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Case report

Incidental leiomyosarcoma found at the time of cesarean hysterectomy for morbidly adherent placenta

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ABSTRACT

Background: Incidental leiomyosarcoma (LMS) is a rare diagnosis in pregnancy or in the puerperium. To our knowledge, this is the first case reported in the literature of incidental LMS after cesarean hysterectomy for morbidly adherent placenta.

Case: We present a case of a cesarean hysterectomy performed for a suspected morbidly adherent placenta in a patient with three prior cesarean deliveries, an anterior placenta previa and a fundal fibroid. Subsequent pathology identified a LMS on final specimen. The patient declined bilateral oophorectomy and removal of her remaining cervix. No chemotherapy or radiation was given for her presumed stage IB disease.

Conclusion: An incidental finding of a LMS is infrequent; the risk of recurrence is > 50% even if the sarcoma is removed in its entirety.

1. Introduction

A cancer diagnosis in pregnancy is rare with an incidence of 1 in 1000; breast and cervical cancers are most common (Matsuo et al., 2009). The incidence of uterine sarcomas in pregnancy is not known, though a systematic review of 40 cases of gynecologic sarcomas showed that the majority (37.5%) were of uterine origin (Matsuo et al., 2009). Of all uterine cancers, uterine sarcomas account for 3–7%, with leiomyosarcomas (LMS) accounting for 25–30% (Park et al., 2011; Lissoni et al., 1998; Gojnic et al., 2005). LMS tumors are usually highly malignant neoplasms with an overall poor prognosis (Park et al., 2011). The diagnosis of a uterine LMS in pregnancy is rare, with only 11 reported cases in the English literature.

Although rapid growth of leiomyomas is not unusual during pregnancy, it may be important to consider the rare possibility of an occult uterine sarcoma when this occurs (Matsuo et al., 2009). Risk factors for LMS are similar to other endometrial cancers and include obesity, hypertension, diabetes, and long-term hormonal therapy. The average age at diagnosis is between 40 and 50 years of age (Gojnic et al., 2005). Presentation of LMS can sometimes include irregular menstrual bleeding and pelvic and abdominal pain.

We present a case of a LMS incidentally diagnosed after cesarean hysterectomy, which was performed for a suspected morbidly adherent placenta in a woman with a placenta previa. Additionally, we have reviewed the literature on peripartum diagnosis of LMS during pregnancy and examined the diagnosis and management.

2. Case

A 33 year old Gravida 5 Para 2113 with complete anterior placenta previa and suspected morbidly adherent placenta was referred at 24 weeks to our Maternal Fetal Medicine (MFM) service. Her antenatal course was complicated by obesity with a body mass index of 36 kg/m^2, a 9.4 cm fibroid, a fetus with single umbilical artery, a history of three prior cesarean deliveries, and one prior preterm birth due to premature rupture of membranes at 35 weeks. Ultrasound confirmed the diagnosis of a complete anterior placenta previa with suspected morbidly adherent placenta. The ultrasound showed the anterior placenta previa merging with the anterior cervical stroma, with shared circulation. The posterior wall of the bladder had an irregular mucosal surface with

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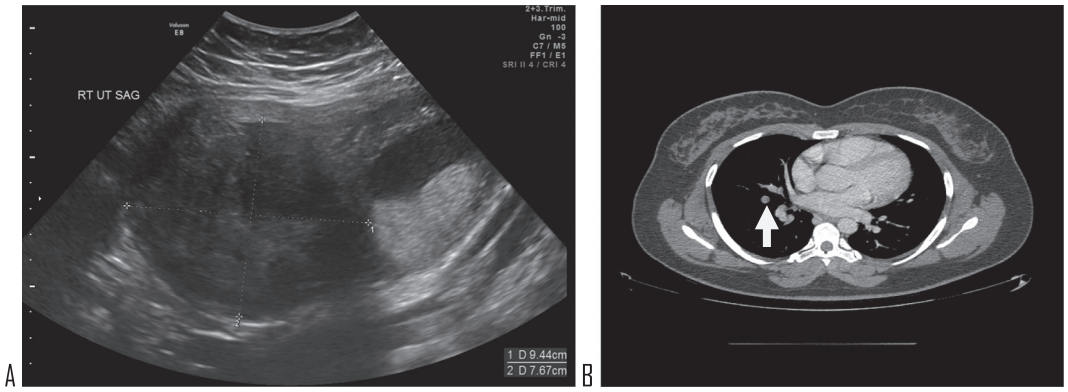

