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Low grade endometrial stromal sarcoma in pregnancy: A case in support of safe abortion access

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ABSTRACT

Background: Endometrial stromal sarcoma (ESS) is extremely rare in pregnancy. It shares clinical and imaging features with more common pregnancy findings such as leiomyoma and molar gestations, which makes diagnosis challenging.
Case: A 36-year-old patient presented at 8 weeks and 1 day gestation for vaginal bleeding. An intrauterine pregnancy with an appropriately sized embryo with heart motion and a 9.5 cm complex uterine mass was found on ultrasound. MRI showed an 11.4 cm cystic mass with nodular septations causing mass effect on the endometrial cavity. After extensive counseling, the patient underwent a gravid abdominal hysterectomy and bilateral salpingectomy. Final pathology showed low grade ESS.
Conclusion: This case highlights the importance of evaluating suspicious uterine masses in pregnancy and the necessity for safe abortion access.

1. Introduction

Malignancy complicates about 1 in 1,000 deliveries, and most malignancies are not uterine in origin. (Smith et al., 2003 Oct) Endometrial stromal sarcoma (ESS) accounts for less than 1 % of all malignant uterine tumors making it an especially rare finding in pregnancy. (Santos and Cunha, 2015) LGESS is an indolent form of ESS. It often presents after age 40 with vaginal bleeding, pelvic pain, and dysmenorrhea but can also be asymptomatic. (D'Angelo and Prat, 2010) For disease confined to the uterus, treatment typically consists of hysterectomy with or without bilateral salpingo-oophorectomy. ESS tumors are sensitive to hormones; however, ovarian preservation can be considered an option for premenopausal women with early-stage disease. (D'Angelo and Prat, 2010) Of note, many patients are diagnosed after hysterectomy for a presumed benign condition. There are limited studies on adjuvant endocrine therapy, but most suggest reduced relapse rate when employed. (Deshmukh et al., 2019 May; Pink et al., 2006 Jun; Chu et al., 2003 Jul) ^{18}F-fluorodeoxyglucose PET and PET/CT have been shown to be accurate methods for detecting recurrence, but data is limited due to low incidence. (Sadeghi et al., 2013 Oct).

In this case, we discuss the uncommon finding of ESS diagnosed during the first trimester of pregnancy. ESS in pregnancy is a particularly challenging diagnosis to make as it shares clinical and imaging features with more common diagnoses such as leiomyoma and molar pregnancies. Furthermore, imaging can be suggestive of ESS but may not be diagnostic. Diagnosis requires pathologic evaluation. After extensive counseling the patient we present chose to terminate her pregnancy to diagnose and safely treat the undefined mass. This is an important case as it emphasizes the value of thorough evaluation of uterine masses in pregnancy and the necessity for patients to have access to safe abortions.

2. Case

A 36-year-old G3P2002 woman was referred to the gynecologic oncology service at 8 weeks and 1 day gestation for vaginal bleeding and ultrasound findings of a 9.5 cm complex uterine mass. Six days prior she had a "large gush" of blood with bleeding tapering off over the following three days. She then passed coffee-ground discharge followed by mild intermittent bleeding. Additionally, she had cramping earlier in pregnancy and her nausea was worse than in prior pregnancies. Her past

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medical history was uncomplicated. She had had two previous cesarean deliveries and no other surgical history. She had no history of abnormal pap smears with her most recent being two months prior to conception. She had never used oral contraceptive pills. She had no history of fibroids on prior ultrasounds. Her initial physical exam was unremarkable except for an enlarged, globular uterus palpable to approximately 16 weeks and a small amount of blood at the external cervical os. Her ß-hCG was within normal limits for gestational age.

