endometrial cancer with Cowden syndrome, germline PTEN mutations did not account for a significant proportion of sporadic endometrial cancers.
The International Cowden Syndrome Consortium developed consensus diagnostic criteria that have been adopted by the National Comprehensive Cancer Network. It is recommended that individuals who meet these diagnostic criteria be offered genetic counseling with germline genetic testing. Based on the above-mentioned studies, endometrial cancer now is included as one of the criteria for consideration for Cowden syndrome testing. The National Comprehensive Cancer Network also has developed guidelines for the treatment of individuals with Cowden syndrome. There currently are insufficient data to recommend endometrial cancer screening for women with Cowden syndrome, and the guidelines suggest that affected women participate in clinical trials to determine the effectiveness of screening modalities.

These recommendations differ from those for women with Lynch syndrome/hereditary nonpolyposis colorectal cancer, an autosomal dominant disorder with a 40% to 60% lifetime risk of endometrial cancer and a 12% lifetime risk of ovarian cancer. It is recommended that these women undergo annual endometrial sampling and transvaginal ultrasound examinations beginning at age 30 to 35 years. In addition, it is recommended that women with Lynch syndrome/hereditary nonpolyposis colorectal cancer be offered prophylactic hysterectomy after age 35 or once childbearing is complete. To date, there are insufficient data to recommend prophylactic hysterectomy in women with Cowden’s syndrome.

There is currently limited information regarding endometrial cancer in women with Cowden syndrome. The true incidence remains unclear, and further study is needed to determine whether endometrial cancer is a true component of Cowden syndrome. The strikingly young age of onset of endometrial cancer in the current case highlights the need for additional study to better understand this entity and to determine what screening and preventive strategies are needed in this population.

REFERENCES
Surgical Reconstitution of a Unilaterally Avulsed Symptomatic Puborectalis Muscle Using Autologous Fascia Lata

S. Abbas Shobeiri, MD, A. Rao Chimpiri, FRCR, Ariel Allen, DO, Mikio A. Nihira, MD, MPH, and Lieschen H. Quiroz, MD

BACKGROUND: The puborectalis muscle is an important muscle for the maintenance of fecal continence. We present a novel surgical technique for repair of symptomatic avulsed puborectalis muscle.

CASE: This woman presented with dyspareunia and fecal incontinence since the vaginal birth of her child 2 years before. The diagnosis of an avulsed right puborectalis was made by physical examination and confirmed by magnetic resonance imaging and three-dimensional ultrasonography. Fascia lata was harvested from the patient’s thigh and used to reconstitute the missing portion of the puborectalis muscle. At 12 months postoperatively, the patient was continent of stool and relieved of dyspareunia.

CONCLUSION: The patient’s dyspareunia and fecal incontinence were alleviated by restoring normal anatomy.

In cases of fecal incontinence unrelated to external anal sphincter injury, the treatments may be limited to physical therapy along with electrical stimulation or neuromodulation. Surgical procedures have been aimed at tightening stretched levator ani muscles. Surgeries such as artificial bowel sphincter procedures, which are aimed at correcting fecal incontinence, do not address levator ani defects. Most recently, Yamana and colleagues described a procedure called perineal puborectalis sling operation for treatment of idiopathic fecal incontinence. In their study they used a mesh sling through a perineal approach to recreate the rectal angle irrespective of the status of the puborectalis muscle.

An OVID search using term puborectalis, levator injury, and fascia lata for 1950 to March 2009 did not produce any articles describing repair of the puborectalis muscle. In the current case, we describe a novel technique for point-specific repair of unilaterally torn puborectalis muscle.

CASE

A woman presented with dyspareunia and fecal incontinence since the vaginal birth of her child 2 years before. Both deliveries had been without third- or fourth-degree lacerations. Her anal incontinence included gas, liquid stool, and solid stool. She had avoided intercourse for the past year due to dyspareunia. On physical examination, the anus and the perineal body were deviated to the left. The digital examination revealed deviation of anus and the rectum to the left side. Although a prominent spasmodic puborectalis was palpable to the left, there was a void of distal levator ani subdivisions on the right side (Fig. 2). Three-dimensional endoanal ultrasonography revealed an intact internal and external anal sphincter complex. Magnetic resonance imaging (MRI) of the pelvis with T1 and T2 weighted images in axial, coronal, and sagittal planes confirmed the diagnosis of avulsed right puborectalis (Fig. 3A).

To develop a surgical approach, six fresh frozen pelves and 12 embalmed cadavers were dissected using a paramedian 3-cm incision, 2 cm lateral to the anococcygeal line into the ischioanal fossa. The following average measurements were obtained in fresh frozen pelves: anococcygeal bone 3.6 cm, puborectalis arm 4.4 cm. The inferior rectal nerve was encountered in all specimens traveling lateral and caudad to the area of dissection. Deep transverse perineal muscles were seen more anteriorly in the same plane. Further dissection was performed to follow the puborectalis to its attachment site at the anterior ischiopubic rami. A 3×5-cm autologous fascia lata graft was sutured with 2.0 polypropylene to levator raphe posteriorly and the ischiopubic rami anteriorly as a conduit to stabilize the contralateral arm of the puborectalis muscle.

Intraoperatively, no puborectalis remnant was identified on the right side. The right puborectalis muscle was recon-
stituted with autologous fascia lata as described above (Fig. 4). To decrease the spasm of the left arm of the levator ani muscle this portion was injected with 100 units of botulinum toxin type A (Botox, Allergen Inc. Irvine, CA) at a concentration of 20 units/mL in 0.2 mL increments using a 22-gauge spinal needle.9 At 3 months, a follow-up MRI confirmed stabilization of the puborectalis sling and major correction of rectal deviation (Fig. 3B). Anal position corrected to a more normal midline anatomic position, but perineal deviation was corrected to a lesser degree. At 12 months, the patient was continent of stool and did not experience dyspareunia.

COMMENT

The levator ani and its components play an important role in anal incontinence.3 Avulsion of puborectalis is a known complication of vaginal birth.4 The best time to repair a torn muscle would be immediately after the incident. Puborectalis avulsion is either asymptomatic or goes unrecognized due to swelling and pain in the vaginal area that is associated with vaginal birth. This injury may manifest itself later in life as pelvic floor weakness and fecal incontinence.

The dilemma remains on what to do with asymptomatic patients whose puborectalis injury is identified at the time of vaginal birth. As illustrated in this case, positioning of the perineal body is determined by a fine balance between different structures that come together to form the perineal body. Correction of the puborectalis defect alone does not correct perineal deviation.

We have described a novel technique that may benefit patients with symptomatic puborectalis injury.
The goals of the procedure were to alleviate the patient’s complaints of dyspareunia and fecal incontinence by restoring normal anatomy.

REFERENCES

Urinothorax
A Rare Complication of Total Abdominal Hysterectomy
Osama Amro, MD, Frances Webb-Smith, MD, and Shiraz Sunderji, MD

BACKGROUND: Urinothorax is defined as the presence of urine in the pleural cavity. This condition is due to the leakage of urine from the peritoneal and retroperitoneal space into the pleural space. We report a case of urinothorax after total abdominal hysterectomy.

CASE: A premenopausal woman underwent total abdominal hysterectomy and left salpingo-oophorectomy for pelvic pain, requiring extensive dissection. Her postoperative course was complicated by right urinothorax, which was diagnosed after a diagnostic thoracentesis and resolved after a therapeutic thoracentesis and the repair of the urinary bladder rent.

CONCLUSION: Urinothorax can occur in cases of undiagnosed urinary tract injury. It presents as postoperative shortness of breath and pleural effusion and should be considered in the differential diagnosis.

