



CASE REPORT

REVISED Case Report: Spontaneous perforation of a bicornuate uterus with concomitant sarcoma [version 2; peer review: 2 approved]

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Abstract

A 47-year-old nulliparous, virginal woman presented to the emergency department with acute abdominal pain. Emergency pelvic ultrasound and abdominal CT were taken, which showed a significant amount of hemoperitoneum and a bicornuate uterus with about 18cm x 10cm mass on left uterus. Since the mass had increased vascularity and irregular margins, we thought that the mass could be a uterine sarcoma. MRI and PET/CT were taken additionally for oncologic evaluation before surgery. Intra operative findings showed a ruptured bicornuate uterus with a large mass within the left uterine horn. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Pathologic analysis confirmed an undifferentiated uterine sarcoma. She was treated with 6 cycles of chemotherapy(etoposide, ifosfamide, cisplatin) postoperatively. Chest and abdomen CT for follow up after chemotherapy showed no sign of cancer recurrence. We suggest a bicornuate uterus with concomitant sarcoma should be concerned as a possible cause of uterine rupture by reviewing this case.

Keywords

Bicornuate uterus, Uterine rupture, Uterine sarcoma

Open Peer Review

Reviewer Status

	Invited Reviewers	
	1	2
version 2		
(revision)		
13 Nov 2020	report	report
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version 1		
16 Sep 2020	? report	? report

1. **Jin-Sung Yuk** , Inje University, Seoul, South Korea
2. **Pallav Sengupta** , MAHSA University, Kuala Lumpur, Malaysia
Sulagna Dutta, MAHSA University, Kuala Lumpur, Malaysia

Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: **Yim S:** Conceptualization, Data Curation, Methodology, Project Administration, Software, Writing – Original Draft Preparation, Writing – Review & Editing; **Yeo I:** Conceptualization, Formal Analysis, Investigation, Software, Writing – Original Draft Preparation; **Lee M:** Writing – Review & Editing; **Kyeong KS:** Methodology; **Cho Hy:** Formal Analysis, Project Administration, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; **Kang JB:** Investigation; **Kyung MS:** Conceptualization, Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

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REVISED Amendments from Version 1

According to the reviewer's comment, we added her post-operative progress, and changed the form of the last sentence not to reads repetitive on abstract. And we changed the order of sentences to explain the relationship between the bicornuate uterus and the uterine rupture. Also, we discuss the objective specifically, rather than mentioning the methods performed.

Any further responses from the reviewers can be found at the end of the article

Introduction

Spontaneous uterine rupture occurs most commonly with labor and delivery¹. When it does occur, the most common cause of rupture is dehiscence of a previous transmyometrial surgical incision, such as that from a cesarean section scar². Spontaneous rupture of a uterus without a previous surgical scar is very uncommon and significantly less is known².

Bicornuate uterus is a common type of congenital uterine malformation: it takes the form of a double uterus with a single cervix and vagina³. Implantation of the zygote in a rudimentary horn of bicornuate uterus is considered an independent risk factor for uterine rupture. Because when a zygote is implanted in a horn of a bicornuate uterus, it is unable to expand as a normal uterus does to accommodate a growing fetus⁴. The walls of the anomalous uterus tend to become abnormally thin as pregnancies advance, and the uterine rupture can happen⁵.

Uterine sarcoma is a rare and aggressive soft tissue neoplasm in women of all ages. It usually presents with abdominal or pelvic pain, vaginal bleeding; sarcoma does not typically cause uterine rupture and hemoperitoneum. To our knowledge, there have been only five cases reported in the literature that describe a uterine sarcoma presenting with rupture and induced hemoperitoneum⁶.

Herein, we report a case from diagnosis to surgical treatment of a 47-year-old woman with bicornuate uterus who had no previous history of spontaneous uterine rupture or uterine surgery. We hypothesize that as the uterine sarcoma advance, uterine rupture can occur as a result of congenitally malformed, bicornuate uterus. Through this case, we suggest that a bicornuate uterus with concomitant sarcoma should be concerned as a possible cause of uterine rupture when a woman presents with hemoperitoneum in the setting of a pelvic mass and uterine anomaly with intact ovaries detected on imaging.