Pelvic ultrasound showed an intrauterine pregnancy (IUP) with normal fetal heart activity and a crown rump length of 13.6 mm consistent with menstrual dating. There was a 9.5 cm diameter mass that appeared to be in the uterine body and to arise separately from the IUP. The mass contained multiple thick septations and internal solid components with significant vascularity as assessed by color Doppler. There were also hypoechogenic components that appeared fluid filled (Fig. 1). An MRI of the pelvis was performed to further assess the characteristics of the mass to rule out extrauterine metastasis. It showed an 11.4 cm cystic mass with nodular septations centered in the right aspect of the uterus causing a mass effect on the endometrial cavity. The mass appeared separate from the ovaries (Fig. 2).

Multiple providers discussed this case including the patient's primary obstetrician, and specialists in the fields of Gynecologic Oncology, Complex Family Planning, Maternal Fetal Medicine, and Radiology. Given the concerning features of the mass, it was agreed that a tissue sample was necessary for diagnosis. Due to the large size of the mass and its effect on the uterine cavity, the patient was informed that fetal growth and development would likely be compromised. Multiple options to obtain tissue diagnosis were reviewed with the patient including attempts to preserve future fertility. The care team offered an aspiration abortion procedure, but it was believed that the mass would not be sampled appropriately with this procedure. The team also counseled the patient on the high chance of bleeding given the vascularity of the mass, which might lead to an urgent hysterectomy. She was also offered the option of excising only the mass. However, given the size of the mass, this surgical option seemed unlikely to be successful. The care team again reviewed with the patient the additional risks of hemorrhage and the potential risk of cancer spread with conservative management. After extensive counseling, the patient opted for a gravid hysterectomy understanding that fertility would not be preserved, and the procedure would terminate the pregnancy. The patient was offered and declined a fertility consult.

At 9 weeks' gestation, the patient underwent a total abdominal hysterectomy and bilateral salpingectomy. Diagnostic laparoscopy was initially performed to confirm no signs of extrauterine disease. The case was then converted to an exploratory laparotomy via vertical midline incision. She underwent a gravid abdominal hysterectomy and bilateral salpingectomy. The uterus was noted to be enlarged and boggy on entry (Fig. 3). The case was completed without complication. She had an unremarkable postoperative course. Final pathology showed low grade endometrial stromal sarcoma (LGESS). There was no evidence of spread to the cervix or either fallopian tube. The patient was counseled regarding risks and benefits of undergoing a bilateral oophorectomy, hormonal therapy, and surveillance. She initially opted for surveillance.

She had a CT C/A/P performed at 2 months post-operatively and was found to have a 5 mm left lower lobe pulmonary nodule which was not amenable to biopsy but was suspicious for metastatic disease. The patient was counseled that observation was no longer recommended. Oophorectomy and hormonal therapy were again discussed. The patient opted for hormonal therapy of megestrol. At 6 months postop, she was found to have an additional right upper lobe pulmonary nodule that has recently increased in size at roughly 19 months postop. The left lower lobe nodule has remained stable in size. A PET/CT scan did not show abnormal ^{18}F-fluorodeoxyglucose (FDG) uptake in pulmonary nodules; the patient has chosen to remain on megestrol with serial CT chest imaging.

3. Discussion

ESS is a rare malignancy especially in pregnancy. It shares clinical symptoms and imaging features with some of the more common uterine masses found in pregnancy. For example, the patient's symptoms of bleeding, enlarged uterine mass, and nausea would fit the clinical picture of gestational trophoblastic neoplasia (GTN), specifically a partial mole. Partial moles often have a ß-hCG within normal gestational age limits. Hydropic placenta with multiple lacunae and presence of a fetus with cardiac activity may be seen on imaging. In the case presented here, GTN was deemed highly unlikely based on imaging findings. On ultrasound, it was clear that the multiseptated uterine mass did not communicate with the gestation directly (Fig. 1). MRI confirmed that this was a predominantly cystic mass centered in the myometrium displacing the gestational sac. Within the T2 bright cystic mass were multiple nodular septations (Fig. 2). The mass was not consistent with a molar pregnancy, which classically presents on MRI as a heterogeneous mass with smaller cystic spaces.