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When the patient was moved to the recovery room and the Foley catheter readjusted, hematuria was noted for the first time. Intravenous pyelography and pelvic CT scan with contrast were performed, which did not disclose any urinary tract injury. On postoperative day 1, the indwelling Foley catheter fell out, and at the patient’s request, no new Foley catheter was inserted. After one episode of straight catheterization to empty the bladder of 500 mL of blood-tinged urine, another Foley catheter was reintroduced at the time of need for second catheterization and left in place until the following day. On postoperative day 3, the patient complained of sudden onset of shortness of breath. Physical examination revealed normal vital signs and decreased breath sounds in the right lung base. There was no clinical evidence of deep vein thrombosis. The abdominal examination was uninformative due to distension and pain. Chest X-ray revealed a large right pleural effusion and associated consolidation of the right lung; the left lung was well aerated and clear. A CT angiogram carried out to rule out pulmonary embolus revealed massive right pleural effusion, with complete consolidation of the right lung, and small left pleural effusion, with left lower lobe segmental atelectasis, and no evidence of pulmonary embolus. A venous duplex ultrasound examination of both legs did not reveal any evidence of deep or superficial thrombosis or valvular insufficiency.

An ultrasound-guided right diagnostic/therapeutic thoracentesis was performed. One liter of yellow fluid was removed, with marked improvement in symptoms. Six hours later, the patient’s symptoms returned, and a second right therapeutic thoracentesis was performed, removing 1.6 L of yellow fluid. At this time a chest tube was left in place.

Pleural fluid creatinine was 9.02, and the ratio of pleural fluid to serum creatinine was 9.02/0.91 = 9.9 mg/dL. The pleural fluid to serum l-lactate dehydrogenase ratio was 60/129 = 0.46, and the pH of the pleural fluid was 8.0, consistent with diagnosis of urinothorax. The patient’s abdomen continued to remain distended and tense, and a CT scan of the abdomen with contrast was performed. This scan showed extravasation of the contrast into the peritoneal cavity and revealed a rent in the posterior aspect of the bladder. A second laparotomy was performed by way of the previous incision; the bladder was mobilized from the vaginal cuff by sharp and blunt dissection to expose the injury. A 2-cm defect in the posterior wall of the bladder was identified, and a cystotomy was performed starting at the dome of the bladder to include the posterior wall defect. The bladder was repaired in two layers, the mucosa with running 2-0 chromic catgut suture and the detrusor muscle with running 2-0 polyglactin (Vicryl, Ethicon Endo-Surgery, Inc., Cincinnati, OH) suture. The integrity of the repair was checked by irrigating the bladder with the three-way Foley. A peritoneal flap was interposed between the bladder and the vaginal cuff using interrupted 2-0 Vicryl suture. An intraperitoneal JP drain was placed at the repair site, and the bladder was drained with a three-way Foley catheter. The patient’s subsequent hospital course was unremarkable, and she was discharged home on postoperative day 8, after removal of the JP drain and the chest tube. A two-way Foley catheter was left in place for 14 days and then removed. A follow-up cystogram showed no extravasation, and the patient subsequently did well.

COMMENT
Our search of the literature restricted to the English language in PubMed using search terms “urinothorax, urothorax pleural effusion and total abdominal hysterectomy or gynecologic surgery” from June 1996 to November 2008 did not reveal any reports of urinothorax associated with gynecologic surgery.

Urinothorax is the presence of urine in the pleural space and is a rare cause of transudative pleural effusion. This condition is due to the leakage of urine from the peritoneum and retroperitoneal space into the pleural space. Two types of urinothorax have been reported: 1) obstructive—due to renal calculi, prostatic hypertrophy, genitourinary malignancy, adult type polycystic kidney disease, and retroperitoneal inflammatory disease; 2) traumatic—due to surgery, urinary tract instrumentation, extracorporeal shock wave lithotripsy, ileal conduit surgery, renal transplantation, and blunt trauma.1 There are three possible routes by which the urine may reach the pleural cavity: 1) lymphatic drainage; 2) direct leakage into the mediastinum followed by rupture into the pleural space; and 3) direct movement of the abdominal fluid into the pleural space through a defect in the diaphragm.

To establish the diagnosis of urinothorax, it is necessary to perform a thoracentesis and evaluate the fluid 1) for color, which should be clear yellow with the smell of urine; 2) for transudate using Light’s criteria;3 for fluid-to-serum creatinine ratio;3 which should be greater than 1 and in most cases greater than 10; for fluid-to-serum l-lactate dehydrogenase ratio, which is less than 0.6; and for fluid pH, which is usually low in cases of exudate.5 The rarity of reports of urinothorax after gynecologic surgery may be explained by the fact that gynecologic surgeons are acutely aware of the risks of potential for urinary tract injury and proactively take measures to identify and repair such injuries intraoperatively. The customary use of continuous bladder drainage by indwelling Foley or suprapubic catheters after gynecologic surgery may also allow healing of unrecognized injuries, thus preventing the occurrence of urinothorax. In our case, the failure to ascertain the integrity of the urinary tract intraoperatively after a difficult and extensive dissection by the time-honored technique of dye instillation, either intravenously or retrograde in the bladder, was an error of omission. The accidental loss of the Foley catheter on postoperative day 1 and the

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insistence by the patient not to have it replaced may have contributed to the breakdown of the injury-weakened area of the bladder, thereby causing leakage of urine into the retroperitoneal space, leading to urinothorax.

Caution should be exercised during surgery so as not to devitalize the tissue when using hemostatic clamps or electrical cautery to achieve hemostasis on the viscus wall, which may subsequently breakdown and cause leakage. Time-honored intraoperative dye instillation with indigo carmine, either intravenously or retrograde in to the bladder, should considered and be carried out with low threshold whenever there is a possibility of urinary tract injury during gynecologic surgery. Identification of the injury to the ureter or areas of the bladder that may have been traumatized or weakened will allow for appropriate repair with continuous drainage of the bladder to facilitate healing and prevent complications like the one encountered in our case.

Recognition of urinothorax is important because the pleural effusion is completely reversible after treatment of the urinary tract lesion, and the patient can be spared further investigations to diagnose the cause of the pleural effusion. Urinothorax is a rare cause of posthysterectomy pleural effusion and should be considered in the differential diagnosis in cases of postoperative shortness of breath associated with rapidly accumulating pleural effusion, particularly when there is possibility of urinary tract injury.

REFERENCES


Successful Use of Botulinum Toxin Type A in the Treatment of Refractory Postoperative Dyspareunia

Amy J. Park, MD, and Marie Fidela R. Paraiso, MD

BACKGROUND: Refractory dyspareunia presents a challenging therapeutic dilemma.

CASE: A woman with defecatory dysfunction and dyspareunia presented with stage 2 prolapse. She underwent laparoscopic and vaginal pelvic floor reconstruction with excision of endometriosis. The patient experienced increased dyspareunia and de novo vaginismus postoperatively that were refractory to trigger point injections, physical therapy, and medical and surgical management. She underwent botulinum toxin type A injections into her levator ani muscles, which allowed her to have sexual intercourse again after 2 years of aparueunia with no recurrence of pain for 12 months.

CONCLUSION: Injecting botulinum toxin into the levator ani muscles shows promise for postoperative patients who develop vaginismus and do not respond to conservative therapy.

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Dyspareunia is a known sequelae of rectocele repair. Surprisingly, dyspareunia is not associated with vaginal topography or vaginal caliber. It has shown to be associated with levator ani plication. Although performing a site-specific repair was previously thought to decrease the risk of dyspareunia as compared with a traditional posterior colporrhaphy, a recent randomized trial comparing these techniques has demonstrated no significant difference in anatomic or subjective cure rates or in dyspareunia rates postoperatively. This trial also demonstrated improvement in defecatory dysfunction, especially with obstructive symptoms such as splinting to defecate. Interestingly, patients often had preoperative dyspareunia that improved after rectocele repair.

