

Treatment of Early Cervical Pregnancy With Cerclage, Carboprost, Curettage, and Balloon Tamponade

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BACKGROUND: Cervical pregnancy, an uncommon variety of ectopic gestation is associated with high morbidity and adverse consequences for future fertility. Currently there are no specific recommendations for the best treatment of this entity.

CASE: A 35-year-old nullipara presented with 8 weeks of amenorrhea and painless brown discharge. The patient was diagnosed with cervical pregnancy with embryonic cardiac activity. A conservative surgical treatment under general anesthesia involved intracervical infiltration of carboprost, cerclage, suction curettage of cervix, and Foley balloon tamponade was performed. The Foley was removed on day 2 and the cerclage on day 7.

CONCLUSION: Early cervical pregnancy was treated with combined cervical cerclage, intracervical infiltration of carboprost, curettage, and balloon tamponade. Severe hemorrhage during suction curettage and the adverse effects and complications of systemic methotrexate treatment were avoided.

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Cervical pregnancy is diagnosed when the gestational sac is located below the level of the anatomical internal os, with an empty uterine cavity and a significantly dilated cervical canal. Pregnancy developing in this area is an uncommon but possibly life-threatening condition due to the risk of severe hemorrhage if it is not diagnosed in time. Historically, the diagnosis was not made until total hysterectomy was performed to control bleeding. It has been reported that a cervical pregnancy cannot be conservatively managed after 20 weeks of gestation,¹ but an effective diagnostic tool, such as a transvaginal ultrasonography, and an early management of this uncommon

implantation of a fertilized ovum can minimize these significant maternal morbidities.

The reported incidence of cervical pregnancy is less than 1% of all ectopics,² with the incidence varying from 1:1,000 to 1:18,000 pregnancies.³ The exact incidence is unclear mainly because most cases are now diagnosed using ultrasonography and then terminated in the first trimester without being reported.⁴

We report a case of cervical pregnancy during the first trimester diagnosed by transvaginal ultrasonography and treated conservatively with cervical cerclage, intracervical infiltration of carboprost tromethamine, dilation and evacuation (D&E), and Foley balloon tamponade.

CASE

A 35-year-old woman presented to the emergency department with a 2-day history of painless brown vaginal discharge without report of active vaginal bleeding, leakage of fluid, or fever before presentation. She had been in good health with regular menstrual periods, the last being 8 weeks before her admission. Her gynecologic history was remarkable for endometriosis diagnosed 4 years ago, syphilis at 17 years old, one first-trimester elective termination, and two spontaneous abortions with dilatation and curettage.

No history of in utero diethylstilbestrol exposure or in vitro fertilization techniques was reported. The patient was stable, with a hemoglobin concentration of 13.4 g/dL, platelet count of 257,000/mm³ and a β -hCG over 50,000 milli-international units/mL. A bimanual examination revealed a slightly enlarged uterus with a 4- to 5-cm soft cervix and a 0.5- to 1-cm dilated external os without active vaginal bleeding. A transvaginal ultrasound examination confirmed the presence of a cervical pregnancy at 7 weeks of gestation. The patient was discharged home in stable condition to be followed up by her primary obstetrician.

A second transvaginal ultrasound examination was done 2 days later at Pennsylvania Hospital and a well-defined gestational sac with a 7-week-old embryo with cardiac activity was visualized below the level of the internal os. (Fig. 1)

In an attempt to preserve fertility, conservative medical and surgical treatment were offered, and the risks and benefits were discussed with the patient. She opted for surgical treatment, and she was counseled regarding the risk for hemorrhage, hysterectomy, and possible massive blood transfusion.

At Pennsylvania Hospital, with the patient under general anesthesia, the cervix was infiltrated with 250 mcg of carboprost tromethamine at 12:00 PM, 4:00 PM, and 7:00 PM to obtain adequate vasoconstriction. A cervical cerclage was placed then and held on tension by an operative assistant, without being tied. A straight 8-mm suction

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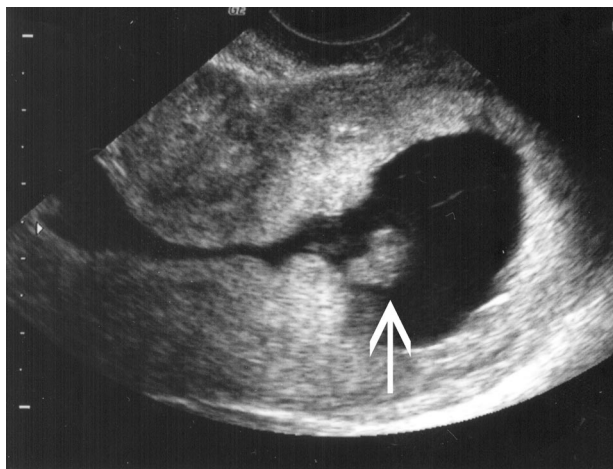


Fig. 1. Seven-week cervical pregnancy (arrow).
De La Vega. *Conservative Treatment of Cervical Pregnancy.*
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curette was inserted and advanced through the external os under transabdominal sonographic control. A large amount of products of conception was obtained from within the cervix and the thickened endometrium was systemically curetted. A 30-mL Foley catheter balloon was then placed within the cervical canal and filled with 25 mL of saline, and the cervical cerclage was tied below the balloon and left in place.

An estimated blood loss of 600 mL was evident at the end of the procedure (400 mL during the procedure and 200 mL collected in the intracervical Foley bag). The pathology specimen was consistent with products of conception. The postoperative course was uneventful, and β -hCG levels decreased to 48,612 milli-international units/mL 24 hours after the procedure and 19,004 milli-international units/mL over the following 2 days. The intracervical Foley balloon was removed on postoperative day 2 with a total of 50 mL of blood collected in the Foley bag. The patient was advised to continue serial hCG level testing and removal of cervical cerclage in 7 days. She was counseled to seek early prenatal care with the possibility of prophylactic cervical cerclage in subsequent pregnancies.

COMMENT

Cervical pregnancy, which results from implantation of the blastocyst within the cervical canal is very rare. Surgical evacuation may cause uncontrolled bleeding which may need hysterectomy. Systemic methotrexate treatment of cervical pregnancy has been reported since 1983⁵. The presence of a live fetus and hCG levels more than 15,000 international units has been considered a relative contraindication associated with higher failure rates and the possibility of sudden massive bleeding.⁶

Adverse effects of methotrexate therapy include pain, pelvic hematoma, neutropenia, alopecia, nau-

sea, vomiting, diarrhea, gastritis, abnormal liver function, stomatitis, transient pneumonitis, and bone marrow suppression.

Several case reports have cited methotrexate as a successful therapy for cervical pregnancies. Kim et al⁷ described clinical outcomes in 31 patients diagnosed with cervical pregnancy between 1993 and 2000. Twenty-two of these patients were treated with methotrexate, and nine underwent surgical procedures without methotrexate therapy. Eight (36.4%) of 22 patients that were treated with methotrexate required additional interventions for a successful treatment outcome.

Other nonsurgical treatment options for cervical pregnancy include uterine artery embolization, balloon catheter tamponade, direct intra-amniotic injection (potassium chloride or methotrexate), and mifepristone therapy. Each of these treatments have been reported in case studies, either solely, or in combination with other therapies.

Fylstra and Coffey⁸ in 2001 reported three cases of cervical pregnancy with β -hCG greater than 50,000 milli-international units/mL. Two of the patients were treated successfully with the technique described above with the only difference that the cervical cerclage was removed immediately after the insertion of the Foley balloon. The third patient underwent a suction curettage plus intracervical carboprost, intramuscular methylergonovine, figure of 8 sutures laterally on the cervix, and a Foley balloon tamponade. The patient required blood transfusion and uterine artery embolization due to active bleeding after the suction curettage. We removed the cervical cerclage 7 days after the procedure because it seems appropriate to follow the hCG titers weekly to ensure inactivity of the placentation site and reduce the risk of bleeding, but it can be done as early with the insertion of the Foley balloon.

We believe that the technique presented here, previously reported by Fylstra and Coffey,⁸ avoids the systemic adverse effects, discomforting patient follow-up of methotrexate therapy, and the potential need for hysterectomy for life-threatening hemorrhage after a routine suction curettage. However, we recommend that this combined therapy should be offered to patients who are hemodynamically stable as an option for the management of this rare entity, keeping in mind that medical therapy or total hysterectomy may still be the more prudent approach. Finally the patient should be counseled about the risk of future ectopic pregnancies, second-trimester pregnancy losses, and the potential need of subsequent prophylactic cervical cerclage.



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Delivery Complicated by Postpartum Hemorrhage and Lower Extremity Compartment Syndrome

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BACKGROUND: Extremity compartment syndrome is a rare surgical complication in which increased intracompartmental pressure threatens the viability of the muscular and nervous tissue. We report a case of a delivery complicated by postpartum hemorrhage and a lower extremity compartment syndrome.