Fig. 1. A. Ultrasound image uterine fibroid at 24 weeks gestational age. B. CT chest at 13 months after cesarean hysterectomy (arrow points to pulmonary nodule).

increased vascularity. A posterior right 9.4 cm fibroid was also visualized (Fig. 1). A cesarean hysterectomy was planned for 34 weeks (Silver et al., 2015).

At 31 weeks 6 days, she presented to the office with severe range blood pressures and an unresolving headache. She was admitted to the hospital for suspected preeclampsia with severe features. The decision was made to proceed with immediate delivery.

As recommended in the literature and per our departmental protocol for treatment of a suspected morbidly adherent placenta, the multidisciplinary team included MFM providers, gynecologic oncologists, urologists, interventional radiologists (IR), neonatologists, cell saver and blood bank staff (Silver et al., 2015). A cesarean hysterectomy and bilateral salpingectomy were planned. A supracervical hysterectomy and bilateral salpingectomy was ultimately performed, as the placenta previa did not involve her cervix. During the surgery, the posterior, right fibroid was noted and appeared unremarkable. Estimated blood loss was 2 l. She was discharged home on postoperative day 7 after resolution of a postoperative ileus.

Final pathology described a 13 cm LMS with unremarkable fallopian tubes and a placenta accreta in the intact hysterectomy specimen (Fig. 2). The specimen showed tumor necrosis, lymphovascular invasion, cytologic atypia, and increased mitotic index > 23/10 high powered field. In light of this unusual finding, the slides were reviewed and confirmed at an outside hospital. Immunohistochemistry stains were positive for smooth muscle actin and negative for CD10.

At the patient's 3 week follow-up visit, both mother and baby were doing well. The patient underwent a CT of her chest, abdomen, and pelvis, which showed no local or distant metastatic disease. Further treatment, including oophorectomy and removal of her remaining cervix versus observation, was reviewed with the patient and she preferred preservation of her ovaries and no surgical resection of her remaining cervix. A surveillance CT of her chest, abdomen, and pelvis, 13 months after surgery, showed no pelvic or abdominal disease, but five new bilateral pulmonary nodules, the largest of which was 1.2 cm (Fig. 3). A video-assisted thoracoscopy with lung wedge biopsy confirmed metastatic LMS 16 months after surgery. The patient is in