Case report

A 47-year-old nulliparous, virginal woman presented to the emergency department with a 2-day fever and acute abdominal pain. She also complained of a 2-month history of foul-smelling vaginal bleeding. She had pyrexia, with a temperature of 38°C (100.4°F), and marked tenderness of the whole abdomen. She has a past medical history significant for breast cancer, which was treated with six cycles of CAF (cyclophosphamide, [doxorubicin] Adriamycin, fluorouracil), adjuvant radiotherapy,

and tamoxifen for 4 years; the doses are uncertain since she had taken those therapies in the other institutes. She has not had a gynecological evaluation for over 8 years since the end of her breast cancer treatment, and she had discontinued her tamoxifen.

Laboratory investigation demonstrated a hemoglobin level of 12.3 g/dL (normal range, 12–16 g/dL), a white blood cell count of 12,600/mm³ (normal range, 4,000–10,000/mm³) and a C-reactive protein of 157.9 mg/L (normal range, 0.1–5.0 mg/L). Mild elevation of her liver enzymes was observed, with a total bilirubin of 2.2 mg/dL (normal range, 0.2–1.4 mg/dL) and a direct bilirubin of 0.7 mg/dL (normal range, 0.0–0.5 mg/dL).

A dynamic CT scan of the liver was performed to evaluate for biliary infection as this patient had been known to have a history of gallbladder stones for years along with complaints of upper abdominal pain. The CT scan revealed a 16-cm uterine mass and increased free fluid in the pelvic cavity, including both paracolic gutters, the perihepatic space, and the perisplenic space. Consequently, she was referred to our obstetrics and gynecology department.

Transrectal ultrasonography showed a bicornuate uterus and an 18.6- × 9.1-cm mass with heterogeneous echogenicity within the left uterus. The mass appeared to extend through the cervix into the vaginal cavity. Its irregular-shaped margins and increased blood flow suggested the possibility of malignancy (Figure 1). Because her vital signs were stable (aside from fever), the patient received an oncological evaluation and antibiotic treatment before surgery. Since F-18 FDG were ordered and needed time to arrive, PET/CT were planned two days later, and the surgery was planned for the next day. Antibiotics (piperacillin 4g, tazobactam 0.5g, metronidazole 0.5g) were injected intravenous every 8 hours, and administered for about 48 hours until just before surgery.

Pelvic MRI was performed on the day after the patient's initial presentation, revealed underlying uterus didelphys with an approximately 15- × 9- × 17-cm mass with mixed signal intensity in the lower abdominal area (Figure 2) and an approximately 6- × 2.7- × 3-cm mass of the left cervix and lower uterine body on T2-weighted imaging. These MRI findings suggested the possibility of hemoperitoneum or cancer peritonei due to rupture of (1) endometrial cancer, (2) uterine sarcoma, or (3) large myoma with degeneration.

A whole-body PET/CT scan was ultimately performed (two days after presentation) and showed an intensely hypermetabolic subserosal mass with accompanying hemorrhage and possible rupture; further, hypermetabolic peritoneal nodules and peritoneal infiltration with ascites were observed (Figure 3).

The patient underwent diagnostic laparotomy three days after presentation. Surgical exploration revealed a ruptured bicornuate uterus with a large mass within the left uterine horn (Figure 4). The mesentery of the small bowel and appendix were partially adhered to the uterine mass. Total abdominal hysterectomy with