CASE: A multigravida in her late 20s was admitted for induction of labor at 41 weeks of gestation. She underwent a cesarean delivery for a nonreassuring fetal heart rate tracing. The delivery was complicated by severe postpartum hemorrhage due to uterine atony, resulting in a cesarean hysterectomy. The patient developed a lower extremity compartment syndrome and underwent an emergent anterior tibial fasciotomy.

CONCLUSION: Extremity compartment syndrome is rarely encountered in obstetric care; however, there may be an association with severe postpartum hemorrhage. (*Obstet Gynecol* 2007;109:507–9)

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Compartment syndrome is an acute increase in pressure in a closed space that impairs blood flow to the structures within. It typically arises as a result of a crush injury to the lower extremity.¹ Well-leg compartment syndrome, first described in the orthopedic literature, is characterized by a compartment syndrome arising in an uninjured leg that was elevated away from the injured leg in the hemilithotomy position. It is typically associated with prolonged lithotomy or hemilithotomy positioning during surgery. Although rarely reported in the obstetric literature, the incidence may be as high as one in 3,500 surgical patients in the lithotomy position.² We report a case of cesarean delivery complicated by severe postpartum hemorrhage followed by a lower extremity compartment syndrome that required an emergent anterior tibial fasciotomy.

CASE

A multigravida in her late 20s was admitted for induction of labor at 41 weeks of gestation. Her medical and surgical history were unremarkable. Her obstetric history was significant for a prior term spontaneous vaginal delivery without complications. Fetal testing was reassuring upon admission, and she underwent labor induction with pitocin and a transcervical Foley catheter. The transcervical Foley was spontaneously expelled and artificial rupture of the membranes was performed 7 hours later. The patient developed chorioamnionitis and was started on ampicillin and gentamicin. She underwent a cesarean delivery for a nonreassuring fetal heart tracing. A viable male infant was delivered without difficulty. The fetal weight was 4,127 g, and the Apgar score at 5 minutes was 7.

There was persistent bleeding from the repaired hysterotomy sight with associated uterine atony. Multiple medical and surgical maneuvers were attempted to achieve hemostasis. They included oxytocin 80 units intravenous infusion, methylergonovine 0.2 mg intramuscular injection, carboprost 0.25 mg intramuscular injection, and 0.25 mg intramyometrial injection, misoprostol 800 mcg per rec-



tum, dinoprostone 20 mg per rectum, bilateral uterine artery ligations, a uterine compression suture, lower uterine segment packing, and finally a supracervical cesarean hysterectomy. The surgery began under regional anesthesia; however, the patient was placed under general endotracheal anesthesia intraoperatively. The patient became coagulopathic during the operation. Intraoperative laboratory studies revealed a hematocrit of 19%, a platelet count of 19,000, a partial thromboplastin time of 48 seconds, and an international normalized ratio of 3.2. Massive volume resuscitation was performed. She received a total of 11.5 L of crystalloid, 500 mL of colloid, 6 units of packed red blood cells, a 6-pack platelet transfusion, and 8 units of fresh frozen plasma. The estimated blood loss was 3,500 mL. The total operation time was 5 hours. The patient remained supine, and pneumatic calf compressors were used throughout the entire case.

The patient was transferred to the surgical intensive care unit under general anesthesia and intubated. Two additional units of packed red blood cells were given overnight. Her hematocrit, platelets, and coagulation studies remained stable after this. She was extubated the following morning. On the evening of postoperative day one, 38 hours after surgery, she reported severe, localized pain to the inferior/lateral aspect of her left lower leg. Physical examination findings were significant for exquisite tenderness to palpation and mild focal edema on the lateral aspect of her left lower leg. Pedal pulses, deep tendon reflexes, and neurological examinations were unremarkable. Doppler ultrasound studies were performed to exclude deep vein thrombosis. Fifteen hours later (53 hours after surgery), an orthopedic consultation was obtained. The patient was taken to the operating room for suspicion of a compartment syndrome where an emergent left anterior tibial fasciotomy was performed. Poor tissue color and ischemia were noted by the orthopedic surgical team. Ninety percent of the extensor digitorum longus muscle and 80% of the distal half of the tibialis anterior muscle were removed. A repeat irrigation and debridement was performed the following day. The patient developed a permanent left-foot drop and continues to undergo physical and occupational therapy.

COMMENT

Compartment syndrome is a symptom complex caused by increased pressure of tissue fluid in a closed osteofascial compartment of the limb which interferes with the circulation of the myoneural components of the compartment. It is most commonly seen after traumatic lower extremity crush injuries, however, it can be seen in the postoperative setting. Well-leg compartment syndrome is the version that develops not from injury, but from abnormal positioning of an atraumatic limb during a surgical procedure. Known predisposing factors include prolonged surgery time, the lithotomy position, the Trendelenburg position, pneumatic calf compressors, obesity, intraoperative hypotension, inadequate

fluid administration, sympathetic blockade, vasoconstricting drugs, peripheral vascular disease, and surgical traction on major vessels. The anterior compartment is most commonly involved. The superficial and deep branches of the peroneal nerve and the tibial and sural nerves course through this compartment.³ Compartment syndrome is potentially life threatening and may be permanently disabling. If not decompressed, it can lead to skin necrosis, residual motor weakness, foot drop, limb loss, rhabdomyolysis, and systemic manifestations such as metabolic acidosis, myoglobinuria, renal failure, and death.¹

The pathophysiology of compartment syndrome is likely related to ischemic-reperfusion events. Ischemia leads to the depletion of intracellular energy stores causing cellular swelling, edema formation, and an increase in venular pressure due to venous outflow obstruction. Intracompartmental pressure eventually equals capillary pressure, stopping nutrient blood flow and leading to tissue infarction.³ A self-perpetuating cycle of ischemia and edema then leads to compartment tamponade, muscle breakdown, and neural injury.

The diagnosis of compartment syndrome can be difficult in the postoperative setting because the most common symptom, pain, can be masked by anesthesia. The affected limb is typically swollen, red, and tender. Pedal pulses are usually palpable. Pain, pallor, and pulseless paralysis are late hallmarks of this syndrome. Magnetic resonance imaging and serum creatinine kinase may be helpful, especially in the sedated patient. An elevated handheld manometer reading confirms the diagnosis and requires immediate intervention. A high index of suspicion is necessary. Treatment is decompressive fasciotomy, optimization of fluid status, and debridement of necrotic tissue. The long-term effects are directly related to the promptness of decompression.¹

Extremity compartment syndrome is rarely encountered in obstetric care. A MEDLINE search, limited to English and humans (1966-December 2005) was performed utilizing the search terms "pregnancy," "cesarean," "postpartum hemorrhage," and "compartment syndrome." Three case reports are in the literature. Jyothi and Cox⁴ reported a case of a vaginal delivery complicated by a retained placenta, postpartum hemorrhage with massive volume replacement, and a lower extremity compartment syndrome. This patient was in the lithotomy position for more than 4 hours. Lecky⁵ reported a case of bilateral lower extremity compartment syndrome after cesarean delivery in a diabetic patient. His patient experienced bilateral foot drop that resolved without orthopedic surgical intervention. Rice and Bowser⁶ reported a case of upper extremity com-



partment syndrome after cesarean delivery for a suspected placenta previa; however, an abdominal pregnancy was discovered. The operation was complicated by significant hemorrhage and multiple blood transfusions. The authors concluded that the upper extremity compartment syndrome was secondary to the infiltration of vasopressors. Our case was notable for postpartum hemorrhage that required a hysterectomy to achieve hemostasis, the use of a vasoconstricting agent, a prolonged operating time, and the use of pneumatic calf compressors. There were no hypotensive episodes during the case, and our patient remained in the supine position during the entire case.

There is scant information linking obstetric care and compartment syndrome. However, there may be an association with severe obstetric hemorrhage. A high index of suspicion for intense extremity pain in the postpartum setting should prompt the obstetrician

to consider compartment syndrome in the differential diagnosis.

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Cotyledonoid Leiomyoma in Pregnancy

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BACKGROUND: Benign smooth-muscle tumors (leiomyomata) are the most frequent tumors found in the female genital tract. They are easy to diagnose in pregnancy and usually managed conservatively. Some variant forms with unusual infiltrative growth pattern have been known, but they are rare in pregnancy. The variant forms pose diagnostic and management difficulties.

CASE: An unusual type of leiomyoma (cotyledonoid), adhering to the bowels and occupying the whole left broad ligament, was excised completely at 14 weeks of gestation, and the pregnancy continued to term.

CONCLUSION: Familiarity with benign uterine smooth-muscle tumors with unusual growth patterns by gynecologists and pathologists is essential in avoiding overtreatment.