Leiomyomas are the most common pelvic mass in females; leiomyomas with cystic degenerative changes and/or high vascularity have been associated with pregnancy. On ultrasound, they can be mistaken for sarcomas as they often appear as a complex uterine mass with cystic lesions. LGESS is better characterized on MRI. It will often appear as a polypoid endometrial mass, typically with myometrial involvement and worm-like lymphatic and vascular invasion. (Santos and Cunha, 2015) Although atypical leiomyomas can be difficult to differentiate from ESS on MRI, Himoto *et al.* found that using a pre-defined MRI system has high sensitivity and specificity to differentiate LGESS from rare leiomyomas. (Himoto et al., 2021 Dec) Specifically, they found that intratumoral low signal intensity bands, cystic necrotic change, and

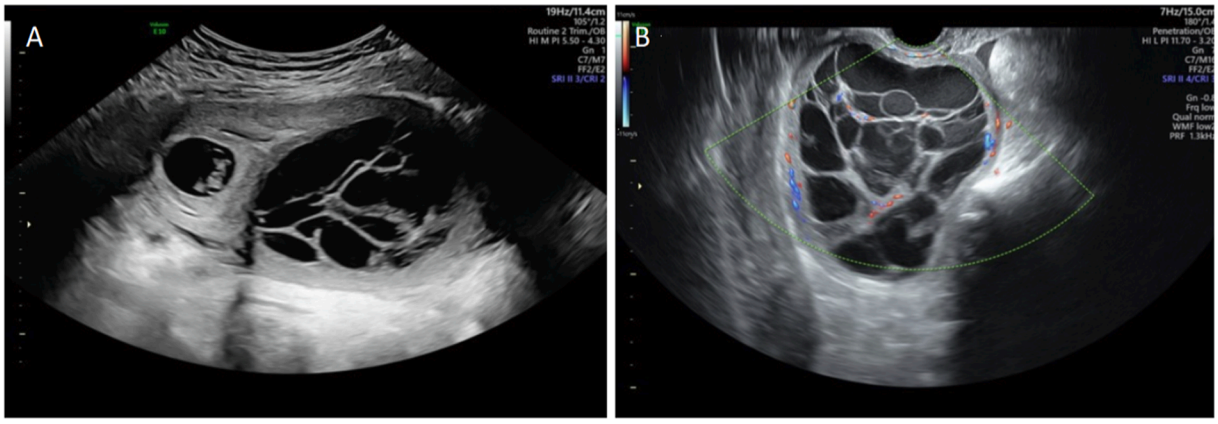

Fig. 1. Transvaginal ultrasound demonstrating an IUP within the uterine cavity and multiseptated mass (A) with thick septations and internal color flow (B).