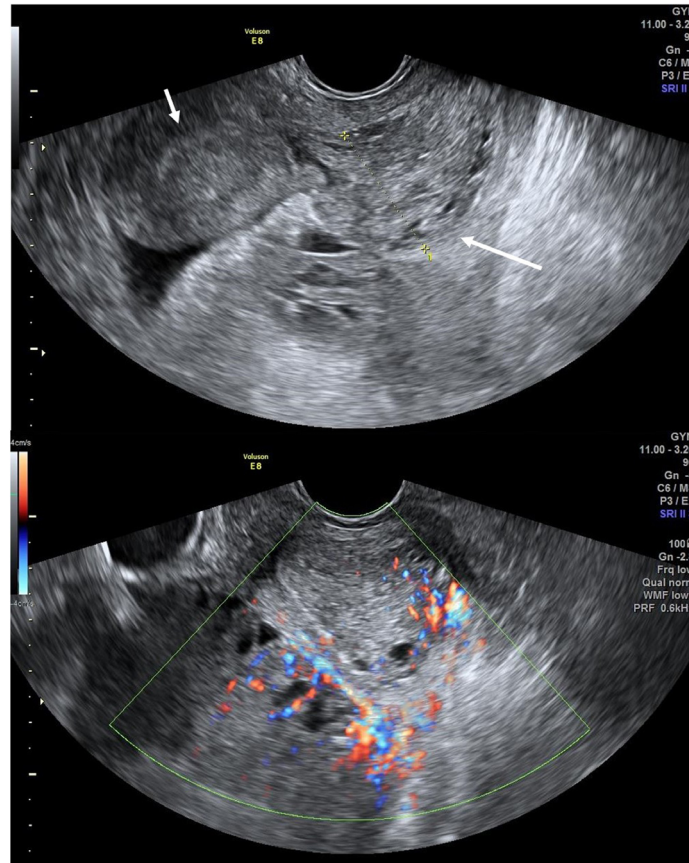


Figure 1. Transrectal ultrasonography. Ultrasonography shows a 1.5-cm-thick endometrial layer in the right uterus (short arrow) and up to 2.69 cm in the left uterus (long arrow). The mass was connected to the left uterus and appeared to be extending into the vaginal cavity. Internal blood flow was increased.

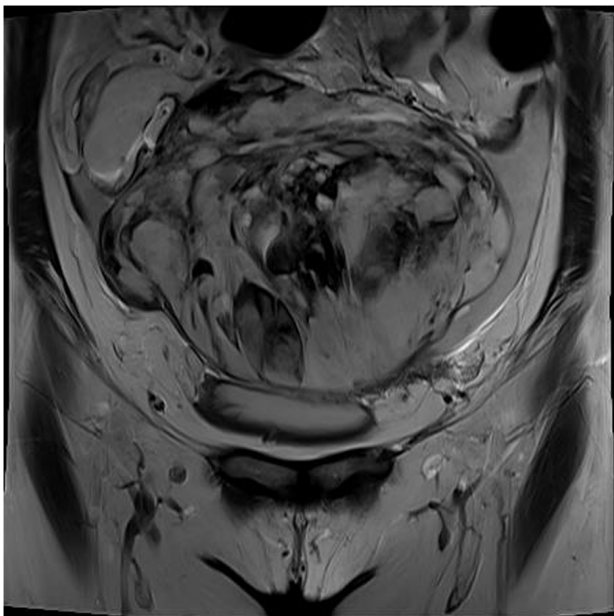


Figure 2. Magnetic resonance imaging (coronal view, T2 W1). This scan shows an approximately 15- × 9- × 17-cm mass with mixed high and low signal intensity and irregular margins in the lower abdomen on coronal view.