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Benign smooth-muscle tumors (leiomyomata) are the most frequent tumors found in the female genital tract. They are present in about 40% of women aged more than 40 years.¹ Most leiomyomata show clear-cut, smooth-muscle differentiation and, as such, create no diagnostic difficulties. A small number of cases, however, create diagnostic challenges and management difficulties. Some variant forms with unusual infiltrative growth patterns have been known, including intravenous leiomyomatosis, leiomyoma with vascular invasion, diffuse leiomyomatosis, and disseminated peritoneal leiomyomatosis.² Roth et al³ have described a rare tumor termed “cotyledonoid dissecting leiomyoma” of the uterus characterized by dissecting growth patterns of smooth-muscle cells with hydropic changes and prominent exophytic components.

CASE

A multipara in her early 30s at 14 weeks of gestation was referred to us from a private clinic because of an abdominal mass. Her presenting complaints were abdominal distension and discomfort of 2-year duration. She was seen in many clinics before pregnancy and reassured. No investigations were done before pregnancy.

The mass was detected by scan done in the third month of pregnancy. The distension became more obvious during pregnancy, and the patient developed pain. Pain was colicky in nature, aggravated by heavy meals. Her menstrual cycles were regular without dysmenorrhoea or menorrhagia. She had three term, normal deliveries, the last one 5 years ago. Abdominal examination revealed distended abdomen, a uterus of 14-week gestational-size deviated to right side and a



28-week gestational-size mass to the left of uterus. The mass was soft, irregular, and inseparable from the uterus.

Ultrasonography showed a live fetus of 14 weeks of gestation with anterior placenta and a worrisome heterogeneous mass extending from suprapubic area to the left hypochondrium. Magnetic resonance imaging with contrast enhancement showed a huge heterogeneous, soft, fleshy extraperitoneal mass extending to the left hypochondrium superiorly, displacing uterus to the right and extending down to the pouch of Douglas. The mass was well encapsulated and showed continuity with the uterine myometrium on the left lateral aspect with parasitization of the uterine vascular supply. There was no retroperitoneal lymphadenopathy or evidence of metastasis within the visible organs. The impression was a uterine myometrial mesenchymal tumor likely to represent a sarcoma or a huge degenerative fibroid.

An exploratory laparotomy was performed a week later, due to the large size and uncertain nature of the mass. The uterus was 16-week gestational size with normal tubes and ovaries. There was a big mass in the left broad ligament extending down to the cervix, with small bowel adherent to the top of the mass and sigmoid colon adherent posteriorly. The mass was multilobulated, soft, and congested with large vessels on the surface. There was no obvious intramural involvement although the tumor was very closely attached to the left lateral wall of the uterus. Adhesions were released with sharp and blunt dissection and the mass was removed completely from its origin. Most of the left broad ligament had to be removed with dissection very close to the left lateral uterine wall. The postoperative course was uneventful.

The patient's pregnancy continued normally, and she underwent an elective *primary* cesarean delivery at 38+ weeks of gestation, yielding a healthy 2,900-g baby girl. At



Fig. 1. Macroscopic appearance of the excised cotyledonoid leiomyoma.

Mathew. *Cotyledonoid Leiomyoma*. *Obstet Gynecol* 2007.

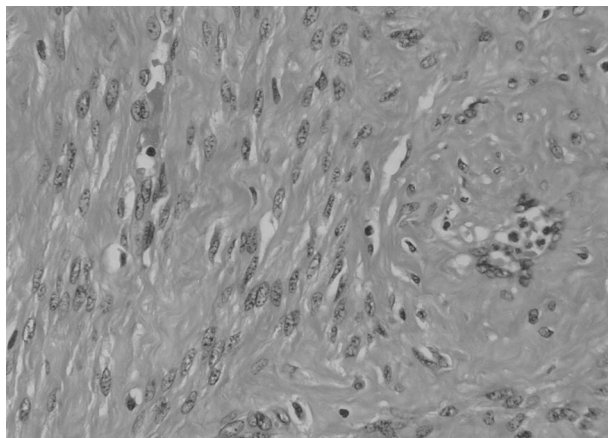


Fig. 2. Hematoxylin-eosin stain $\times 600$ showing bland smooth-muscle fibers.

Mathew. *Cotyledonoid Leiomyoma*. *Obstet Gynecol* 2007.

the time of cesarean delivery, there was no evidence of any residual disease or adhesions.

The tumor mass consisted of multiple broad bulbous protrusions joined together at the root, was soft in consistency, and weighed 3,200 g (Fig. 1). It was approximately 30×25 cm. The outer surface was smooth, purplish in color, with prominent blood vessels. The cut surface showed whorled nodular areas intersected by grayish solid tissue. The root portion was comparatively narrow with dilated blood vessels surrounded by rubbery yellow-white myometrial tissue with cord-like, firm white extensions of the main lesion.

Microscopic examination showed a neoplasm composed of fascicles of spindle-shaped cells with marked hyaline changes and extensive hydropic degeneration. Blood vessels were numerous, large, and thick walled. There was no evidence of nuclear atypia, increased mitotic activity, or necrosis (Fig. 2). Immunohistochemical studies showed strong positivity to desmin and actin confirming the smooth-muscle origin of the tumor.

COMMENT

Leiomyomata are the most frequent tumors found in the female genital tract. They are thought to be estrogen dependent and mostly asymptomatic, and most do not pose diagnostic difficulties. Leiomyomata tend to grow during pregnancy and undergo various types of degenerations including red degeneration. Although the management during pregnancy is usually conservative, the uncertain nature of the mass, the rapid increase in size, and the acute pain compelled us operate on this patient during pregnancy.

Cotyledonoid leiomyomata were first reported by Roth et al³ in 1996. They described the tumor as a "very rare variant of uterine leiomyoma characterized by the presence of numerous deep red, exophytic, and bulbous protrusions over the uterus resembling



the cotyledons of placenta.” This type of tumor had previously been reported under the designation “grapeliike leiomyoma.”⁴ It is also called Sternberg tumor in recognition of the contribution of the late William H. Sternburg, who had originally studied the tumor as “a red seaweed lesion.”³

There are 14 reported cases (in nonpregnant state).⁵ The tumor usually presents as a pelvic mass, with abdominal pain or abnormal uterine bleeding or both. The usual treatment is resection of the tumor with total abdominal hysterectomy. The age group of patients varied from 23 to 67 years. In most of these cases, intraoperative diagnosis of a malignant neoplasm was considered. The impression of malignancy can be attributed to the lack of familiarity with the alarming fungating appearance of cotyledonoid leiomyoma, the large size of the tumor, and the apparent widespread infiltrative growth with extension into the pelvic cavity, broad ligament, and the retroperitoneal space.

The histologic features of the tumor are those of a bland-looking and mitotically inactive leiomyoma, and clinical outcomes have been uniformly benign.^{5,6} All reported cases except two had an intramural dissecting component.⁵ Ours seems to be the third case without an intramural dissecting component. Frozen section should be done to avoid radical surgery in a benign condition,^{4,5} but it was not done in this patient as she was pregnant and hysterectomy consent was obtained only for uncontrollable hemorrhage. There were no intraoperative clinical features of malignancy at laparotomy. The bizarre, sarcoma-like gross appearance of the tumor apparently results from a combination of several uncommon growth factors, including subserosal growth, dissecting growth, and perinodular hydropic degeneration.⁷ Flow cytometric studies by Fukunaga et al⁸ showed

that such tumors were DNA diploid with relatively low S-phase fractions, consistent with a benign nature.

The pregnancy continued uneventfully resulting in a term, healthy baby born by elective cesarean delivery. There was no residual disease or adhesions at the time of cesarean delivery in contrast to the extensive adhesions reported by Allison et al.⁴ The ability of the uterus to coordinate contractions in labor and the risk of uterine rupture raises the question of the mode of delivery after myomectomy in pregnancy.⁴ Cesarean delivery was performed because we were not sure as to the best mode of delivery in this patient although the myoma was not obviously intramural. Familiarity with benign uterine smooth-muscle tumors with unusual growth patterns by gynecologists and pathologists is essential in avoiding misdiagnosis and overtreatment.

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Mifepristone as Treatment of Recurrent Progesterone Receptor–Positive Uterine Leiomyosarcoma

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BACKGROUND: Prolonged treatment with antiprogesterin results in shrinkage of benign uterine leiomyomata. Leiomyomata and uterine leiomyosarcomas share some common features, and they both often express progesterone receptors. Thus, treatment of uterine leiomyosarcomas with antiprogesterins has been suggested.

CASES: The antiprogesterin mifepristone was administered (50–200 mg/d) to three patients with recurrent uterine leiomyosarcomas. A dramatic response lasting more than 3 years was observed in a case of recurrent low-grade (G1) progesterone receptor–positive leiomyosarcomas. In two other patients, with G3 leiomyosarcomas, the disease progressed despite several months of mifepristone therapy.

CONCLUSION: We speculate that mifepristone has a role in the management of some cases of recurrent uterine leiomyosarcomas.