Once dyspareunia occurs, several treatment options exist, such as the use of topical anesthetics,
lubricants, vaginal estrogen, trigger point injections with local anesthetics and steroids, or anxiolytics such as benzodiazepines. Physical therapy with the optional use of dilators is also a noninvasive method to address this problem. If the patient has a palpable band of tissue due to incorporation of the levator ani muscles into the rectocele repair, the surgeon may elect to release the band of muscle intraoperatively through the use of monopolar cautery. Decreased vaginal caliber and vaginal tightness may be addressed through the use of a graft, either autologous or cadaveric, to increase vaginal caliber and diameter.

If these measures fail, the remaining options to patients and physicians are few. The following case demonstrates the successful use of botulinum A toxin into the levator muscles for a case of refractory dyspareunia after a site-specific rectocele repair, ilio-coccygeus fascia suspension, and concomitant laparoscopic pelvic floor reconstruction and excision of endometriosis.

**CASE**

The patient was a 49-year-old gravida 1 para 1 who presented with defecatory dysfunction consisting of splitting to defecate, chronic constipation that was not relieved with oral psyllium fiber or milk of magnesia, and pain after bowel movements. The patient attributed her constipation to tramadol and hydrocodone/acetaminophen use, which she took for her back pain.

She initially presented to a colorectal surgeon who diagnosed a rectocele and performed a flexible sigmoidoscopy that revealed the presence of diverticulosis and significant perineal descent with straining. A defecating proctogram was obtained due to the suspicion of intussusception which confirmed the presence of a rectocele and enterocoele.

The patient was then referred to the urogynecology department for further work up. Upon further questioning, she stated that she had dyspareunia, with the specific reports of tenderness at the vaginal apex and superficial burning at the introitus during intercourse that would resolve by the next day. She reported rare urge incontinence with leakage but no further stress incontinence after the next day. She reported rare urge incontinence with leakage but no further stress incontinence after the next day.

The patient's obstetric history was significant for one vaginal delivery of a 5-lb 14-oz infant with an episiotomy. Her medical history consisted of a congenital tricuspid valve prolapse quantification staging system. The measurements were as follows: Aa -1, Ba -1, C -4, gh 3, pb 4.5, TVL 8.5, AP +1, BP +1. She was prescribed polyethylene glycol (peg) 3350-oral for her constipation and vaginal estrogen for vaginal atrophy and was referred to physical therapy.

Given the patient’s history of dyspareunia at the vaginal apex, a laparoscopic approach was performed to evaluate for endometriosis, in addition to a rectocele repair for her posterior vaginal prolapse and history of defecatory dysfunction. Given her medical comorbidities, medical clearance was obtained before her procedure. The patient underwent a laparoscopic uterosacral ligament vaginal vault suspension, enterocoele repair, enterolysis, bilateral salpingo-oophorectomy, excision of endometriosis, and site-specific rectocele repair. Intraoperative findings were consistent with bilateral enteroceles, left pararectal endometriosis, adhesions of the left fallopian tube and ovary to the left pelvic sidewall and to the left uterosacral ligament, left ovarian endometrioma, and adhesions of the bowel to the vaginal apex and pelvic sidewalls.

Because of the intraoperative findings of endometriosis, the vaginal estrogen was discontinued. At her 4-month postoperative visit, the patient reported intermittent vaginal bleeding, spasms in the perineal area, and still having to splint to defecate. On physical examination, the patient had vaginal atrophy and granulation tissue just inside the hymenal ring from an undissolved polydiallyxanone suture from the rectocele repair. Silver nitrate was applied to the area of granulation tissue and vaginal estrogen was restarted as the biopsy results were negative for endometriosis. Five months postoperatively, her vaginal bleeding, granulation tissue, and stitch erosion had resolved. However, she reported dyspareunia that was significantly increased compared with her preoperative reports of apical tenderness and introital burning. Physical examination revealed a vaginal caliber of three finger breadths and point tenderness at the band of scar tissue on the right iliococcygeus muscle. A trigger point injection with 9 mL of 0.25% bupivicaine and 1 mL of dexamethasone was performed. She was again referred for physical therapy, which improved the patient's symptoms by 60%. The patient was also started on a low-oxalate diet and titrated up on gabapentin and amitriptyline, which she took for back pain, for presumed vulvar vestibular syndrome, as she still had the symptom of superficial burning with intercourse that she had had preoperatively. Eventually, the pain management center, who was co-managing this patient, discontinued the gabapentin and amitriptyline and changed to levetiracetam.

The patient continued to have dyspareunia refractory to conservative management and therefore 1 year after her initial surgery went to the operating room for a vaginoplasty, bilateral levator release with a full thickness dermal graft harvested...
from the abdominal pannus. Intraoperative examination revealed a vaginal stricture just cephalad of the hymenal ring, and at the end of the procedure four fingerbreadths were easily inserted into the vagina. She was managed postoperatively on pelvic rest and vaginal dilators. Nevertheless, approximately 1 month after this procedure, she lost her vaginal graft and had granulation tissue at the levator release sites at 4 and 8 o’clock, which was treated with silver nitrate and vaginal estrogen.

Subsequently the patient reported aperpeunia, vaginal discharge, and continued vaginal bleeding due to granulation tissue. On examination, she had a constriction of the left levator muscles and was given another trigger point injection with the bupivacaine and dexamethasone into the left pubococygeus muscle.

The patient continued to have significant dyspareunia and levator spasm. Four months after the vaginoplasty graft operation, she was injected with a total of 40 units of botulinum A toxin, initially at five sites with 10 units each of botulinum A toxin in the levator ani muscles bilaterally and one into the right bulbocavernous muscle. One month later, a second round of botulinum toxin injections was performed with 10 units each in four sites at 10 o’clock, 2 o’clock, 4 o’clock, and 8 o’clock in the levator/obturator muscle complex (Fig. 1). No local or intravenous anesthesia was used during the botulinum injections. Before undergoing these injections, the patient was extensively counseled that bladder and bowel dysfunction may occur as a result of paralyzing the levator musculature.

At the 2-month follow-up from the second botulinum toxin injection, the patient reported that she was able to successfully have intercourse, without pain, for the first time in 2.5 years. For almost a year after botulinum injection, she had no recurrence of her symptoms but subsequently experienced recurrence and gradual exacerbation of dyspareunia. She underwent repeat botulinum toxin injections 18 months after her first treatment. She now is having pain-free intercourse.

**COMMENT**

Botulinum toxin type A blocks the transmission of acetylcholine at the neuromuscular junction, resulting in muscular paralysis that can treat conditions of hypertonicity. It has demonstrated efficacy in the treatment of cervical dystonia, limb spasticity after cerebrovascular accidents, and headache.

In terms of pelvic floor complaints, Ghazizadeh and Nikzad enrolled 24 women with severe vaginismus refractory to previous therapy in their case series to receive 150–400 units of botulinum toxin type A into three sites on each side in the puborectalis muscle. The etiology of the vaginismus was not specified in the inclusion criteria. After a mean follow-up of 12 months, none of the patients had recurrent vaginismus, and 75% were able to achieve satisfactory intercourse. Abbott et al performed a double-blinded randomized controlled trial that demonstrated botulinum injections of 80 units into two sites bilaterally of the pubococcygeus and puborectalis muscles were superior to placebo in the treatment of vaginismus. Women included in this study had to have objective evidence of pelvic floor myalgia, with painful contracted levator muscles on examination and elevated resting vaginal pressures on manometry. The majority of patients included in this study had a history of endometriosis, and about 90% in each group had undergone a previous laparoscopy or abdominal surgery. Of note, neither study demonstrated any adverse side effects in terms of bowel or bladder dysfunction subsequent to the botulinum injections.

This case demonstrates the successful use of botulinum A toxin for a patient who presented with dyspareunia that increased after pelvic floor reconstruction and excision of her endometriosis.