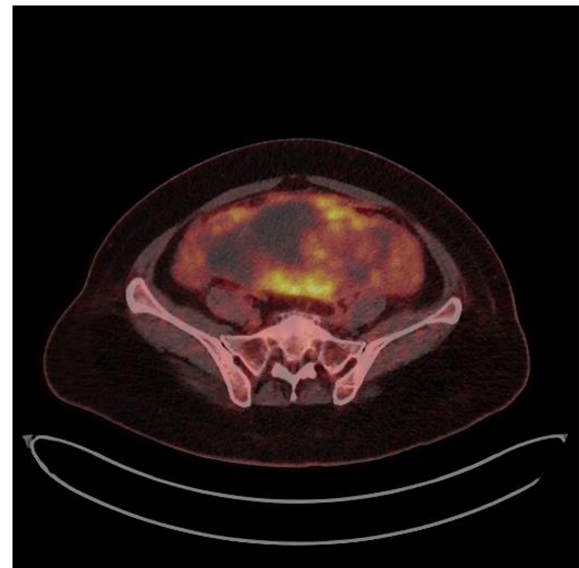


Figure 3. Positron emission tomography/computed tomography. An approximately 13-cm intensely hypermetabolic hemorrhagic mass is noted in the pelvic cavity, suggestive of a subserosal uterine mass possibly connected with a cervical lesion. There are regions of hypermetabolic peritoneal thickening and nodules with a small amount ascites.

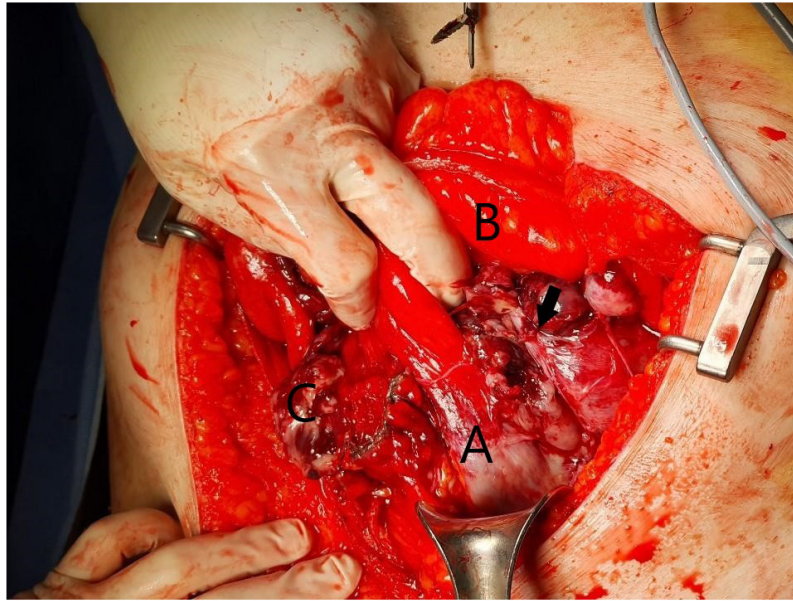


Figure 4. The arrow is pointing the ruptured portion of left uterine horn of the bicornuate uterus. Rupture length was about 3cm. Mesentery of small bowel was partially adhered to the uterine mass. A significant amount of hemoperitoneum was observed. Estimated blood collection in cul-de-sac was 1000 to 1500 mL. (A) Left uterus (B) Small bowel (C) Mass.

bilateral salpingo-oophorectomy was performed, and invasive cancer implants within the bowel were removed. Estimated surgical blood loss was approximately 1500 mL.

Pathological analysis confirmed an undifferentiated uterine sarcoma with tumor size up to $23 \times 13 \times 6$ cm. Because a tumor in her left fallopian tube and one of her bowel mass implants tested positive for cancer, she was diagnosed with FIGO Stage IIIA (from the International Federation of Gynecology and Obstetrics cancer staging system)⁷.

Postoperatively, the patient was treated with a combination of etoposide (150 mg/m^2 for 3 days), ifosfamide (1.5 g/m^2 for 3 days), and cisplatin (70 mg/m^2 for 1 day) once every 3 weeks. Chest and abdomen CT were performed for follow up 2 weeks after. There were no sign of cancer recurrence in the chest and abdominal CT.