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Uterine leiomyosarcoma is rare gynecologic malignancy, representing approximately less than 1% of all uterine cancers. Primary treatment consists of hysterectomy plus salpingo-oophorectomy (depending on age) with or without lymph node dissection. In advanced cases chemotherapy has been used, although the response rates have been relatively poor, varying from 12% to 53%. The role of radiotherapy in the treatment of leiomyosarcoma is uncertain.¹ The rate of recurrence is high, ranging from 45% to 73%.¹ The prognosis of recurrent leiomyosarcoma is poor, and median survival times of 7–18 months have been reported when using

second-line chemotherapy.² Overall 5-year survival rates have been reported to be 25–75%.¹ In only a few studies have the effects of hormone therapy in cases of recurrent leiomyosarcoma been assessed. In a study by Wade et al,³ hormone therapy (medroxyprogesterone acetate, tamoxifen, or both) of uterine sarcomas was not effective.

Uterine leiomyosarcoma shares some common features with benign leiomyoma. Progesterone controls the growth of benign leiomyoma, and 90% of benign leiomyomas express progesterone receptors. Similarly, progesterone receptors have been reported to be present in 37–60% of cases of leiomyosarcoma.^{3,4} In addition, the presence of steroid receptors has been associated with better prognosis of leiomyosarcoma.⁴

Prolonged administration of the antiprogesterin mifepristone results in shrinkage of benign uterine leiomyomata.⁵ The potential value of antiprogesterins in the treatment of uterine leiomyosarcoma has been hypothesized, and a case of primary leiomyosarcoma of bone, treated successfully with mifepristone over prolonged periods, has been reported.⁶ We therefore speculated that mifepristone treatment may also be valuable in selected cases of uterine leiomyosarcoma. In this case report, we describe our experience of mifepristone treatment in three patients with recurrent uterine leiomyosarcoma, resistant to standard chemotherapy.

CASE 1

A 55-year-old nulligravid woman underwent complete cytoreduction of stage Ic grade 1 uterine leiomyosarcoma in 1992. Ten years after the primary operation and chemotherapy (etoposide-ifosfamide) she experienced recurrence: there were metastases in the lungs, liver, and pelvis. The size of the pelvic metastasis was 10.8 × 7.8 cm and those of the liver metastases (two of equal size) were 1.5 × 1.5 cm. The patient refused chemotherapy. A trial with mifepristone, approved by the Institutional Review Board of Helsinki University Central Hospital, was proposed. After the patient signed an informed consent document, the treatment was started using a daily dose of 50 mg of mifepristone. Progesterone receptor status of the primary tumor was analyzed immunohistochemically using progesterone receptor–antibody and Envision-detection kit from Dako (Glostrup, Denmark); the tumor tissue was strongly positive for progesterone receptors. We followed-up with her monthly (clinical status and several laboratory tests concerning safety) during the first year and thereafter every 3 months. Response was estimated using computerized tomography (CT), which was performed at 3- to 6-month intervals. Because there was no response after 3 months of therapy, the dose of mifepristone was increased to 100 mg daily. Three months later, shrinkage of the liver and pelvic metastases was evident. The liver metastases were barely detectable, and the

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size of the pelvic metastasis was 9.7×6.7 cm. Thereafter, shrinkage of the metastases continued, and a partial response has now (December 2005) been achieved after 36 months; the liver metastases are no longer detectable, and the larger dimension of the pelvic metastasis has diminished from 10.8 to 2.2 cm (Fig. 1). However, the sizes of the lung metastases

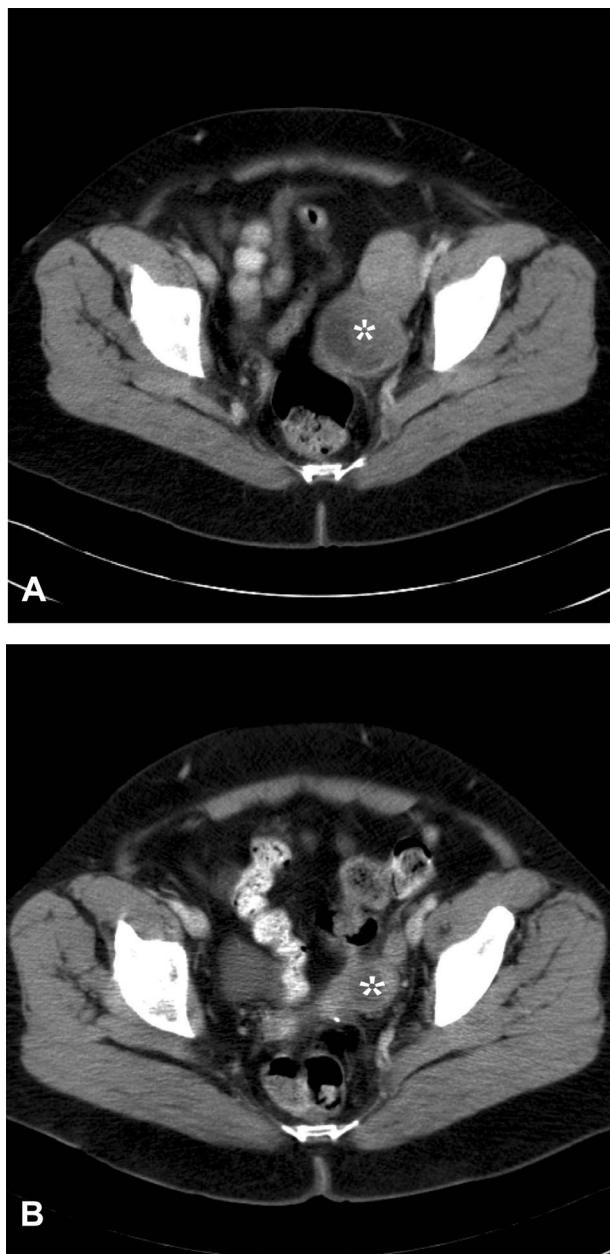


Fig. 1. Computerized tomography scans showing the size of the pelvic metastasis (asterisk) at initiation of mifepristone treatment (A) and after 36 months of therapy (B) in case 1. The maximal dimension of the pelvic metastasis diminished from 10.8 cm to 2.2 cm.

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have remained unchanged. The patient has tolerated mifepristone treatment well and reported night sweats as the only side effect. The results of liver (alanine aminotransferase, aspartate aminotransferase) and thyroid function tests (thyrotropin and free T4), and creatinine levels, have remained within normal ranges throughout the treatment (Table 1).

CASE 2

A 60-year-old nulliparous woman was operated on in April 2004 because of stage IV (lung metastases) grade 3 uterine leiomyosarcoma. Supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed, but a thin pelvic residual tumor was left. Despite operation and four cycles of etoposide-ifosfamide, the disease progressed. Mifepristone treatment (100 mg/d) was started in August 2004. The primary tumor was progesterone receptor-negative. The first CT scan revealed stable disease 3 months after the initiation of mifepristone therapy. Thereafter the disease progressed with the appearance of convulsions, and brain metastases were diagnosed after 4.5 months of treatment. Mifepristone was no longer continued. The patient died 7 months after discontinuation of the medication.

CASE 3

A 49-year-old nulliparous woman was treated in October 2003 for stage IV (lung metastases) grade 3 uterine leiomyosarcoma, by means of total hysterectomy (without salpingo-oophorectomy) followed by four cycles of etoposide-ifosfamide. A CT scan revealed a complete response after the therapy. Recurrence with lung metastases was diagnosed 7 months after the primary therapy. New cycles of chemotherapy were started: four cycles of etoposide-ifosfamide followed by six cycles of paclitaxel-carboplatin. Lung metastases progressed despite the chemotherapy. Because the primary tumor was progesterone receptor-positive, mifepristone therapy was proposed and initiated with a daily dose of 100 mg in June 2005. Despite the therapy, the lung metastases grew progressively, as assessed by CT performed at 3 months after initiation of the mifepristone therapy. In addition, she developed pleural effusion and mild dyspnea. Mifepristone treatment was continued at a daily dose of 200 mg. However, the dyspnea and pleural effusion worsened, necessitating repeated pleural drainage. Mifepristone treatment was stopped after 6 months; the patient died within a few weeks.

COMMENT

Among the present three patients with recurrent leiomyosarcoma, one has displayed a dramatic response to mifepristone treatment, lasting for more than 3 years, whereas administration of mifepristone for several months appeared to have little effect on the progression of leiomyosarcoma in the other two patients.

The reasons for the variable response to mifepristone are likely to be multifactorial. In case 1 the histologic grading of the leiomyosarcoma was grade



Table 1. Summary of the Three Leiomyosarcoma Cases and Results of Mifepristone Treatment

Cases	Stage	Grade	PR Status	Time of Recurrence	Mifepristone Therapy	Response to Treatment
Case 1	I	1	+	120 mo	9/2002–	Partial
Case 2	IV	3	–	PD	8/2004–1/2005	PD, DOD (16 mo)
Case 3	IV	3	+	7 mo	6/2005–11/2005	PD, DOD (26 mo)

PD, progressive disease; DOD, dead of disease.