**REFERENCES**

Sacral Neuromodulation in the Treatment of Vulvar Vestibulitis Syndrome

Laura B. Ramsay, MD, Johnnie Wright Jr, MD, and John R. Fischer, MD

BACKGROUND: Vulvar vestibulitis syndrome is a chronic pain syndrome that typically results in pain and irritation of the vulvar vestibule and has few effective options for treatment.

CASE: A 42-year-old woman presented with symptoms consistent with chronic vulvar vestibulitis syndrome that was refractory to multiple attempted therapies. The patient was offered sacral neuromodulation for treatment. She underwent a standard two-phase surgical implantation with good result at 2 years postimplantation.

CONCLUSION: Sacral neuromodulation was shown to be a valid treatment option for this patient and resulted in excellent patient satisfaction at 2-year follow-up. Although the exact mechanism of action is unknown, sacral neuromodulation may be a viable option for the management of chronic pain syndromes of the vulva and vagina.

(Obstet Gynecol 2009;114:487–9)

Vulvar vestibulitis syndrome is a subset diagnosis of vulvodynia. It consists of unexplained vulvar pain frequently accompanied by physical disabilities, limitation of daily activities (such as sitting and walking), sexual dysfunction, and psychologic disability.1 Age distribution for this condition ranges from the 20s to the 60s, and white women are affected predominantly. Obstetric and gynecologic history is usually unremarkable. Risk-taking sexual behavior is rare, but a history of genital infections has been identified as a risk factor for vulvar vestibulitis syndrome.2 Vulvar pain frequently has an acute onset. At times, the pain can be associated with episodes of vaginitis or certain therapeutic procedures of the vulva (eg, cryotherapy, laser therapy, vaginal delivery) and often is described as burning or stinging. Patients with vulvar vestibulitis syndrome have been shown to have an increased density of neutrophils in the vulvar and vestibular region.3 It is theorized that these patients have a defect in their respective spinothalamic pathway that predisposes them to longstanding neuropathic pain. In most cases, this syndrome can last for months to years.

The cause of this pain syndrome is unknown. Treatment tends to be guided by patient symptoms and the health care provider’s clinical experience because there is a paucity of published data on effective treatments to guide the clinician. Current treatment modalities include topical, oral and injectable medications, physical therapy, dietary modifications, and surgery.2,4

Sacral neuromodulation, or InterStim (Medtronic Inc., Minneapolis, MN), is a technology based on the surgical implantation of a device that allows chronic electrical stimulation of the sacral nerves using a battery-powered pulse generator. Sacral neuromodulation has been approved by the U.S. Food and Drug Administration for the treatment of urinary retention and the symptoms of overactive bladder, including urinary urge incontinence and urinary urgency or frequency or both in patients who have failed or could not tolerate more conservative treatments.5 Case re-

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The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army, Department of the Navy, Department of the Air Force, or the Department of Defense.
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port of the use of sacral neuromodulation in interstitial cystitis also have shown benefit in the pain associated with the disease process. A recent case report highlights the use of S4 nerve root stimulation via lumbar epidural placement for the treatment of vulvodynia. We present a case of the use of sacral neuromodulation in the treatment of refractory vulvar vestibular syndrome.

**CASE**

A 42-year-old woman, gravida 2 para 2, with a known diagnosis of chronic vulvar vestibular syndrome since the vaginal delivery of her first daughter 13 years earlier presented to the urogynecology clinic for referral. The patient reported that the pain and pressure sensation in her vaginal area had worsened since the delivery of her twins in 2004, such that she had to wear loose clothing and was unable to sit. She reported not having intercourse in the previous 2 years secondary to the vulvar pain and stated that it had affected her marriage negatively. She described the intensity to be a 10/10 on the visual analogue scale at worst and never better than 4/10.

The patient’s past medical history was remarkable for Hashimoto’s thyroiditis, osteopenia, and psoriasis. She was allergic to latex but had no known medication allergies. Her surgical history was notable for one cesarean delivery, two modified vestibulectomies, and a loop electrosurgical excision procedure. She denied alcohol and tobacco consumption. Her obstetric history was significant for one vaginal delivery and the cesarean delivery of her 38-week twins 2 years prior. Current medications included Synthroid and Fosamax.

The patient had exhausted various therapies with some improvement but always with return of symptoms over time. Her treatments included trigger-point injections with lidocaine, botulinum toxin A injections, interferon alpha injections, antidepressants (including desipramine and amitriptyline), peeling creams, topical lidocaine, 8 weeks of injections, antidepressants (including desipramine and amitriptyline), peeling creams, topical lidocaine, 8 weeks of pelvic floor physical therapy, and eventually two partial vestibulectomies.

Her physical examination was notable for normal external female genitalia and tender hyperesthesia to Q-tip from 5–8 o’clock at the introitus. The levator ani muscles were nontender, and pelvic examination was negative for levator spasms, but her presenting symptoms made dilator therapy and intercourse impossible.

Given the refractory nature of the patient’s disease process, sacral neuromodulation was considered as a possible treatment option. PubMed and MEDLINE searches were conducted in the English language from January 1, 1997–January 31, 2007, regarding the potential role of sacral neuromodulation placement in the treatment of chronic vulvar pain using the following terms: neuromodulation, chronic vulvar pain, vulvar vestibular syndrome, pelvic pain, InterStim, interstitial cystitis, and sacral stimulation. No prospective trials existed involving the use of implantable sacral neuromodulation in the treatment of vulvar vestibular syndrome. After extensive counseling, the patient was offered implantable neuromodulation. She was counseled on potential risks associated with the procedure, including pain at the implantation site, lead migration, infection, pain at the lead site, transient shock, and device malfunction requiring surgical revision or explant or both.

The patient underwent the standard two-phase surgical implantation, which initially involved placement of a quadripolar lead transforaminally onto the third sacral nerve root (S3). This was followed by a screening test period during which patient symptoms were monitored closely to determine whether there was improvement with stimulation using an external battery pack. Response to test stimulation was determined by the patient’s pain scores, documented via the visual analogue scale. The patient had documented reduction in the visual analogue scale from 10/10 to 2/10 with stimulation. Given her positive response to initial stimulation, a permanent implantable pulse generator was placed 2 weeks after initial placement of the quadripolar lead.

At 6 weeks after permanent implantation, the patient had significant improvement of her symptoms. She noted that she had not had a “flare” since the placement of the device and was able to resume her daily activities as well as dilator therapy. She continued to have some premenstrual discomfort 2 days before menses, but reported that it was substantially more tolerable.

Twenty-four months postimplantation, the patient continued to have substantial benefit. Dilator therapy progressed such that she was able to resume coital intercourse with her spouse. She noted both an increase in the number of pain-free days and an overall decrease in intensity of pain during flares.

**COMMENT**

The results of this case are very promising. Sacral neuromodulation was shown to be beneficial for this patient and resulted in both objective and subjective improvement in her symptoms as early as 6 weeks that have persisted up to 24 months postimplantation. InterStim (Medtronic Inc., Minneapolis, MN) has been shown to be a viable management option for refractory urinary dysfunction, including urgency/frequency and nonobstructive urinary retention. It also has been shown to be of benefit in the management of fecal incontinence.

The authors believe that vulvar vestibular syndrome is a neuropathic pain disorder characterized by an increase in nociceptive nerve fibers (c-fibers) with altered receptor expression and activation of the sympathetic nervous system. Although the exact mechanism of action in this patient is unknown, we postulate that chronic stimulation of the sacral nerve roots (specifically S3) resets...
the central pain response by altering the density of nociceptive nerve fibers in the vulvar region.