Discussion

The uterus is pear shaped and consists of two major but unequal parts. The upper, larger portion is the body or corpus, whereas the lower smaller cervix projects into vagina. The bulk of the uterine body is muscle. Almost the entire posterior wall of the uterus is covered by serosa, that is, visceral peritoneum. Uterine rupture can present with both complete rupture involves the full thickness of the uterine wall and incomplete rupture occurs with the visceral peritoneum remains intact. Both types of uterine rupture are rare but serious events. Several risk factors have been identified. The most common risk factor is previous transmyometrial surgical incision, typically the result of a cesarean section^{1,2}. Other significant risk factors for uterine

rupture include oxytocin-induced labor, antepartum fetal death, and first trimester miscarriages⁸. There have been several reported cases of uterine rupture in Müllerian anomalies where the zygote implants within a rudimentary horn. Higher rates of uterine rupture have been reported in patients with Müllerian duct abnormalities who elect to undergo a trial of labor after cesarean delivery when compared with patients without Müllerian duct abnormalities, suggesting that these anomalies may be an independent risk factor for uterine rupture⁵.

The uterus is formed by the fusion of two paramesonephric ducts (Müllerian ducts) during embryogenesis. The separate ducts fuse into a single uterine body between the sixth and eighth weeks of gestation⁹. Failure of complete fusion of the Müllerian ducts leads to various types of malformations of the female genital tract¹⁰. The incidence of uterine anomalies is 0.06% to 38% in the general population¹¹. Bicornuate uterus is a common type of uterine malformation, taking the form of a double uterus with a single cervix and vagina. Each uterus has a single horn linked to an ipsilateral fallopian tube that faces its ovary³. The bicornuate uterus often has unusually thick and strong round ligaments along with a thick vesicorectal fold running between them¹². This fibrous band in the form of a rectovesical ligament has a restrictive effect on the expansion of the pregnant horn of a bicornuate uterus, thereby weakening the medial aspect of the horn¹³. Rupture of a bicornuate uterus during a growing pregnancy occurs due to inability of the malformed uterus to expand as a normal uterus would⁴. The walls of the anomalous uteri tend to become abnormally thin as the pregnancy advances. Rudimentary horn rupture is likely to occur in the late first trimester or even in the second trimester³.

Some cases are associated with leiomyoma of the uterus. Potential etiologies for spontaneous rupture of leiomyomas are degeneration or sarcomatous changes of uterine leiomyomas. The most likely mechanism behind spontaneous rupture of a leiomyosarcoma is tumor necrosis. Hemoperitoneum is the result of spontaneous rupture of the superficial vessels overlying leiomyomas¹⁴ or the result of avulsion of a pedunculated myoma by trauma^{15,16}. Uterine rupture with resulting hemoperitoneum has been described particularly for leiomyomas, and approximately 100 cases have been reported. Because uterine sarcoma is a rare neoplasm; therefore, uterine rupture as a result of sarcoma is even more unusual. A patient with uterine rupture typically presents in hypovolemic shock with severe abdominal pain that requires emergency care. Because a patient's condition can deteriorate rapidly after uterine rupture, most patients will need immediate blood and fluid replacement therapy and an exploratory laparotomy to be done without a clear preoperative diagnosis before surgery. Most uterine sarcomas are diagnosed after surgery by postoperative biopsy¹⁷.

We formulated two hypotheses regarding the etiology of uterine rupture in our patient: (1) the sarcoma itself had necrotic changes that led to uterine rupture and (2) the patient had an underlying bicornuate uterus, which exerted a restrictive effect on the ability of the myometrium to expand in the setting of a growing sarcoma.

Pelvic ultrasonography or CT imaging is commonly used for preoperative diagnosis of uterine sarcoma. Ultrasonography can also be the initial examination measure performed urgently in the setting of acute pelvic symptoms. However, ultrasonography remains insufficient to differentiate between a remodeled myoma and a sarcoma based on morphologic criteria alone. As a result, color Doppler ultrasonography can be used to measure resistance indexes which reveal a significant difference between leiomyomas (resistance index 0.01–0.59) and sarcomas (resistance index 0.06–0.41)¹⁸

Ultrasonography is useful when performed properly, but it has a limitation for revealing a large mass. CT imaging is superior to ultrasonography especially for evaluation of a large mass. Also CT imaging has good diagnostic value, because extravasation of contrast enhancement can be used to evaluate for active bleeding. Further, a diagnosis of hemoperitoneum can be made by assessing the Hounsfield unit (HU), a measure of radiodensity. The attenuation values of unclotted extravascular blood usually measure between 30 and 45 HU, whereas clotted blood is between 45 and 70 HU because of its high protein content¹⁹. However, a CT imaging is not sensitive enough to distinguish between a leiomyosarcoma and a necrotic leiomyoma²⁰.