1. However, in the two other patients the primary tumor was grade 3, suggesting a more aggressive nature of the disease. The delay in recurrence of almost 10 years is also in line with a more insidious nature of the disease in case 1. Patient 3 had recently failed to respond to several combinations of chemotherapy. This may have selected particularly resistant cell types with little resemblance to those in the progesterone receptor–positive primary tumor. Progesterone receptor negativity of the primary tumor is likely to have been a major factor contributing to failure in case 2. Thus, a patient with progesterone receptor–positive, low-grade leiomyosarcoma and late recurrence might be an optimal candidate for mifepristone therapy.

In previous studies, a daily dose of 50 mg or more of mifepristone has resulted in shrinkage of benign uterine leiomyomata.⁵ Administration of 200 mg of mifepristone per day over a prolonged period results in activation of the hypothalamo-pituitary-adrenal axis as a sign of potentially significant antiglucocorticoid effects of the drug.⁷ In addition, development of subclinical hypothyroidism has been described during prolonged administration of mifepristone to patients with nonresectable meningioma.⁷ We thus chose to start the treatment with daily doses of 50 or 100 mg of mifepristone. In case 1, clinical effect of mifepristone was seen during daily administration of 100 mg but not 50 mg. Therefore the dose of 100 mg of mifepristone may be optimal for the treatment of recurrent leiomyosarcoma. In previous trials in which the efficacy of mifepristone in the treatment of meningioma, breast cancer, or recurrent ovarian cancer has been evaluated, the medication has been well tolerated.⁸ Similarly, among the present three patients, only mild side effects were reported. In addition, the results of several laboratory parameters concerning safety, including liver and thyroid function tests, remained normal throughout the treatment.

Thus, safety and good tolerability would be major advantages, should mifepristone prove efficacious in long-term therapy of recurrent leiomyosarcoma.

In conclusion, a dramatic response to mifepristone exceeding 3 years was seen in a patient with recurrent, low-grade, progesterone receptor–positive leiomyosarcoma. However, mifepristone was without effect in two patients with more aggressive leiomyosarcoma. We speculate that mifepristone has a role in the management of some cases of recurrent uterine leiomyosarcoma. Given the rarity of the disease, the efficacy of mifepristone in leiomyosarcoma should be evaluated in a multicenter trial.

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Meningioma Mimicking Puerperal Psychosis

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BACKGROUND: Meningiomas are slow-growing benign brain tumors. They can be sensitive to sex hormones, increasing in size with pregnancy and leading to clinical presentation either before or immediately after delivery. Initial symptoms and signs can present in the antenatal as well as the postnatal period.

CASE: A patient presented with confusion associated with complaints of déjà vu and auditory hallucinations on day 1 postcesarean delivery. Meningioma was diagnosed by computed tomography and treated successfully with steroids, anticonvulsant, and craniotomy.

CONCLUSION: It is imperative to perform a thorough neurologic examination in a patient who presents with atypical psychiatric symptoms in the antenatal or postpartum period. Neuroimaging should be performed in the presence of any neurologic abnormality to exclude intracranial lesions such as meningioma.

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Meningiomas are slow-growing benign brain tumors. The incidence of meningioma in pregnancy is unknown, but is thought to be the same as in nonpregnant, reproductive-age women, which has been quoted as 4.5 in 100,000.¹ They are thought to arise from the arachnoid cells that form the arachnoid villi and account for 18% of all intracranial tumors.² Meningiomas variably express progesterone and androgen receptors and to a lesser extent estrogen receptors.^{3,4} The development and accelerated growth of meningiomas in pregnancy^{5,6} may be due to endogenous hormonal exposure,⁷ water retention, or vessel engorgement.^{7,8} Several cases have reported initial presentation in the antenatal as well as the postnatal period mimicking more common pregnancy conditions such as hyperemesis gravidarum⁸ or

eclampsia.⁹ This case report illustrates meningioma occurring postpartum in a woman who presents with symptoms of puerperal psychosis.

CASE

A young gravida 2 para 1, had close antenatal surveillance because she had a history of corrected Tetralogy of Fallot with aortic valve replacement. She had cardiology and anesthetic reviews during pregnancy with no detectable problems. An elective cesarean delivery at 39 weeks of gestation was planned due to a previous fourth-degree perineal tear. At 38 weeks of gestation, she was admitted with spontaneous rupture of membranes and subsequently had an uneventful cesarean delivery under regional anesthesia.

On day 1 postpartum, our patient presented with a sudden onset of confusion associated with complaints of déjà vu and auditory hallucinations, lasting for 30 minutes. She wandered around the postnatal ward and seemed to be speaking to herself. She claimed that she could hear voices and felt that she was reliving the same situation over and over again.

There was no loss of consciousness, headaches, or focal neurologic symptoms. She had no past history of epilepsy or psychiatric illness. On recovery, she had no recollection of her symptoms. The initial diagnosis was postpartum psychosis, but examination also revealed a mild left-sided motor weakness, with normal tone, symmetrical reflexes, and no sensory disturbance. Cardiac and respiratory examinations were unremarkable. Electrocardiogram, blood glucose, full blood count, and liver and renal function tests were all normal except for a raised C-reactive protein level at 126 mg/L.

Our patient's husband then reported for the first time that she had similar absence-type episodes in the preceding 3 months, averaging five times per week, each lasting 30 seconds to 2 minutes. She had no recollection of these events. She had also been experiencing severe headaches for the first 3 months of pregnancy.

Later on the same day, she had a generalized seizure accompanied by tonic-clonic limb movements, irregular respiration, and transient drop of oxygen saturation to 80%, followed by deep sleep lasting for 10 minutes. On waking, she was alert and orientated with a completely normal neurologic examination. A magnetic resonance imaging scan revealed a 4 cm × 4 cm extra-axial mass centered on the right sphenoid, with associated mass effect and vasogenic edema in the surrounding brain (Fig. 1).

A course of oral dexamethasone and phenytoin was started, which resulted in a dramatic resolution of her symptoms. She was discharged home on day 6 postpartum. Because drug therapy had controlled her symptoms, surgery was delayed for 6 weeks postpartum. The patient then underwent a right pterional craniotomy and macroscopic excision of the tumor, which was found to have a broad dural base along the middle cranial fossa floor. She made an uneventful postoperative recovery with no neurologic

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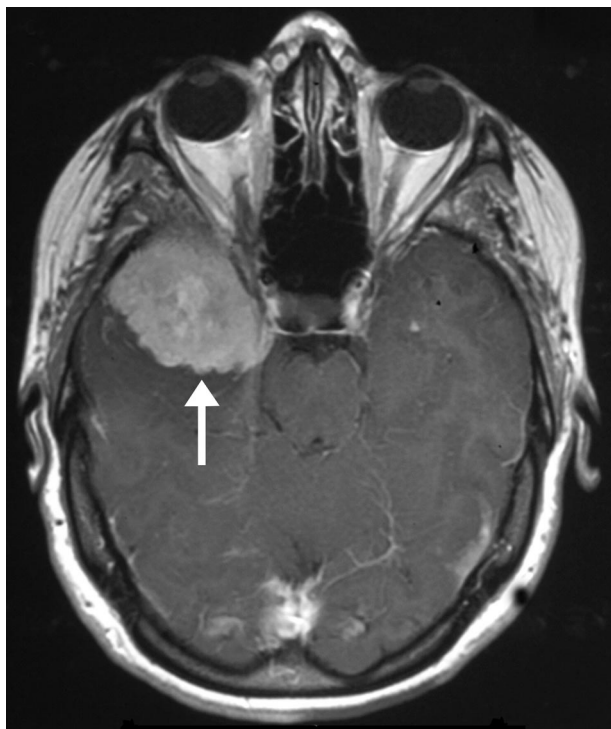


Fig. 1. Gadolinium-enhanced T1-weighted magnetic resonance imaging of the brain in the axial plane showing an extra-axial mass (arrow) arising from the right sphenoid bone. Low signal in the adjacent temporal lobe indicates cerebral edema.

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deficit. She was weaned off steroids and remained on phenytoin. Neuropathology confirmed the diagnosis as meningioma (World Health Organization grade I).

COMMENT

Meningiomas may present with symptoms of raised intracranial pressure, seizures, or focal neurologic deficits. In our case, the patient presented with symptoms of déjà vu and auditory hallucinations on day 1 postpartum preceding a tonic-clonic seizure. Postpartum psychosis does not usually present until the second or third day after delivery. Other differential diagnoses are epilepsy, cerebrovascular accident, and biochemical or metabolic causes of acute confusional state, such as hyponatremia, hypoxia, and drugs. This case highlights the need to perform neuroimaging to exclude an intracranial lesion when a pregnant patient presents with atypical psychiatric symptoms. The magnetic resonance imaging scan is preferred to the computed tomography scan in the antenatal period because it has no radiation effects on the fetus and has a high-sensitivity diagnostic effect.⁸

Most women with meningiomas diagnosed antenatally

are able to safely continue their pregnancies to term with close fetal and maternal monitoring. There is no contraindication for a vaginal delivery if there are no signs of raised intracranial pressure. Steroids have been shown to effectively resolve neurologic symptoms and symptoms resulting from raised intracranial pressure, because they tend to reduce the vasogenic edema in the surrounding brain caused by the meningioma. Anticonvulsants are usually used in combination with steroids to achieve optimal seizure control.