The authors acknowledge that sacral neuromodulation was used off label for the treatment of vulvar vestibular syndrome in this case. Although we are excited for this patient in particular and about the possible applications in patients with chronic pain syndromes, larger randomized studies are necessary to better understand the role of this therapy. A significant concern is the cost associated with sacral neuromodulation. A recent study attempted to assess the efficacy of the use of sacral neuromodulation for the management of patients with urinary dysfunction. Although there are no studies that specifically address its cost-effectiveness with respect to pain, perhaps the same argument could be made for patients suffering from chronic pain syndromes such as vulvar vestibular syndrome if one were to consider the cost of frequent specialist consultations, rehospitalization, ongoing therapy, and diagnostic tests.

The encouraging results of this report suggest that sacral neuromodulation may be an effective and reversible therapy for the management of vulvar vestibular syndrome.

REFERENCES

Martius Graft for the Management of Tension-Free Vaginal Tape Vaginal Erosion

Khalid Al-Wadi, MBBS, and Ahmed Al-Badr, MBBS, FRCS(C), FACOG

BACKGROUND: The tension-free vaginal tape (TVT) procedure has become standard for the treatment of stress urinary incontinence in women. The procedure carries a risk of vaginal erosion and exposure of the mesh. When this occurs, most surgeons recommend removal of the tape for immediate relief of symptoms. However, this poses a risk of recurrence of urinary incontinence. CASE: A premenopausal woman had an exposed vaginal mesh after a TVT procedure. After failed conservative treatment, she was treated successfully using a Martius graft, with preservation of the mesh.

CONCLUSION: The Martius procedure was a practical alternative for treating this patient with synthetic-mesh-induced vaginal erosion. It allowed preservation of the sling, thereby preventing recurrence of urinary incontinence.

The tension-free vaginal tape (TVT) procedure gained worldwide acceptance for the treatment of stress urinary incontinence because of long-term effectiveness and a presumed low complication rate. The widespread use of this procedure, however, led to an increasing number of reports of associated complications.1 Vaginal erosion after TVT or transobturator tape placement is well-documented, with an incidence ranging from 0.2% to 22%.2 The exact cause of vaginal erosion is unclear, although subclinical wound infection, excessive sling tension, small mesh pore size, poor mesh incorporation, and thin vaginal walls that may occur after radiation therapy or surgery have been suggested.1 Most surgeons recommend removal of the tape, either partially or completely, for immediate relief of the symptoms; however, there is an accompanying risk of recurrent urinary incontinence.1,3
We report a case of vaginal erosion after TVT placement that was treated surgically successfully using Martius bulbocavernosus fat pad graft after failure of conservative treatment.

CASE

A woman aged 43 years presented with stress urinary incontinence, urgency, and frequency for 1 year. She had had six normal vaginal deliveries, and her medical and surgical history were unremarkable. Pelvic examination revealed a wide genital hiatus with anterior and posterior pelvic prolapse (grade 2 of 4) based on the Baden-Walker System but no cervical prolapse. Uroflowmetry was normal. The patient was diagnosed with urge-predominant mixed urinary incontinence with pelvic organ prolapse.

The patient was treated initially with pelvic floor exercise and bladder drills. She was offered and declined anticholinergic medications. After 2 months, she reported incomplete resolution of her symptoms and requested surgical treatment. Accordingly, after counseling, she underwent anterior and posterior vaginal repair with Gynecare TVT (Ethicon, Somerville, NJ) insertion and cystoscopy (done by A.A.). At the initial follow-up 2 months after the procedure, the patient was continent with no complaints. Pelvic examination revealed, incidentally, an exposed piece of mesh (1 to 2 cm) in the midline with thinned, eroded vaginal epithelium. The area was tender to touch, and there was no discharge. Topical conjugated estrogen vaginal cream was prescribed for 2 months as conservative treatment but with no improvement, and, in fact, the patient began to experience dyspareunia.

Cystourethroscopy showed normal bladder and urethra. Subsequently, the patient was counseled regarding the treatment options for isolated vaginal erosion after TVT insertion and potential complications. The superior part of the graft was clamped and ligated. Options that have been suggested for management of this erosion include observation, using epithelial tissue flaps to cover and preserve the mesh, and surgical removal of the tape. Successful conservative management comprising observation and abstinence from sexual intercourse was reported by Kobashi et al for four patients with vaginal erosion after TVT placement. In that case series, the vaginal defects were small (0.5 to 1.0 cm) and underwent complete epithelialization in approximately 6 weeks. Other research has demonstrated that conservative management alone is frequently unsuccessful, especially if the vaginal defect is larger than 1.0 cm.

Recently, successful primary closure of the vaginal epithelium over eroded TVT tape without compromising continence was reported in five patients. This may prove to be an effective, less invasive method for managing isolated vaginal erosion; however, vaginal erosion after placement of the synthetic slings is a well-documented, potentially devastating complication. Using synthetic materials in suburethral slings provides the advantage of eliminating complications related to harvesting autologous fascia; however, vaginal erosion after placement of the synthetic slings is a well-documented, potentially devastating complication. The superior part of the graft was clamped and ligated. Options that have been suggested for management of this erosion include observation, using epithelial tissue flaps to cover and preserve the mesh, and surgical removal of the tape. Successful conservative management comprising observation and abstinence from sexual intercourse was reported by Kobashi et al for four patients with vaginal erosion after TVT placement. In that case series, the vaginal defects were small (0.5 to 1.0 cm) and underwent complete epithelialization in approximately 6 weeks. Other research has demonstrated that conservative management alone is frequently unsuccessful, especially if the vaginal defect is larger than 1.0 cm.

Recently, successful primary closure of the vaginal epithelium over eroded TVT tape without compromising continence was reported in five patients. This may prove to be an effective, less invasive method for managing isolated vaginal erosion; however, one of the patients was treated by excising the extruded portion of the tape, and the free edges of the tape were buried under the vaginal mucosa. Using a tissue graft to cover the defect and preserve the mesh is described by Lee et al in three
Unusual Presentation of Severe Intrahepatic Cholestasis of Pregnancy Leading to Fetal Death

Nathalie Favre, MD, Armand Abergel, MD, PhD, Pierre Blanc, MD, Vincent Sapin, PharmD, PhD, Laurence Roszyk, PharmD, and Denis Gallot, MD, PhD

BACKGROUND: We report an unusual presentation of intrahepatic cholestasis of pregnancy complicated by fetal death and associated with homozygous bile salt export pump polymorphism.

CASE: A secundigravida presented at 31 weeks of pregnancy with discrete pruritus and highly elevated bile acid levels (223 μmol/L) suggestive of intrahepatic cholestasis of pregnancy, despite normal serum aminotransferase levels. She had a 6-year history of ulcerative colitis, and her previous pregnancy (3 years before) had been uneventful. Initial contractions and vaginal bleeding subsided spontaneously, and corticosteroids were administered for fetal lung maturation. However, in utero fetal death occurred 9 hours after normal cardiotocography. Follow-up confirmed progressive decrease of bile acid level, but the aminotransferase levels remained elevated. Molecular biology revealed a homozygous mutation for bile salt export pump protein.

CONCLUSION: This case illustrates an unusual presentation of very severe intrahepatic cholestasis of pregnancy in a homozygous patient carrying bile salt export pump mutation.

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commonly starts on the palms of the hands and the soles of the feet before spreading in an ascending pattern. Jaundice typically develops 1–4 weeks after the onset of pruritus but occasionally can be the initial symptom. Serum aminotransferase activity is 2-fold to 10-fold higher than normal in 20–60% of patients with pruritus and may exceed 1,000 units/L in exceptional cases. The most specific and sensitive marker of intrahepatic cholestasis of pregnancy is serum bile acid above 10 micromoles/L. Intrahepatic cholestasis of pregnancy usually occurs during the third trimester of pregnancy but has been reported from 20 weeks of pregnancy. Adverse fetal outcomes of intrahepatic cholestasis of pregnancy include preterm delivery, meconium staining of amniotic fluid, fetal distress, and intrauterine fetal demise (0.4–4.1%).