Pelvic MRI is a useful diagnostic tool for the detection and characterization of uterine sarcoma, as well as for an assessment of disease staging. MRI images of uterine sarcomas generally have irregular margins and are isointense or hypointense on T1-weighted imaging (compared to the signal from the myometrium) with possible hemorrhagic zones. In T2-weighted imaging, uterine sarcomas have an intermediate-to-high signal. In contrast, leiomyomas have regular margins and low-to-intermediate signals on both T1-weighted and T2-weighted imaging. Although the radiological findings of these lesions can overlap, characteristic features can help narrow the differential diagnosis and guide adequate treatment selection and follow-up. In addition to morphologic features, diffusion-weighted imaging seems to be a potentially useful tool in the characterization of large uterine lesions²¹.

In our patient case, it was uncertain whether the uterine rupture was due to endometrial cancer, uterine sarcoma, or degenerated myoma. The mass appeared to be extending through the cervix into the vaginal cavity, but vaginal examination and endometrial biopsy could not be performed because the patient is a virgin. The patient had stable vital signs other than pyrexia, and her pain was not severe. Therefore, we decided to perform PET/CT scan additionally to distinguish between leiomyoma and sarcoma to determine the scope of preoperative surgery.

The treatment of uterine sarcomas is surgical intervention. It includes a total hysterectomy with bilateral adnexectomy in the event of a tumor limited to the uterine body. The indication for adjuvant treatment remains a topic of debate²². The prognosis for uterine sarcomas remains poor. The probability of survival at 5 years is estimated at 30%, all stages combined²³.

Though uncommon, uterine rupture in the setting of a bicornuate uterus with concomitant sarcoma should be highlighted as a possible cause of hemoperitoneum when a woman presents with severe abdominal pain, particularly in the setting of a pelvic mass and uterine anomaly with intact ovaries detected on imaging. CT imaging is useful when ultrasonography shows no definite evidence of uterine rupture. We recommend the use of MRI imaging to help differentiate between leiomyoma and sarcoma before surgical intervention takes place.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

We received written informed consent from the patient for the use and publication of the patient's data.

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Open Peer Review

Current Peer Review Status:  

Version 2

Reviewer Report 04 January 2021

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Pallav Sengupta 

Department of Physiology, Faculty of Medicine, Bioscience and Nursing, MAHSA University, Kuala Lumpur, Malaysia

Sulagna Dutta

MAHSA University, Kuala Lumpur, Malaysia

The authors have revised the article as per the given comments. I recommend publication of the article in its present form.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Reproductive Endocrinology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 20 November 2020

<https://doi.org/10.5256/f1000research.30570.r74759>

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Jin-Sung Yuk 

Department of Obstetrics and Gynecology, Sanggye Paik Hospital, School of Medicine, Inje University, Seoul, South Korea

I think you've made a good correction.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Endocrinologic Gynecologist

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 23 October 2020

<https://doi.org/10.5256/f1000research.28649.r72608>

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Pallav Sengupta

Department of Physiology, Faculty of Medicine, Bioscience and Nursing, MAHSA University, Kuala Lumpur, Malaysia

Sulagna Dutta

MAHSA University, Kuala Lumpur, Malaysia

The case report on 'Spontaneous perforation of a bicornuate uterus with concomitant sarcoma' by Yim et al is describing an interesting finding. The authors have described the physical and laboratory investigations and operative and post-operative procedures well. The report can be accepted in F1000Research. However, the presentation of the literature in various sections can be improved further to improve the readability of the article.