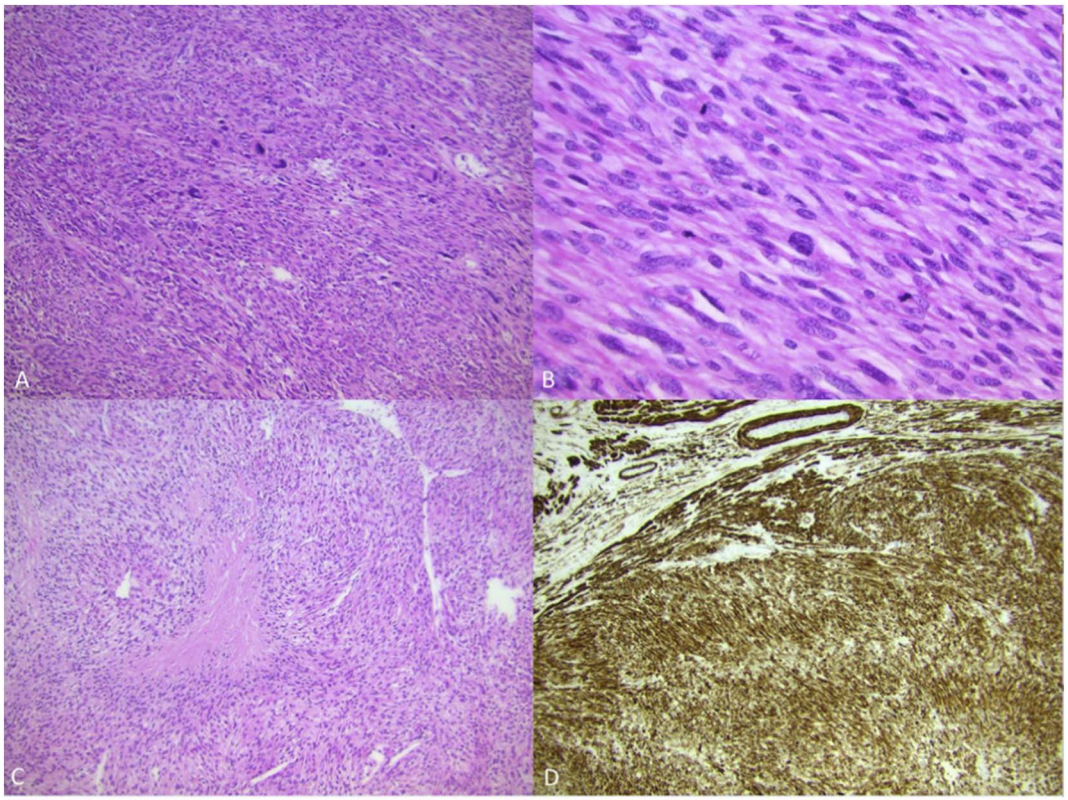

Fig. 2. A. Nuclear atypia, 100 × H & E, B. Increased mitotic activity, 400 × H & E, C. Tumor necrosis, 100 × H & E, D. Immunohistochemical stain for smooth muscle actin 100 ×, H & E.

Table 1
Pregnancy Outcomes in cases of leiomyosarcoma.

Article	Case #	Year	Country	Time of diagnosis	GA at delivery (weeks)	Mode of delivery	Live birth	BW (grams)	Adjuvant treatments	Ovarian preservation	Follow up (months)	Comments
Hand et al.	1	2015	United States	Postpartum	31	Cesarean hysterectomy	Y	1454	N	Y	16	Concurrent bilateral salpingectomy.
Bodner-Adler et al. (2008a, b)	2	2008	Austria	At delivery	34	CD, myomectomy	Y	2917	Y	N	19	Followed by TAH/BSO/omentectomy/ para-aortal lymph node dissection. 6 cycles of epirubicin and ifosfamide for concurrent meningioma.
Gojnic et al. (2005)	3	2005	Serbia	Postpartum	38	SVD	Y	3100/3000	-	Y	-	Twin pregnancy.
	4			Postpartum	-	CD	Y	-	-	Y	-	All patients underwent hysterectomy, omentectomy, and removal of lymph nodes.
	5			Postpartum	-	CD	Y	-	-	Y	-	
	6			Postpartum	-	CD	Y	-	-	Y	-	
	7			Postpartum	-	CD	Y	-	-	Y	-	
Lau and Wong (1994)	8	1993	Hong Kong	At delivery	25	SVD	N	-	N	N	18	Followed by TAH/BSO/pelvic lymph node dissection.
	9			Postpartum	35	CD	Y	2420	N	Y	1.5	Followed by subtotal hysterectomy.
Younis et al. (1990)	10	1990	Israel	At delivery	33	CD, myomectomy	Y	1690	–	Y	36	No further operation.
Kyodo et al. (1989)	11	1989	Japan	At delivery	37	CD, myomectomy	Y	2640	Y	Y	3	TAH two weeks postpartum. Picibanil for one month.
King et al. (1980)	12	1979	United States	At delivery	–	–	N	–	–	N	–	At pregnancy termination in 1st trimester. Followed by TAH/BSO.

Abbreviations: Y-yes, N-no, CD-cesarean delivery, TAH-total abdominal hysterectomy, BSO-bilateral oophorectomy, SVD-spontaneous vaginal delivery. Blank cells indicate information was not published.

the process of receiving chemotherapy with gemcitabine and docetaxel. The patient provided written consent to publish this case.