Liver, meconium staining of amniotic fluid, fetal hepatic cholestasis of pregnancy include preterm delivery at 39 weeks. Her medical records included a 6-year history of ulcerative rectocolitis treated by azathioprine and topical betamethasone (no medication required during pregnancy). Three days later, the patient reported extreme pruritus. Laboratory results showed normal serum aminotransferases and very high bile acid levels (223 micromoles/L), suggesting intrahepatic cholestasis of pregnancy. Cardiotocography demonstrated normal fetal heart rate pattern. Ultrasound examination of liver and biliary tract excluded obstructive gallstone disease. Serologic tests performed for viral hepatitis A, B, and C, cytomegalovirus, Epstein-Barr virus, and human immunodeficiency virus infections were negative. It was decided to assess bile acid levels 1 day later. At this time, the patient reported aggravated pruritus. In utero fetal death was recorded 9 hours after normal cardiotocography. Bile acid level was 252 micromoles/L. The patient delivered a stillborn male fetus weighing 1,690 g by cesarean (cord blood bile acid level 170 micromoles/L). Bile acid chromatography performed on maternal and fetal blood samples demonstrated no qualitative anomaly (cholate over chenodeoxycholate ratio at 1.35 and 2.6, respectively). Amniotic fluid was meconium-stained, with amniotic bile acid level at 2,515 μmol/L (N<4 micromoles/L). Necropsy revealed acute anoxia with no fetal or placental abnormality. Maternal follow-up confirmed an elevated serum aminotransferases and hyperbilirubinemia (27 μmol/L) associated with a progressive decrease in bile acid levels (15 μmol/L at day 20). Biliary tract magnetic resonance imaging performed 5 weeks later revealed no obstruction. Liver biopsy demonstrated no cholangitis. All the coding regions of the ABCB4, ATP8B1, and ABCB11 genes were sequenced. No mutations were detected in the ABCB4 or ATP8B1 genes. The mother was homozygous for the 1331T>C mutation in the ABCB11 gene, resulting in the substitution of valine by alanine at position 444 in the bile salt export pump protein.

**COMMENT**

Our case illustrates a very uncommon presentation of severe intrahepatic cholestasis of pregnancy, with the absence of elevated serum aminotransferases despite highly elevated bile acid levels in association with homozygous bile salt export pump polymorphism. We observed a transitory increase in aminotransferases over the days that followed delivery, leading to the comprehensive picture of intrahepatic cholestasis of pregnancy with spontaneous resolution after delivery. The context of ulcerative rectocolitis prompted the use of biliary tract magnetic resonance imaging and liver biopsy to rule out sclerosing cholangitis definitively. Numerous authors have demonstrated a highly significant correlation between intrahepatic cholestasis of pregnancy and homozygous status for the ABCB11 (bile salt export pump) 1331T>C polymorphism. Bile salt export pump expression in healthy liver tissue has been found to be lower in carriers of the 1331C allele. This might offer one valuable explanation for the increased susceptibility to the develop-
ment of cholestasis under specific circumstances, such as hormonal challenges. Moreover, bile acid levels are usually higher with the CC genotype of the \textit{ABCB11} gene compared with the TT genotype. A very severe case of intrahepatic cholestasis of pregnancy already has been observed in a patient with the CC genotype. This patient presented with severe pruritus from the first trimester of pregnancy, with aminotransferases more than 40-fold higher than the upper limit of normal, and the patient carried an additional \textit{ABCB4} mutation and had already developed severe cholestasis under previous use of oral contraceptives. Incomplete efficacy of ursodeoxycholate treatment with persistently high bile acid levels was associated to reduced bile acid secretion. In our case, discrete pruritus occurred during the last trimester, aminotransferases were normal, the patient was not carrying an \textit{ABCB4} or \textit{ATP8B1} mutation, and, most surprisingly, cholestasis did not occur during the previous pregnancy. Fetal death occurred before the use of ursodeoxycholate treatment. Fetal complications are thought to occur secondary to the increase in bile acid levels. In vitro studies have demonstrated a vasoconstrictor effect of bile acids on human placental choriocarcinoma veins and a more intense response to oxytocin stimuli in myometrial cell preparations from women with intrahepatic cholestasis of pregnancy compared with healthy women. In our case, bile acids reached a highly elevated level (greater than 250 micromoles/L). We recorded similar bile acid concentrations in fetal and maternal serum, with a normal cholate over chenodeoxycholate ratio. Elevated bile acid concentrations in amniotic fluid already have been reported in intrahepatic cholestasis of pregnancy, with mean values about 70-fold higher than in controls; here we recorded 600-fold higher bile acid concentrations. Abnormal placental bile acid transport from fetal to maternal circulation, increased maternal bile acid levels, and immaturity of fetal transport systems all may contribute to the elevated fetal bile acids. One study reports that fetal complications (preterm delivery, asphyxial events, and meconium staining of amniotic fluid) did not arise until bile acid levels were greater than 40 micromoles/L. Nevertheless, fetal death has been reported despite low bile acid levels after initiation of ursodeoxycholate treatment. Simple logistic regression analyses showed that the probability of fetal complications increased by 1–2% per additional micromoles/L of serum bile acids. Based on bile acid levels above 200 \(\mu\)mol/L, our case was at very high risk of fetal complications, as reflected in the occurrence of fetal death within 24 hours of a normal cardiotocograph. Conventional monitoring of fetal wellbeing does not, in most cases, predict fetal death. Fetal cardiac monitoring is designed to recognize a failing placenta, but it cannot forecast an acute event such as sudden fetal cardiac decompensation or arrhythmia. Proactive management is warranted in women with intrahepatic cholestasis of pregnancy when lung maturity is achieved to protect against intrauterine fetal demise. We opted not to proceed with elective caesarean delivery at the time of the initial bile acid result owing to the uncommon presentation with early gestational age (31 weeks of pregnancy). As illustrated by our observation, no association has been demonstrated between maternal symptoms and serum bile acid levels. Therefore, our group now considers pruritus during the last trimester an indication to assess bile acid level whatever the intensity or duration and whatever the aminotransferase levels. Physicians should be aware that uncommon presentation of severe intrahepatic cholestasis of pregnancy can reveal genetic predisposition.

REFERENCES

Successful Outcome in Pregnancy With Arterial Tortuosity Syndrome

Victoria M. Allen, MD, MSc, S. Gabrielle Horne, MBBS, PhD, Lynette S. Penney, MD, Ivan L. Rapchuk, MD, Jo-Ann K. Brock, MD, PhD, Deborah L. Thompson, MD, and Dora A. Stinson

BACKGROUND: Arterial tortuosity syndrome is a rare, autosomal recessive, severe, connective tissue disorder caused by a mutation in the SLC2A10 gene. We describe the pregnancy and delivery with this high-risk connective tissue disorder involving generalized abnormalities of the vasculature.

CASE: A woman with an undefined connective tissue disorder was referred for tertiary prenatal care. Diagnostic imaging demonstrated multiple pulmonary artery aneurysms and arterial tortuosity, consistent with a clinical diagnosis of arterial tortuosity syndrome. With a team considering all potential complications, a delivery plan was undertaken involving cesarean delivery and intensive perioperative and postpartum monitoring. The outcome was optimal for mother and neonate. Concurrent molecular testing demonstrated homozygosity for the SLC2A10 gene.

CONCLUSION: Optimal maternal, fetal and neonatal outcomes were obtained with comprehensive multidisciplinary care and close maternal and fetal surveillance.

Arterial tortuosity syndrome is a rare, autosomal recessive, connective tissue disorder caused by a mutation in the SLC2A10 gene and has traditionally been considered to confer a short life expectancy. Clinical manifestations are variable and include characteristic dysmorphism, arterial changes, cardiac valvular abnormalities, thromboembolic stroke, as well as skin involvement, hernias, and joint laxity. There is some overlap with features of other connective tissue disorders such as Marfan, Ehlers-Danlos, and Loeys-Dietz syndromes. Molecular evaluation for mutations in the SLC2A10 gene allows definitive diagnosis. We describe pregnancy and delivery with this high-risk connective tissue disorder involving the vasculature.