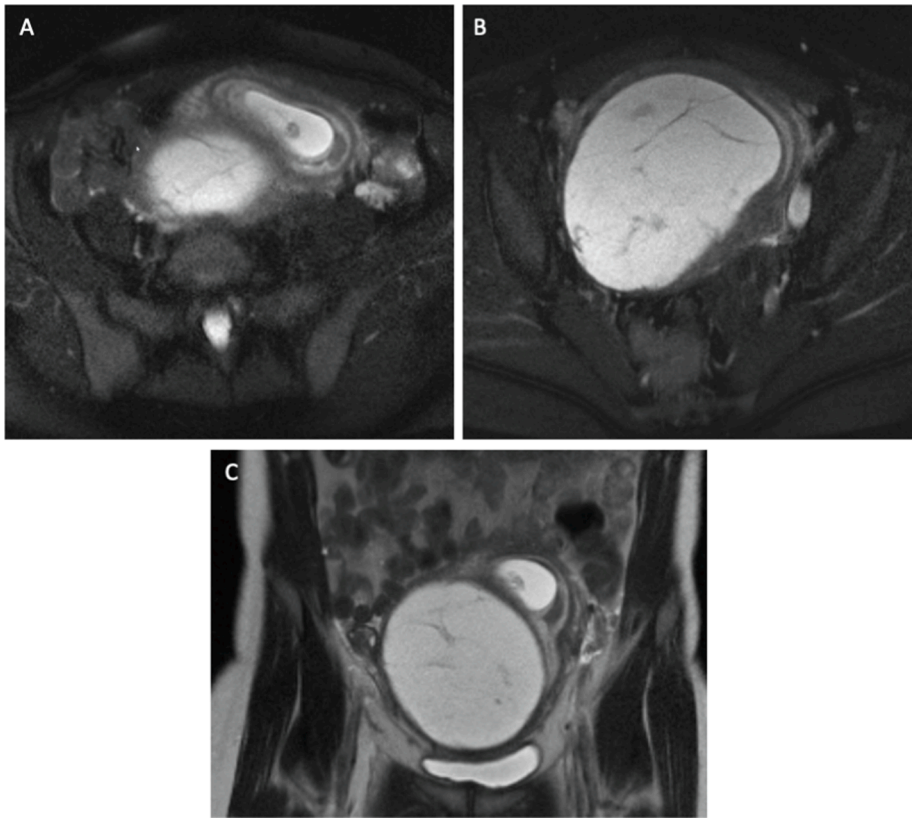

Fig. 2. Axial T2-weighted, fat-saturated MR images show the early gestational sac (A) as well as a large, predominately cystic submucosal mass with nodular internal septations (B). Note the relationship of the mass to the gestational sac on coronal T2 weighted image (C).

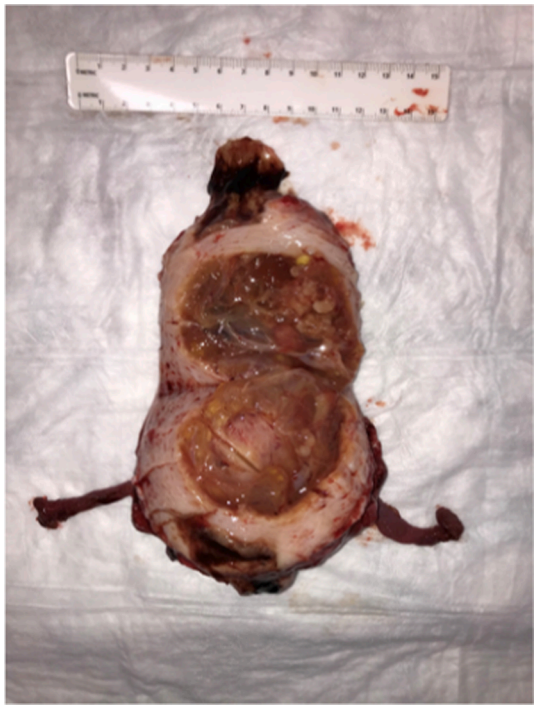

Fig. 3. Operative specimen demonstrating mass within uterus.

absence of speckled appearance are key features to suspect LGESS over rare leiomyoma variants. Features on MRI that were concerning for malignancy over leiomyoma in this case were the nodularity of the internal septations and the lack of internal hemorrhage on T1 weight images. Additionally, she had no history of fibroids noted on prior ultrasounds. Thus, the imaging findings were highly concerning for malignancy. Of note, needle biopsy is a noninvasive diagnostic measure that has been shown to be highly sensitive and specific for distinguishing sarcoma for leiomyomas. (Tamura et al., 2014 Jul) Biopsy was not a favored option for the patient presented her due risk of hemorrhage in a gravid uterus.