1. Abstract: This section is well-presented. However, it is preferable to discuss some information on operative as well as post-operative procedures with the lab investigations. Please also try to rewrite the last sentence which reads repetitive.
2. Introduction: Nicely written. The last paragraph should discuss the objective specifically, rather than mentioning the methods performed.
3. Case Report: Well described.
4. Discussion: Please start with the discussion of normal uterine structures and development (as done in the second paragraph) and continue with the structural abnormalities and so on. The rest has been discussed well.
5. The authors are requested to provide the ethical approval to publish the study along with the patient consent details (already provided).

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Reproductive Endocrinology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 10 Nov 2020

Inji Yeo, Hallym University Medical Center, Hwaseong, South Korea

Thank you for your very informative and appropriate comments.

Reviewer's comment 1 : Abstract

-> We added her post-operative progress, and changed the form of the last sentence not to reads repetitive

Reviewer's comment 2: Introduction

-> We added more contents about objective of this article

Reviewer's comment 3: Discussion

-> We added contents about normal uterine structures as commented

Competing Interests: No competing interests were disclosed.

Reviewer Report 22 October 2020

<https://doi.org/10.5256/f1000research.28649.r73429>

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Jin-Sung Yuk

Department of Obstetrics and Gynecology, Sanggye Paik Hospital, School of Medicine, Inje University, Seoul, South Korea

The second paragraph on page 1: it would be helpful to first explain the relationship between the bicornuate uterus and the uterine rupture in the third sentence.

Figure 4 on page 4: The anatomical structure of the photograph cannot be distinguished. I think it will be helpful to put text on the picture to distinguish it.

The first paragraph of the discussion: It is very similar to the first paragraph of the introduction. Variations such as changing the form of the sentence or describing the content in more detail are needed.

The 3rd paragraph of discussion: "rupture of the superficial overlying vessels" is the result, not the cause of rupture of leiomyoma.

The 4th paragraph on discussion: These sentences ("Uterine rupture with ~ by trauma.") fit the previous paragraph rather than this one. It would be nice to integrate with the previous paragraph and reduce the content.

The 4th paragraph on page 5: In the conclusion of the last paragraph, it was argued that CT is helpful when sono cannot discriminate. Write something to support this. For example, "CT is superior than sono in circumstances that ~~~".

The 7th paragraph on page 5: This sentence ("In our patient~~or degenerated myoma.) appears to be the result of the MRI reading. From the point of view, it would be better to move it backwards than the CT at the end of this paragraph.

The 7th paragraph on page 5: In the last sentence ("CT imaging revealed~ PET/CT scan)", it is unclear why the MRI and PET/CT scans were performed. (bicornuate uterus? The distinction between leiomyoma and sarcoma? The distinction between rupture?)

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Endocrinologic Gynecologist

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 10 Nov 2020

Inji Yeo, Hallym University Medical Center, Hwaseong, South Korea

Thank you for your very informative and appropriate comments.

Reviewer's comment 1: The second paragraph on page 1

-> we changed the order of sentences to explain the relationship between the bicornuate uterus and the uterine rupture

Reviewer's comment 2: Figure 4 on page 4

-> we put text on picture, and added description

Reviewer's comment 3: The first paragraph of the discussion

-> We added normal structure of uterus, and changed the form as commented

Reviewer's comment 4: The 3rd paragraph of discussion

-> we removed that sentence

Reviewer's comment 5: The 4th paragraph on discussion

-> We changed the order of sentence, and integrated the 4th paragraph with 5th paragraph

Reviewer's comment 6: The 4th paragraph on page 5

-> we removed the sentence that is in argue, and added pros of CT over sono.

Reviewer's comment 7: The 7th paragraph on page 5:

-> we moved above sentence backward to the end of paragraph about MRI reading

Reviewer's comment 8: The 7th paragraph on page 5

-> We performed the PET/CT to make distinction between leiomyoma and sarcoma before surgery.

Competing Interests: No competing interests were disclosed.

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