Surgical excision can be performed during pregnancy and tends to be reserved for progressive neurologic deficits or signs of impending brain herniation despite medical treatment. If symptoms can be controlled with steroids and anticonvulsants, it is best to defer surgery until after the delivery of the fetus. It may be even more beneficial to delay debulking surgery to more than 6 weeks postpartum to avoid the increased risk of thromboembolism associated with the postpartum period. The prognosis for a World Health Organization grade 1 meningioma with a complete macroscopic excision (Simpson grade 1) is very good, and the chance of remaining recurrence free at 10 years is approximately 90%.

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Kawasaki Disease With Coronary Artery Sequelae

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BACKGROUND: Kawasaki disease is an acute febrile illness characterized by mucosal inflammation, skin rash, and cervical lymphadenopathy, with potential for cardiac sequelae, including coronary aneurysms with subsequent thrombosis, infarction, and death. Pregnancy in affected women presents multiple maternal risks.

CASE: A woman with Kawasaki disease complicated by coronary aneurysms underwent two consecutive pregnancies without further difficulty. She was maintained on therapeutic enoxaparin, alpha-methyldopa, and labetalol, with labor induction, passive second stage, and continued anticoagulation for 6 weeks postpartum. During gestations she was assessed with echocardiography, electrocardiography, and cardiac event monitor and managed by a maternal-fetal medicine and cardiology team.

CONCLUSION: Kawasaki disease with coronary aneurysms presents challenges for obstetric management; obstetricians should be familiar with the disease, implications, and management in pregnancy.

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Kawasaki disease, an early childhood illness, is characterized by febrile mucocutaneous inflammation, skin rash, cervical lymphadenopathy, and potential for cardiac involvement, with 1% to 2% mortality from cardiac failure.¹ Late cardiac manifestations include coronary artery aneurysm formation with subsequent thrombosis, infarct, arrhythmia, and valvulopathy.^{1,2} Very few cases are reported in association with pregnancy or the postpartum period^{3–6}; we report here the case of a woman with childhood Kawasaki disease complicated by cardiac sequelae who was able to achieve two successful pregnancies.

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CASE

A woman with a history of Kawasaki disease starting at the age of 9 years presented at 12 weeks gestation and was referred to a tertiary center for maternal-fetal medicine consultation. She remained asymptomatic after her acute illness, pursuing an active lifestyle, until age 22 when she experienced atypical chest pain. She underwent coronary angiography revealing a 6-mm aneurysmal dilatation at the origin of the left anterior descending and left circumflex coronary arteries (Fig. 1), sequelae of the Kawasaki disease, and she was begun on daily aspirin (81 mg/d) and managed with periodic echocardiograms. She planned her initial pregnancy 3 years later, although without pre-pregnancy consultation from her cardiologist or obstetrician.

Initial evaluation included echocardiogram and verification of 6-mm coronary aneurysms. Because of increased risk of thrombosis of the aneurysms, full anticoagulation with enoxaparin (80 mg subcutaneously every 12 hours) and meticulous control of blood pressure and heart rate with alpha-methyldopa 250 mg twice daily was begun, with goals of maintaining systolic pressures less than 130 mm Hg and diastolic pressures less than 80 mm Hg. Interval echocardiograms, showing normal cardiac function, anti-factor Xa levels to assure therapeutic enoxaparin, and fetal growth and well-being assessments were performed. At 35 weeks of gestation, worsening blood pressures with proteinuria and edema developed, and preeclampsia was diagnosed. Magnesium sulfate was begun, enoxaparin discontinued, and intravenous heparin initiated; cervical ripening

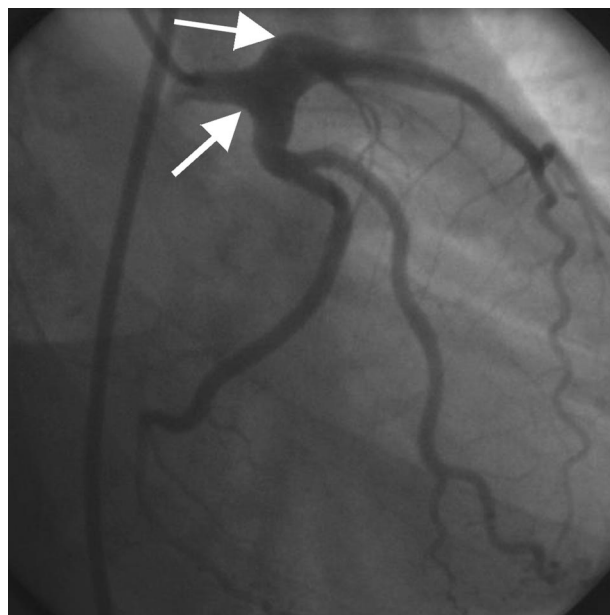


Fig. 1. Coronary angiography demonstrating aneurysmal dilatation at the origin of left anterior descending (top arrow) and left circumflex arteries (bottom arrow).

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with a prostaglandin agent and induction of labor with oxytocin was performed. An epidural for pain control was administered after discontinuation of heparin 4 hours previously. The second stage of labor was shortened with outlet forceps delivery of a healthy female infant. The preeclampsia resolved, and the patient was maintained on full anticoagulation with enoxaparin for 6 weeks postpartum; antihypertensives were not required, and thereafter daily aspirin was reinitiated. The patient presented again 6 months later with complaints of chest pain and shortness of breath, underwent repeat coronary angiography, but no change in coronary anatomy was noted.

Three years later she presented with her second planned gestation, and the same medical regimen was initiated. At 30 weeks of gestation she complained of shortness of breath with exertion, orthopnea, and dizziness, but electrocardiogram and echocardiogram remained normal. She wore a cardiac event monitor for 1 month without documented arrhythmia. At 35 weeks, blood pressures increased and labetalol was added to her antihypertensive regimen. Brain natriuretic peptide was normal, electrocardiogram and echocardiogram unchanged, and thereafter blood pressure remained well controlled. At 37 3/7 weeks of gestation her labor was induced with oxytocin after discontinuation of enoxaparin; epidural was administered, and the second stage of labor was shortened with outlet vacuum delivery of a healthy male infant. Enoxaparin was continued for 6 weeks postpartum, after which daily low-dose aspirin was again initiated; antihypertensives were not required. Seven months later she experienced chest pain and shortness of breath; coronary angiography revealed no change in status, and she was asymptomatic thereafter.

COMMENT

Although the cause of Kawasaki disease is unclear, clinical and epidemiologic features suggest an infectious cause in genetically predisposed individuals, but no organism has been identified.⁷ The acute febrile phase of Kawasaki, 1 to 2 weeks in duration, includes fever for at least a 5-day period, conjunctivitis, mucosal inflammation, cutaneous erythema, and lymphadenopathy. This is followed by 2–4 weeks of subacute illness with thrombocytosis, arthritis, and desquamation of the hands and feet, but resolution of fever, rash, and lymphadenopathy, and presents the greatest risk for coronary arteritis and thrombosis. Resolution of all clinical signs occurs 6–10 weeks later.⁷ Coronary arteritis, leads to aneurysm formation in 20% to 25% of untreated patients. Aspirin is used acutely at high doses for its anti-inflammatory action in conjunction with intravenous immune globulin in the initial phases of the illness, although therapy may not actually lower the incidence of coronary anomalies.⁸ Although one half of the coronary aneurysms regress over time, those that persist and enlarge may be

associated with coronary artery stenosis, thrombosis, dissection, and rupture, as well as early onset atherosclerosis, angina, acute myocardial infarction, and sudden death.² Rarely valvulopathy occurs. Giant aneurysms, more than 8 mm in diameter, present the greatest risk of progressive coronary disease, and full anticoagulation is recommended, whereas smaller aneurysms are treated with low-dose aspirin for its anti-thrombotic effect; additional therapy depends upon the extent of coronary involvement.^{7,8} Coronary artery bypass surgery, percutaneous coronary intervention, mitral valve replacement, and cardiac transplant have been used to treat cardiovascular sequelae.