CASE

A 27-year-old nulliparous woman was referred to a tertiary care center for ongoing prenatal care at 20 weeks of gestation. She had been followed since early childhood by Medical Genetics and Cardiology. As an infant, she showed features of cutis laxa, although in later childhood, with stable skin extensibility but with the development of joint hyperextensibility, a mild form of Ehlers-Danlos type III was considered. As a child, she was noted to have a borderline enlarged ascending aorta and mitral and tricuspid valve prolapse without significant regurgitation. She also had numerous episodes of rectal prolapse, an inguinal hernia, and a hiatal hernia, all managed conservatively, and various infections, including pneumonia. There was no history of easy bruising, bleeding, or poorly healed scars. Her four grandparents were born in the same small rural community, but there was no known consanguinity. Her family history was negative for connective tissue disorder.

Physical examination demonstrated height at the 90th percentile and weight at the 25–50th percentile, with an arm span less than her height. She had a long, narrow face with sagging cheeks, down-slaning palpebral fissures, a beaked nose and micrognathia. Her uvula and palate were normal. Her skin had a “dough-like” consistency. She had some joint laxity but a Beighton score of 4 of 9 (within normal limits). There were no skeletal abnormalities or Marfanoid features. Her clinical picture suggested a connective tissue disorder, with features inconsistent with well-described vascular connective tissue disorders: Marfan, Ehlers Danlos type IV, or Loeys Dietz.

She had had an uneventful obstetric course, with normal first- and second-trimester screening. A maternal echocardiogram at 22 weeks of gestation demonstrated a mildly myxomatous mitral valve and mild mitral and tricuspid regurgitation. Unenhanced magnetic resonance imaging of the thorax and abdomen was performed at 33 weeks of gestation to assess whether her vasculature was affected. This demonstrated diffuse tortuosity of the maternal pulmonary arteries and dilatation of the right pulmonary artery, with a beaded appearance consistent with multiple aneurysms. The aortic arch was mildly tortuous, with elongation but no frank coarctation segment (Fig. 1); the remainder of her vasculature was normal. There was interposition of the intestine between the anterior abdominal wall and the liver (Chilaiditi syndrome). With this new information, and in the...
context of the rest of the clinical picture, a diagnosis of arterial tortuosity syndrome was suspected and genetic testing was initiated on an urgent basis. Unenhanced magnetic resonance imaging of the head and neck demonstrated dilated and tortuous carotid arteries, with marked tortuosity of the vertebral arteries and intracranial vasculature (Fig. 2). The pulmonary artery pressure was reassessed echocardiographically and found to be normal; however, new biatrial enlargement was noted. Fetal assessment showed normal amniotic fluid volume, breech presentation, and an estimated fetal weight of 2,213 g (41st percentile weight for gestational age) at 33 4/7 weeks.

A multidisciplinary team (see Box 1) counseled the woman and her family regarding the unquantified risk of maternal vascular catastrophe or thromboembolic stroke with an ongoing pregnancy. She was made aware of the potential risk for uterine rupture, postpartum hemorrhage, and poor wound healing. The team advised against prophylactic acetylsalicylic acid therapy for stroke prevention before imminent delivery in view of her sensitivity to nonsteroidal antiinflammatory medication and the increased risk of postpartum hemorrhage. A plan for primary cesarean delivery for maternal reasons was organized by 34 weeks after administration of antenatal steroids to accelerate fetal lung maturity. The cesarean delivery with the obstetric, obstetric anesthesia, and neonatal team was performed with informed consent in the cardiovascular surgical operating room with cardiovascular anesthesia, cardiology, and cardiovascular surgery teams also in attendance (see Box 1). Cesarean delivery of a preterm breech under regional anesthesia was uneventful, with an estimated blood loss of 600 mL. Polydioxanone #1 was used to reapproximate the fascial layer, and metal clips were placed for reapproximation of the skin incision. The woman received intensive postpartum monitoring for 72 hours postoperatively in the cardiovascular intensive care and coronary care units. Staples were removed before discharge on postoperative day 7 after an unremarkable postpartum course. She was counseled against estrogen-containing contraception, and advised regarding the use of multiple methods of birth control. The female neonate weighed 2,250 g at birth, was admitted to neonatal intensive care unit for care, and had an uneventful neonatal period, with discharge to home hospital on day 10.

Concurrent genetic testing of the mother confirmed the diagnosis of arterial tortuosity syndrome 1 day postpartum, which demonstrated homozygosity for the c.685C>T truncating mutation of the SLC2A10 gene. At day 8 postpartum, low-dose acetylsalicylic acid (81 mg daily) for empiric stroke prophylaxis was started after aspirin desensitization, in view of the patient’s cervical and intracranial arterial tortuosity and the established association with stroke in arterial tortuosity syndrome. At her follow-up visit at 6 weeks postpartum, she was in stable cardiovascular status, and had a well-healed Pfannenstiel incision. Family planning included use of condoms and the Nova T intrauterine device (Berlex Laboratories, Inc., Wayne, NJ).

COMMENT
Arterial tortuosity syndrome (Online Mendelian Inheritance in Man [Johns Hopkins University, Balti-
more, MD] 208050) is an autosomal recessive disorder that is associated with dysmorphic facial features (elongated face, down-slanting palpebral fissures, sagging cheeks, and micrognathia, as seen with our patient), hyperextensible skin with abundant subcutaneous tissues (described as “doughy”), hypotonia in infancy, joint laxity, diaphragmatic and inguinal hernias, elongation of the intestine, recurrent respiratory infections, and laryngotracheomalacia.\(^1,2\) The cardiovascular features include valvular stenosis or regurgitation, pulmonary and systemic arterial elongation and tortuosity, large artery aneurysms, and pulmonary and systemic large artery stenotic segments. Stenotic segments of the aorta may have the effect of a coarctation, whereas peripheral pulmonary stenosis may produce right ventricular pressure overload.\(^1\)

Arterial tortuosity syndrome has significant phenotypic overlap with other connective tissue disorders, such as Marfan, Ehlers-Danlos, and Loeys-Dietz syndromes. Arterial tortuosity syndrome can be distinguished from these disorders by molecular delineation of the mutation in the \(SLC2A10\) gene mutation, which encodes the facilitative glucose transporter GLUT10.\(^3\) The GLUT10 deficiency is associated with the upregulation of the TGF-\(\beta\) pathway in the arterial wall, a finding also observed in Loeys-Dietz syndrome. Characteristic dysmorphisms differ among connective tissue disorders, as does prognosis.

A systematic review of the world literature was performed using PubMed and Science Citation Index with the search term “arterial tortuosity syndrome” and unlimited time duration, which identified 33 articles related to arterial tortuosity syndrome. The abstract of each article was reviewed and, where relevant, the text and bibliographies of each article were examined for content and other references. No other report of pregnancy with arterial tortuosity syndrome was identified. Although early case reports evaluating arterial tortuosity syndrome focused on clinical and pathologic findings in children and suggested a very limited life expectancy due to pulmonary stenosis, pulmonary hypertension, and aneurysms associated with tortuous and elongated arteries,\(^3,4\) more recent case series have reported individuals with arterial tortuosity syndrome living into adulthood.\(^1\) With no information related to arterial tortuosity syndrome and pregnancy, the management of our patient took into consideration the obstetric, medical, and anesthetic risks associated with other high-risk connective tissue disorders with vascular involvement (Table 1), such as Marfan, Ehlers-Danlos type IV, and Loeys-Dietz syndromes.