There are limited reports of ESS diagnosed in pregnancy. Gu *et al.* and Woytoń *et al.* discuss two cases of presumed leiomyomas that were found to be ESS postpartum. (Gu et al., 2021 Feb 6; Woytoń et al., 2002) In the case presented by Gu *et al.*, the patient delivered via cesarean section and simultaneously underwent fertility sparing resection for the previously presumed myoma. This mass which ultimately was diagnosed as LGESS was fully encapsulated; thus, fertility sparing management was feasible. The patient went on to successfully conceive and delivered a live infant at term via cesarean section. The patient Woytoń *et al.* describe was also delivered via cesarean delivery. However, excision was postponed given the size and vascularity of the mass. Imaging was then performed showing metastasis to lymph nodes and lungs; despite attempted chemotherapy, the patient died after 4 months. Grade was not specified but given the rapid progression it is likely to have been high grade. The consequence of ESS intrapartum is further demonstrated by Leunen *et al.* They report a high-grade ESS (HGESS) at the uterine fundus found to be the cause of postpartum hemorrhage requiring chemotherapy, surgical management, and radiation. (Leunen et al., 2003 Oct) Lastly, Amant *et al.* describe a case of HGESS in pregnancy with peritoneal spread. (Amant et al., 2010 Aug) They were able to obtain a peritoneal tissue sample without disrupting the pregnancy. This was extremely advantageous as it allowed for counseling and decision to terminate the pregnancy with a concrete understanding that a malignancy was coinciding with pregnancy.

In the case we present, there was not a definitive pathologic

diagnosis to guide management. As discussed, the unknown nature of the mass made it particularly challenging. Unlike the cases presented by Gu *et al.* and Woyton *et al.*, the imaging findings were strongly suspicious for malignancy as reviewed above. (Gu et al., 2021 Feb 6; Woytoń et al., 2002) This mass warranted further timely evaluation. The team caring for the patient was concerned that postponing a diagnosis could have put the patient at risk of tumor growth, metastasis, and postpartum hemorrhage as prior reports have shown. (Koskas et al., 2009; Leunen et al., 2003; Woytoń et al., 2002) The patient was also counseled that, despite the concerning features, there was a possibility that it could be a benign mass. The patient was presented with various tissue sampling options and was counseled that pregnancy termination would likely be necessary for proper and safe tissue sampling, but that it might be possible to maintain future fertility. The patient was given support, resources, and time to consider her options and discuss with family. Using shared decision-making, she ultimately decided to have the pregnancy terminated and a gravid hysterectomy in favor of a timelier diagnosis and definitive treatment as she determined she did not desire ongoing fertility. Thus, it was felt that regardless of final pathology, this was the right treatment plan for this patient.

It is important to acknowledge that the legal landscape regarding abortions has changed dramatically since this patient had her surgery. Although most states with restrictive laws make exceptions for medical emergencies and life-threatening pregnancies, it is not always clear what constitutes a lifesaving procedure. While abortion care is acknowledged as essential healthcare, a case such as this demonstrates the need to be able to provide such care even when there is not a definitive diagnosis of malignancy or other life-threatening medical conditions.(Jensen, 2023 Feb) A patient in a similar position presenting today may face more challenges in accessing the same treatment plan, and the care team may have more restricted options to offer as a result of institutional and state legal prohibitions on such care. This rare case of ESS exemplifies the importance of fully considering and evaluating masses in pregnancy. It also demonstrates the value of safe abortion access.

4. Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

Rachel L. Furuya: Conceptualization, Writing – original draft, Writing – review & editing. **David L. Eisenberg:** Data curation, Writing – review & editing. **Diana L. Gray:** Data curation, Writing – review & editing. **Vincent M. Mellnick:** Data curation, Writing – review & editing. **Premal H. Thaker:** Data curation, Writing – review & editing, Supervision.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: David L. Eisenberg, MD,MPH has served on the Advisory Board for Merck & Co. He has been a consultant for Evofem Biosciences, FemaSys and Sebela. He has received honoraria from Omnia Education. His university department receives contraceptive research funding from Evofem Biosciences, Medicines360, Merck & Co.,and Myovant.

Premal H. Thaker MD, MS receives grants/contracts from Merck and Galxo Smith Kline. She participates on a Data Safety Monitoring Bboard or an Advisory Board for the following entities: Iovance, Immunon, Glaxo Smith Kline, Clovis Oncology, Astra Zeneca, Merck, Aadi Biosciences, Novocure, Immunogen, Seagen, R Pharmaceuticals, Zentalis, and Mersana. She has stock in Immunon.

Diana L. Gray, MD, Vincent M. Mellnick, MD, Rachel L. Furuya, MD have no conflict of interests to report.

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