Kawasaki disease complicating pregnancy has been reported rarely^{3–6}; those with persistent coronary involvement are at greatest risk during pregnancy, due to hypercoagulability and risk for acute coronary thrombosis and myocardial infarction. Therapeutic anticoagulation is recommended throughout pregnancy and for 6 weeks postpartum. Aneurysm enlargement and dissection, especially in those with uncontrolled hypertension, demands strict control of blood pressure and heart rate, typically with alpha-methyldopa or β -blockade. Serial echocardiogram or magnetic resonance imaging may be safely performed in gestation to further assess size or progression of aneurysms. Angiography, with increased risks of radiation exposure to the fetus, is reserved for gravidas with acute severe symptoms and suspicion of acute coronary syndrome or infarction. Calcium or β blockade and nitrates can be added as anti-ischemic therapy in symptomatic patients (labetalol was used in our patient) in addition to standard antihypertensive agents such as alpha-methyldopa or hydralazine. Statin and ACE inhibitor therapy are contraindicated in pregnancy.

Further, obstetric supervision should include frequent prenatal visits to monitor maternal blood pressure, heart rate, and therapeutic levels of enoxaparin and keen observation for signs of preeclampsia. Serial ultrasonography for fetal growth is suggested, especially in the setting of β blocker therapy. Induction of labor, discontinuation of enoxaparin, and administration of an early epidural for pain relief to maintain stable hemodynamics is recommended. Shortening of the second stage of labor is recommended to decrease cardiac load, blood pressure, and heart rate to lessen the risks of aneurysm enlargement or dissection. Cesarean delivery should be reserved for obstetric indications only. Endocarditis prophylaxis is not warranted at the time of delivery in the absence of significant associated valvular pathology. Enoxaparin should be reinitiated 6–12 hours after delivery, and maintained for 6 weeks or until anticoagulation with warfarin is achieved for this time



period. Breastfeeding is safe and encouraged, and contraception with medroxyprogesterone acetate (depot medroxyprogesterone acetate) or barrier methods is preferred, avoiding estrogen-containing agents with thrombogenic propensity.

Kawasaki disease with coronary aneurysms presents challenges for obstetric management; obstetricians should be familiar with the disease, implications and management in pregnancy. Kawasaki's with cardiac involvement is best managed by an maternal-fetal medicine and cardiology team, ideally with evaluation and workup before conception and throughout gestation.

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A 14-Week Abdominal Pregnancy After Total Abdominal Hysterectomy

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BACKGROUND: Pregnancy after hysterectomy is rare. Because this clinical phenomenon is so uncommon, the diagnosis is not always considered in the evaluation of pain in a reproductive-aged woman after hysterectomy. Delay in diagnosis can result in potentially catastrophic intra-abdominal bleeding.

CASE: A 31-year-old multigravida underwent a total abdominal hysterectomy for menometrorrhagia. She experienced several weeks of postoperative abdominal pain and ultimately was diagnosed with a 14-week size intra-abdominal pregnancy. Surgical evacuation of the fetus and products of conception were complicated by significant intra- operative bleeding.

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CONCLUSION: In reproductive-aged women undergoing hysterectomy, it is vital to obtain preoperative urine hCG levels immediately before surgery and to consider ectopic pregnancy in the differential diagnosis of these women when severe or persistent abdominal pain occurs postoperatively.

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Since the first case of posthysterectomy pregnancy was reported in 1895, only 35 additional cases have been described in the literature.¹ The majority of cases occur as a result of pre-existing pregnancies at the time of surgery. Women with abdominal pregnancies after hysterectomy will most commonly present with severe pain as a result of peritoneal irritation from intra-abdominal bleeding. Because the diagnosis of pregnancy is not usually entertained in these women, a delay in diagnosis will occur in most cases and can lead to life-threatening consequences.

CASE

A 31-year-old woman, gravida 10, para 8, ectopic 2, underwent total abdominal hysterectomy at a community hospital for menometrorrhagia. A urine hCG test performed 2 days before her scheduled surgery had negative results, but for unclear reasons, the patient's surgery was postponed for several days. The patient reported her last menstrual period as occurring 6 days before her actual surgery date, and a pregnancy test was not repeated on the day of her procedure.

Intraoperatively, the patient was noted to have a 10-



week size uterus, dense adhesions at the uterine fundus and right adnexal regions, but otherwise, she had normal-appearing pelvic structures. The hysterectomy was performed without noted complications, with a final uterine pathology of simple hyperplasia without atypia.

Although the estimated blood loss of surgery was 200 mL, postoperatively the patient's hemoglobin dropped 4 g/dL, and she was transfused with four units of packed red blood cells. She was discharged from the hospital in stable condition on postoperative day three.

Nine weeks after surgery, the patient presented to her local community with a chief complaint of several days of lower abdominal pain that had suddenly worsened. A computed tomography (CT) of the abdomen and pelvis revealed a "5-cm cystic fluid collection probably representing a hematoma" (Fig. 1). The patient was admitted overnight for pain management and discharged the next morning. Three weeks later, she presented to the same emergency department with severe abdominal pain. A repeat CT of the abdomen and pelvis demonstrated a 7×8-cm cystic structure within the pelvis containing fetal parts (Fig. 2). Scattered soft tissue densities were also seen within the pelvis, likely representing placental tissue. The patient was taken immediately to the operating room for exploratory laparotomy. A 2-liter hemoperitoneum surrounding a free-floating, 14-week size fetus was encountered upon entering the abdominal cavity. The fetus and blood were evacuated without difficulty; the placenta, however, was attached to the right adnexa, sigmoid colon, and mesentery. Most of the placenta was removed, but due to concern for further hemorrhage, small, placental fragments were left undisturbed in the peritoneal cavity. Pathologic analysis of the fetus revealed it to be an intact, normal-appearing female fetus at approximately 14 week of gestational age with a second-trimester placenta. The patient required five units of packed red blood cells for severe anemia and was



Fig. 1. Computed tomography of pelvis: 9 weeks post-hysterectomy with 11-week intra-abdominal pregnancy. Nickles Fader. *Abdominal Pregnancy After Hysterectomy*. *Obstet Gynecol* 2007.



Fig. 2. Computed tomography of pelvis: 12 weeks post-hysterectomy with 14-week intra-abdominal pregnancy.

Nickles Fader. *Abdominal Pregnancy After Hysterectomy*. *Obstet Gynecol* 2007.

discharged in stable condition on postoperative day three. Four days later, she presented once again to the same institution reporting severe abdominal pain. A CT scan of the abdomen and pelvis demonstrated "a multiloculated pelvic collection, most likely representing an abscess." The patient was transferred to our institution at that time for further management.

Upon presentation, the patient was afebrile and hemodynamically stable. Abdominal examination revealed diffuse tenderness with voluntary guarding but no rebound tenderness. A pelvic examination was limited due to the patient's discomfort. Laboratory values on admission included a white blood cell count of 7,300 (normal differential), hemoglobin of 11.2 g/dL, and a quantitative β -hCG of 1391 milli-International Units/mL. Given the preliminary reading of pelvic abscess from the outside institution, the patient was initiated on ampicillin, gentamycin, and clindamycin. During the patient's 5-day hospitalization, her pain gradually improved, she remained afebrile, and her hemoglobin remained stable.

While she was hospitalized at our institution, the patient's quantitative β -hCG levels declined from 1,391 to 511 milli-International Units/mL. Methotrexate therapy was withheld given the decreasing trend in her laboratory values suggesting spontaneous resorption of the retained placental fragments. The patient was discharged on hospital day five and instructed to follow up at our institution for serial monitoring of quantitative β -hCG levels. Twenty days after discharge, her β -hCG was 40 milli-International Units/mL, and 4 months later, it had fallen to below 10 milli-International Units/mL.

COMMENT

The etiology of ectopic pregnancy after hysterectomy can be classified as either pre-existing or late occurring.



Of all such reported pregnancies, most were discovered within weeks to months of the hysterectomy and were theorized to be pre-existing at the time of surgery.¹ In other words, the conceptus was present either as an implanted, unrecognized tubal pregnancy or as a fertilized egg in transit in the fallopian tube at the time of hysterectomy. There are, however, eight reports of fertilization occurring up to twelve years after a total hysterectomy, most commonly after vaginal hysterectomy.² In these late-occurring pregnancies, it was not unusual to discover a fistulous channel through the vaginal cuff as often diagnosed by fistulography.³

Once discovered, the majority of these ectopic pregnancies are terminated surgically. There is only one reported case of a post-hysterectomy abdominal pregnancy that was carried successfully to term,⁴ but this is not recommended due to the risk of life-threatening maternal hemorrhage with progression of the pregnancy.

This case of a woman with post-hysterectomy abdominal pregnancy is representative of a pre-existing pregnancy. The patient later admitted to unprotected intercourse in the weeks before her hysterectomy. In most cases, obtaining a urine hCG in a reproductive-aged woman before her surgery is helpful. It may or may not have been useful in this case, however, as the patient was approximately 2 weeks pregnant at the time of her surgery, making detection of a pregnancy by most commercial urine hCG tests difficult.