Some hereditary connective tissue diseases carry an increased risk of obstetric and vascular complications with pregnancy and delivery, in particular uterine and great vessel rupture. The obstetric concerns of increased risks for cervical incompetence, premature rupture of the membranes, intrauterine growth restriction, uterine prolapse, uterine rupture, severe hemorrhage, poor wound healing, and increased wound dehiscence are dependent on the type of connective tissue disorder, but can affect women with Ehlers-Danlos type IV or Loeys-Dietz syndromes.\(^5,6\) In women with Ehlers-Danlos type IV (vascular type) and Loeys-Dietz syndromes, mode and timing of delivery is controversial.\(^5,6\) Assisted vaginal delivery with forceps or vacuum to reduce the risk of aortic dissection or other vascular events may have an increased risk of perineal trauma and bleeding, whereas cesarean delivery before or during labor may be complicated by increased blood loss.\(^7\) A planned assisted vaginal or cesarean delivery will be influenced by the degree of maternal cardiovascular compromise, fetal status, and the availability of cardiovascular medical and surgical resources at the time of delivery. The option of administration of antenatal corticosteroids to accelerate fetal lung maturity would be dependent on gestational age.

**BOX 1. CONNECTIVE TISSUE DISORDERS WITH CARDIOVASCULAR INVOLVEMENT IN PREGNANCY TEAM MEMBERS**

| Maternal–Fetal Medicine/Obstetrics |
| Cardiology |
| Medical Genetics |
| Obstetric/Cardiovascular Anesthesia |
| Neonatology/Pediatrics |
| Radiology |
| Cardiovascular Surgery |
| Operating Room Team |
| Obstetrics |
| Cardiovascular Surgery |
| Vascular Neurology |
| Intensive Care Unit Team |
| Cardiovascular Intensive Care Unit |
| Coronary Care Unit |
| Clinical Nurse Specialists |
| Perinatal and Genetics |
| Neonatal |
| Cardiology |

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The magnitude and nature of the risk of vascular complications in pregnancy in connective tissue disorders is predicated on the specific diagnosis. Marfan syndrome most often affects the aortic root, and the risk of dissection in pregnancy is higher in the presence of a dilated aortic root. On the other hand, Loeys-Dietz and Ehlers-Danlos syndromes are associated with a very high risk of vascular catastrophes in pregnancy (up to 15% mortality), and this often occurs with minimal aortic root dilatation.

Although no consistent coagulation disorder has been identified in association with connective tissue disorders with vascular involvement, bleeding may complicate arterial, peripheral, or central line, and neuraxial needle placement. Regional analgesia may optimize fluid distribution and cardiovascular stability, whereas administration of general anesthetic may be complicated by possible spine involvement, periodontal disease, propensity for gingival bleeding, and oropharyngeal tissue fragility, as well as the possibility of pneumothorax with high airway pressures. Postoperative concerns include the persistent risk of postpartum hemorrhage and poor wound healing seen with other connective tissue disorders with vascular involvement. Arterial tortuosity syndrome, more than other vascular connective tissue syndromes, has been associated with stroke, with these events reported to occur from infancy onwards. Stroke has been reported to be ischemic in cause, to be associated with carotid artery dissection, and is influenced by the prothrombotic nature of pregnancy and the immediate postpartum period.

The obstetric and vascular issues complicating pregnancy in a woman with arterial tortuosity syn-

<table>
<thead>
<tr>
<th>Issue</th>
<th>Management/Action</th>
</tr>
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<tbody>
<tr>
<td>Antepartum course</td>
<td>Regular multidisciplinary follow-up</td>
</tr>
<tr>
<td>Maternal Fetal Medicine Clinic—Prenatal care and fetal imaging</td>
<td></td>
</tr>
<tr>
<td>Cardiology Clinic</td>
<td></td>
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<tr>
<td>Timing of delivery</td>
<td>Dependent on maternal, fetal, and cardiovascular status—consider 32–34 wk after prophylactic antenatal corticosteroids for acceleration of fetal lung maturity</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>Dependent on maternal, fetal, and cardiovascular status—consider contraindications to vaginal delivery, assisted second stage to reduce/eliminate Valsalva, and logistics of multidisciplinary care</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>Evaluation of airway, skeletal abnormalities, and vascular abnormalities for consideration of regional vs general anesthesia</td>
</tr>
<tr>
<td>Tissue quality</td>
<td>A definitive diagnosis, the patient’s past surgical history, or both may provide information on tissue quality and healing. Consider delayed absorbable sutures such as PDS for fascial repair</td>
</tr>
<tr>
<td>Intraoperative cardiopulmonary compromise</td>
<td>Possibility of hypercompliant vasculature, prone to exaggerated fluid shifts. Cardiopulmonary bypass immediately available should there be a major cardiovascular event. Transesophageal echo and transthoracic echocardiography immediately available, as well as vascular imaging (no precontrast scanning but contrast-enhanced CT imaging from neck to femoral vessels) immediately available</td>
</tr>
<tr>
<td>Intraoperative obstetric hemorrhage</td>
<td>Regional (epidural) anesthesia performed after establishing (ultrasound-assisted) peripheral arterial monitoring (challenging due to mobile vasculature). All medical and surgical options for management of intrapartum/immediate postpartum hemorrhage available</td>
</tr>
<tr>
<td>Intraoperative neurologic event</td>
<td>Immediate neuroimaging and neurosurgeons available in the event of a cerebrovascular event (hemorrhagic or thrombotic) with tortuous neck vessels and hypercoagulability in pregnancy and the postpartum period</td>
</tr>
<tr>
<td>Intraoperative fetal compromise</td>
<td>Neonatal team present in the operating room. Washed red cells if hypovolemia in the neonate associated with intraoperative maternal hemorrhage and volume shift to placenta from fetus</td>
</tr>
<tr>
<td>Postoperative cardiopulmonary compromise</td>
<td>Monitor in CVICU, CCU, or both</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>Medical options for management of postpartum hemorrhage immediately available in CVICU and CCU</td>
</tr>
<tr>
<td>Postoperative neurologic event</td>
<td>For arterial tortuosity syndrome only: ASA 81 mg PO, once daily</td>
</tr>
<tr>
<td>Long-term follow-up</td>
<td>Cardiology, Medical genetics, Family planning/preconception counseling</td>
</tr>
</tbody>
</table>

PDS, polydioxanone; CT, computed tomography; CVICU, cardiovascular intensive care unit; CCU, coronary care unit; ASA, acetylsalicylic acid; PO, by mouth.
drome highlight the necessity for adequate family planning, preconception counseling, and multidisciplinary prenatal, intrapartum, and postpartum care in patients with connective tissue disorders. A thorough family pedigree, history, and physical examination may facilitate the identification of women eligible for testing in the form of prenatal diagnosis in the case of an autosomal dominant disorder. Accessibility of appropriate medical and surgical resources is essential and must be considered in the multidisciplinary prenatal, intrapartum, and postpartum care of connective tissue disorders with vascular involvement.

We describe pregnancy and delivery with a rare high-risk connective tissue disorder involving generalized abnormalities of the vasculature. In managing such cases, emphasis should be placed on striving for the correct diagnosis and ensuring adequate vascular imaging, particularly where there is diagnostic uncertainty. The care of such patients should be centered on a multidisciplinary, comprehensive approach to pregnancy and peripartum care, with close maternal and fetal surveillance to optimize maternal, fetal, and neonatal outcomes. Awareness of the full clinical spectrum of the hereditary connective tissue disorders is important. The reciprocal effect of arterial tortuosity syndrome and pregnancy remains unclear, but may be very high risk, given that the reported life expectancy for arterial tortuosity syndrome is less than that of other vascular connective tissue disorders, including Marfan, Ehlers-Danlos type IV, and Loeys-Dietz syndromes. The long-term prognosis for a woman with arterial tortuosity syndrome after pregnancy is also unknown.

REFERENCES