3. Discussion

With the rising number of cesarean deliveries in the United States, an increased number of cases of morbidly adherent placenta are being identified. Concurrently, there is an increased awareness of occult LMS secondary to morcellation and thus, increased concern regarding dissemination and upstaging of disease (Lissoni et al., 1998). The incidence of post-operatively diagnosed sarcomas (LMS and endometrial stromal sarcoma) has been estimated to be between 1:350 to 1.4:500 in patients undergoing hysterectomies or myomectomies (Park et al., 2011; Lissoni et al., 1998; Food and Drug Administration, 2014; Kamikabeya et al., 2010). The largest single institution series showed the incidence of sarcomas to be 20:4785 patients (Cui and Wright, 2016).

A LMS diagnosis in pregnancy is unusual. In our review of the English literature, there have been 12 reported uterine leiomyosarcomas in pregnancy, including this case (Table 1) (Matsuo et al., 2009; Lau and Wong, 1994). Our case is the first to be diagnosed after cesarean hysterectomy.

In both gravid and nongravid patients, symptoms of a LMS are generally nonspecific and include abdominal pain, irregular menstrual bleeding, and increased uterine size (Matsuo et al., 2009). It should be noted that even though a rapidly growing uterus may anecdotally raise concerns about a uterine sarcoma, the actual incidence of uterine sarcoma found after hysterectomy performed for this reason is rare at 0.27% (Parker et al., 1994). Pregnancy complicates this presentation given that a quarter of fibroids will routinely enlarge in pregnancy (Matsuo et al., 2009). Although cancer diagnosis in pregnancy is uncommon, it may become increasingly important to be aware of this possibility in order to better counsel patients who have a known fibroid uterus that require a hysterectomy at the time of delivery. Evaluation with physical exam, ultrasound, and possibly surgical intervention may be warranted if suspicious symptoms are present (Matsuo et al., 2009). Since surgery is not always an option early in pregnancy, close observation may be necessary. In our case, the patient's care was transferred to our institution in the second trimester so it was difficult to notice an increase in the size of the fibroid. Additionally, the placenta previa complicated matters, as this was the assumed reason for her intermittent vaginal bleeding.

The most effective curative treatment for a LMS is surgical excision including hysterectomy, with or without bilateral salpingo-oophorectomy, tumor debulking and removal of enlarged lymph nodes (Roque et al., 2016). Preservation of the ovaries is a reasonable management strategy in premenopausal women with early stage, low grade disease, as a significant difference in disease free survival or overall survival has not be seen in non-gravid patients (Park et al., 2011). Neither radiation nor adjuvant chemotherapy are supported as a standard treatment for patients with early stage disease (Roque et al., 2016). Despite uterine limited disease that is kept intact during removal, there is still > 50% chance of recurrence (Hyman et al., 2014). Agents for disseminated disease include gemcitabine and docetaxel, although a first line agent has not been established (Hyman et al., 2014).

It is unclear if pregnancy influences the progression of aLMS. The majority of patients we reviewed in Table 1 had early stage disease at the time of diagnosis. None had metastasis or had died of their disease at time of publication. Matsuo et al. looked at genital sarcomas during pregnancy and given that the majority of the infants were male, they postulated that the Y chromosome could promote cell growth. This data was insufficient to draw any conclusions (Matsuo et al., 2009). When reviewing all cancers in pregnancy, outcomes are similar in pregnant and non-pregnant patients when compared at different stages. There has been no data showing that the prognoses of cancers change with a pregnancy (Moran et al., 2007).

This case report highlights the potential importance of talking with patients about the risks of occult malignancy, especially when performing a hysterectomy on a uterus that contains fibroids. Prior to Physicians may additionally want to include a discussion of this rare situation during preoperative counseling prior to any cesarean hysterectomy for morbidly adherent placenta in patients with a presumed fibroid uterus. There is not enough data to state if intraoperative pathologic assessment should be a component of benign hysterectomies as the incidence of occult LMS is still rare. If LMS is diagnosed, surgical management should include the removal of the uterus, cervix, tubes, and possibly ovaries depending on patient factors and after appropriate counseling.

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