Other than obtaining preoperative pregnancy tests on all appropriate patients, the best way to prevent post-hysterectomy pregnancy is to emphasize to our patients the importance of practicing reliable contraception before surgery. For patients reporting unprotected intercourse and with a negative urine pregnancy test before surgery, it is unknown whether routine preoperative testing with a quantitative β -hCG would reduce the likelihood of post-hysterectomy pregnancy. Theoretically, utilizing this more sensitive test could help rule out pregnancy too early to be detected by urine hCG. Furthermore, meticulous attention to proper operative technique to prevent complications at the surgical site, such as pelvic hematomas and surgical site infections (eg, vaginal cuff cellulitis and abscess), may be important to reduce postoperative cuff fistula formation and subsequent post-hysterectomy ectopic pregnancy.

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Fetal Leukemia With Umbilical Artery Embolism and Circulatory Failure

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BACKGROUND: This is a case report of fetal leukemia associated with hydramnios.

CASE: When the hydramnios was treated with amnioreduction, near-term bradycardia was recorded ultrasono-

graphically, resulting in immediate cesarean delivery. At birth, neonatal leukemia was diagnosed and there was no evidence of chromosomal abnormalities. The infant died of pulmonary hemorrhage. Autopsy showed umbilical venous embolization with tumor cells, and there was arterial invasion of the vessel wall by tumor.

CONCLUSION: Fetal leukemia is extremely rare, and its prenatal diagnosis is difficult. In cases of hepatomegaly, fetal leukemia should be considered in the differential diagnosis.

(*Obstet Gynecol* 2007;109:521–3)

The incidence of acute myeloid leukemia in infants aged less than 1 year is estimated at 10.6 per million per year.¹ Transient leukemia, a benign form of leukemia, occurs frequently in newborn infants with Down syndrome, and this disease disappears spontaneously in most cases. Epidemiologic and molecular genetic investigations report that chromosomal translocations of *MLL* (myeloid/lymphoid, or mixed lineage, leukemia) genes occur at late gesta-

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tional ages in some infant leukemias.² We report a euploid case of fetal leukemia with *MLL* translocation in which sudden circulatory failure occurred before birth due to leukemic cell thrombosis of the umbilical artery after amnioreduction for hydramnios and prenatal chromosomal diagnosis.

CASE

A 36-year-old woman, multipara, was referred to our hospital at 36 weeks of gestation with hydramnios and hepatomegaly. Her abdominal circumference had been increasing rapidly from the 34th week of gestation, and she complained of coughing and dyspnea. Ultrasonographic findings indicated an amniotic fluid index of 25.5 cm and fetal hepatomegaly.

Amnioreduction was performed to relieve the abdominal distension before fetal magnetic resonance imaging was attempted. Immediately after the amnioreduction, a nonstress test showed a reassuring fetal heart rate of approximately 130 beats per minute, but 1 hour later the fetal heartbeat was suddenly lost. Doppler ultrasonography recorded a fetal heart rate of 79 beats per minute and diastolic flow disruption, indicating exacerbation of the fetal bradycardia. An emergency cesarean delivery was therefore performed. No major anomalies were identified, but the female infant exhibited systemic stiffness, with many nodules measuring approximately 20 mm in diameter and petechiae observed over the entire body surface (Fig. 1). The infant was intubated immediately after delivery. Her Apgar score was 0 at both 1 and 5 minutes, and her heart started beating after 8 minutes. Blood examination showed a white blood cell count of $92.6 \times 10^6/\text{mL}$, hemoglobin count of 2.5 g/dL, and platelet count of $225 \times 10^6/\text{mL}$. Prothrombin time and activated partial throm-

boplastin time were longer than 180 seconds. The infant died at 4 hours and 22 minutes after delivery due to lung hemorrhage; an autopsy was performed with consent.

Monocytic leukemia (M5) was diagnosed based on the morphology and the state of differentiation of leukocytes in the peripheral blood (Fig. 2). No cytomegalovirus, chromosomal aberration, or chimeric gene was detected. However, rearrangements of the *MLL* gene were found, implying that the rearrangements occurred in utero. Specific staining of cell surface markers produced negative staining for CD2 and CD19 and positive staining for CD13, CD14, CD33, and CD68, indicating myelogenous leukemia.

Although the autopsy showed no major anomalies, subcutaneous nodes were found over the entire body, and hepatomegaly was extensive, with yellowish-greenish masses observed macroscopically on the heart and chest wall, in the bowel, and in the left ureter. Swollen mesenteric lymph nodes were also found. Pleural effusion was observed, and petechiae were found in the pleura, diaphragm, peritoneal, and alimentary canal mucosa.

The heart and most parts of the liver were occupied by leukemic cells. The leukemic cell invasion of the wall of the umbilical artery near the placenta and vasoconstriction of the umbilical cord caused by a tumor cell embolism in the umbilical vein (Fig. 3) seem to have contributed to abnormal circulation and enhancement of the accelerator and fibrinolysis system. Inhibition of gas exchange by pneumorrhagia and deep infiltration of the lung stroma by leukemic cells seem to have been the direct causes of death. Stenosis of the umbilical artery by tumor invasion and tumor embolism of the umbilical vein may also have induced sudden death.



Fig. 1. "Blueberry muffin-like baby." There were numerous purple nodules (color not shown), approximately 20 mm in diameter, occupied by leukemic cells. Petechiae were observed over the entire body surface.

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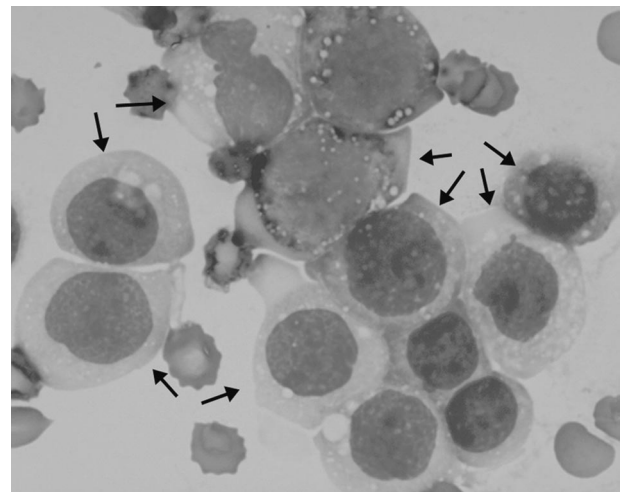


Fig. 2. Blood smear, May-Grunwald-Giemsa stain. Acute monocytic leukemia, poorly differentiated (FAB AML-M5a). Monocytes (arrows) in the peripheral blood are large, approximately 12 to 20 μm in total diameter. The nucleus is round to oval with reticular chromatin ($\times 1000$, original magnification).

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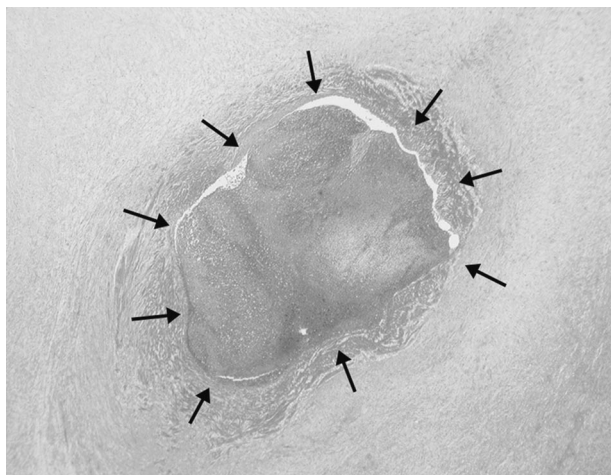


Fig. 3. Hematoxylin and eosin stain. Arrows show leukemia cells in the umbilical vessels ($\times 100$, original magnification).

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COMMENT

Fetal leukemia has been reported to occur as a complication in cases of Trisomy 21, Turner Syndrome, or Chromosome 7p Deletion. In the present case, however, there was no evidence of chromosomal abnormalities.

Translocations of the *MLL* gene at the chromosome band 11q23 are the most common cytogenetic alterations in de novo leukemia in infants. Although *MLL* translocations are pathogenetically important, additional mutational events may be required for complete leukemogenesis.^{3,4} In the present case, therefore, both *MLL* translocation and additional cooperative somatic mutations may have occurred at an early gestation age. Although the fetal leukemia was

advanced, no neoplastic cells were observed in the mother's blood, indicating that the fetal leukemia did not affect the mother.

Experimental research has shown that acute umbilical-placental embolization results in increased placental vascular resistance and reduction of umbilical blood flow⁵; neoplastic embolism could have caused diastolic flow disruption and bradycardia in the present case. Embolism and infarctions may have occurred after amnioreduction.

Fetal leukemia is a rare disease; clinical prenatal diagnosis is difficult, and there is no established treatment. In hepatosplenomegaly cases, the possibility of leukemia could be investigated early using cordocentesis, currently the only diagnostic procedure available for identifying fetal hematologic abnormalities. With early diagnosis the leukemia could be monitored, improving knowledge of and response to the disease.

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