International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Howford M et al. Int J Reprod Contracept Obstet Gynecol. 2026 Jul;15(7):2766-2770
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20262135

Case Report

Endometrial stromal sarcoma in a large fibroid uterus presenting with sepsis-like picture, extensive pelvic thrombosis and severe menorrhagia

Megan Howford[1]*, Nicholas Matthews[2], Madhavi Gudipati[2], Shamma Al-Inizi[2]

[1]University of Sunderland, Chester Road, Sunderland, England
[2]South Tyneside and Sunderland NHS Foundation Trust, Kayll Rd, Sunderland, UK

Received: 04 May 2026
Accepted: 03 June 2026

***Correspondence:**
Dr. Megan Howford,
E-mail: bi25gp@student.sunderland.ac.uk

ABSTRACT

This case report aims to demonstrate the diagnostic challenges of uterine sarcomas, presenting with presumed benign symptoms. Missed clinical clues and consequently a delayed diagnosis demonstrates the importance of considering uterine sarcomas as a differential, particularly in premenopausal women. This case report describes the case of a woman in her early 40s, who presented with symptoms of fibroids, before receiving an incidental diagnosis of endometrial stromal sarcoma, almost a year after her initial hospital presentation. The patient had an extensive investigative period, repeatedly returning to hospital with symptoms including lower abdominal pain and heavy vaginal bleeding, and imaging and biopsies not pointing clinicians to the diagnosis. Many findings and reports presented clues which should have pointed towards an alternative diagnosis-raised LDH, extensive pelvic thrombosis, the presence of a pelvic lymph node, and lack of response to treatment-none of which were considered as consequences of a uterine sarcoma. Diagnostic interpretation was complicated by factors such as a raised BMI, continuous bleeding, and the need for anticoagulation, making the final diagnosis hard to reach. This case demonstrates the criticalness of considering uterine sarcomas as a mimic for benign gynaecological conditions and symptoms. Timely recognition and early consideration is critical to improve outcomes, and uterine sarcomas should always be discussed as a potential diagnosis, especially in premenopausal women.

Keywords: Endometrial stromal sarcoma, Uterine sarcoma, Abnormal uterine bleeding, Pelvic thrombosis, Diagnostic delay

INTRODUCTION

Uterine sarcomas are mesenchymal tumours, and despite accounting for roughly 3-7% of uterine cancers, are often diagnosed following presumed benign findings.[1-3] They lack specific features that may direct clinicians to a diagnosis early, and are aggressive, contributing to a poorer prognosis.[4] The classical presentation of uterine sarcomas involves a pelvic mass alongside vaginal bleeding and abdominal/pelvic pain, although symptoms vary with histological subtypes.[4,5] Histologically, uterine sarcomas are divided into four classes: carcinosarcomas, leiomyosarcomas, endometrial stromal sarcomas (ESS) and undifferentiated sarcomas.[3] For ESS's, irregular vaginal bleeding is the most common symptom.[5] Symptoms of uterine sarcomas overlap heavily with presentation of leiomyomas (or fibroids). These benign tumours, although up to 70% are asymptomatic, present with features including abdominal pain and abnormal uterine bleeding, and are hormonally responsive, making fibroids a likely differential, particularly in reproductive years.[6]

CASE REPORT

This case review discusses a female in her early 40s, with no known drug allergies, a medical history of anxiety and depression, for which she takes 50 mg of sertraline, heavy periods, and a BMI of 52. This patient had no abnormal smears, with 5 previous childbirths (4 vaginal births and 1

caesarean section). She presented to the emergency department (ED) complaining of lower abdominal pain. The pain was unrelated to menstruation and ongoing for two months before her ED visit which as increased in intensity. The patient was assessed, reassured, and discharged with a supply of simple pain killers with the request that the patient's general practitioner (GP) considered an outpatient pelvic ultrasound.

Three months later, she attended ED with heavy prolonged vaginal bleeding lasting for few weeks. The patient had been passing palm sized blood clots and was leaking through clothes. The paramedics estimated 500-700mls of blood loss, and the patient was extremely weak and lethargic, with no urinary symptoms and no changes to her bowel habits. Vaginal examination was inconclusive due to her body habitus. She was eventually sent home on oral progesterone and tranexamic acid (TXA), with advice to return if symptoms continued or her condition deteriorated, and an ultrasound scan was arranged and showed the presence of at least two uterine leiomyoma with the largest being 80 mm length with the endometrium measuring approximately 11 mm.

The patient presented a third time, just over two months later, with abdominal pain. She described the lower abdominal pain, described as a pressure but experienced a sharp pain bilaterally in the iliac fossas, groin and flank. On examination, the patient presented with a septic- like picture-she was tachycardic, with low grade pyrexia, and was found to have raised inflammatory markers, with low haemoglobin level of 84G/L. The patient elicited guarding to the right iliac fossa, leading to the suspicion of appendicitis. Abdominal and pelvic CT scan and MRI were arranged which identified thrombosis in the right common iliac vein, possible degeneration of fibroids and a bulky uterus, with no signs of appendicitis (Figures 1-3). Thrombosis was further confirmed by a pelvic venogram where extensive thrombosis of ovarian and uterine vessels was detected. It also reported a left deep pelvic lymph node measuring 12 mm.

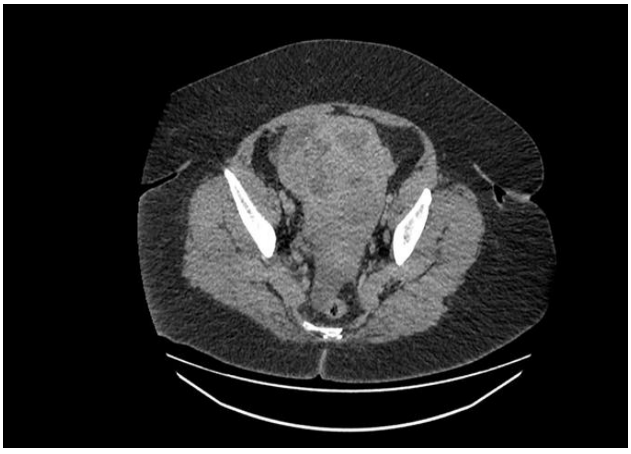

Figure 1: Displaying AP pelvic CT axial view scan indicating a bulky fibroid uterus occupying most of the pelvis.

Figure 2: Displaying AP pelvic CT coronal view scan indicating the lateral view of the large fibroid uterus.

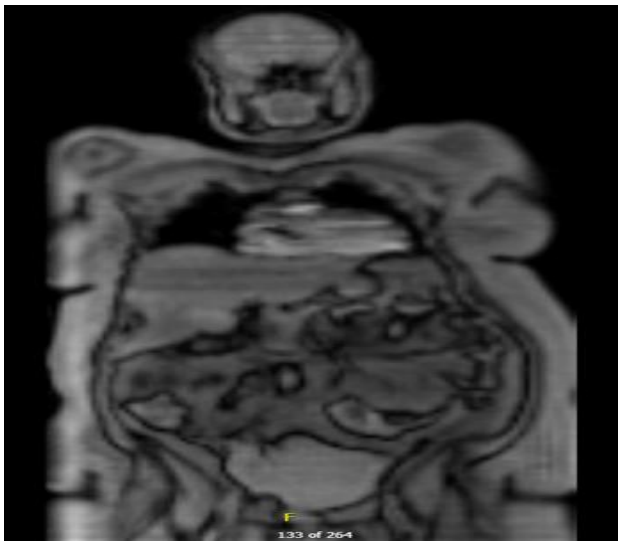

Figure 3: Displaying MRI coronal view scan indicating the large fibroid uterus occupying most of the pelvis.

During this admission, the patient explained that she had tried medroxyprogesterone acetate and norethisterone but continued to bleed. There was suprapubic abdominal tenderness and to the right side. A mobile mass was palpated, and a bulky uterus was identified, with a bimanual exam revealing a nodular cervix. The plan was to commence treatment dose of enoxaparin (170 mg) and withhold tranexamic acid which she was taking over the last few weeks. The haemoglobin was 66 gm/dl and 2 unit of red cells were transfused and she was restarted on medroxyprogesterone acetate. The patient's lactate dehydrogenase was reported to be elevated 299 U/L (135-214 U/L). An endometrial biopsy was taken and a

Levonorgestrel intrauterine system (IUS) was inserted. The biopsy indicated a menstruating endometrium. She continued to bleed heavily vaginally resulting in a drop in haemoglobin to 72 gm/dl and a further unit of blood transfusion was give.

A few weeks later, she returned with further heavy bleeding. A pelvic ultrasound scan confirmed that the IUS was still in place. The enoxaparin was withheld until bleeding stabilised, and further blood transfusion was provided. It was explained to the patient that a hysterectomy would not be ideal due to the high BMI and current deep venous thrombosis. The patient was offered uterine artery embolization (UAE) which she declined. As she continued to bleed heavily despite the oral progestogens, extensive discussions with the multidisciplinary team (MDT) took place, and a hysterectomy was planned with patient`s consent. Overall, the patient received 11 units of blood prior to the operation.

Total abdominal hysterectomy and bilateral salpingoopherectomy was performed. Advanced malignancy was suspected during surgery after having significant difficulty to safely ligate the uterine vessels as the tumour had invaded the pelvic side wall, needing a further 10 units of blood transfusion and ITU admission. The patient then recovered and went home.

Histology revealed low grade endometrial stromal sarcoma, with involvement of the uterus, cervix, bilateral parametria and adnexa (Figure 4 and 5).

Following discussing the case on the regional sarcoma MDT, a CT scan repeated 3 months post-surgery was suggestive of progressive pelvic disease, and the patient was commenced on megestrol acetate (160 mg).

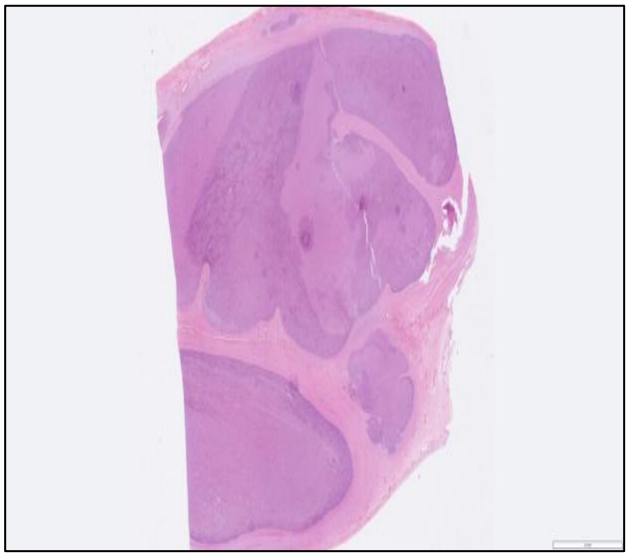

Figure 4: Displaying low power histology slide of hysterectomy indicating some smooth muscle bundles of benign fibroid with myometrial invasion with ESS and into lymphovascular spaces.

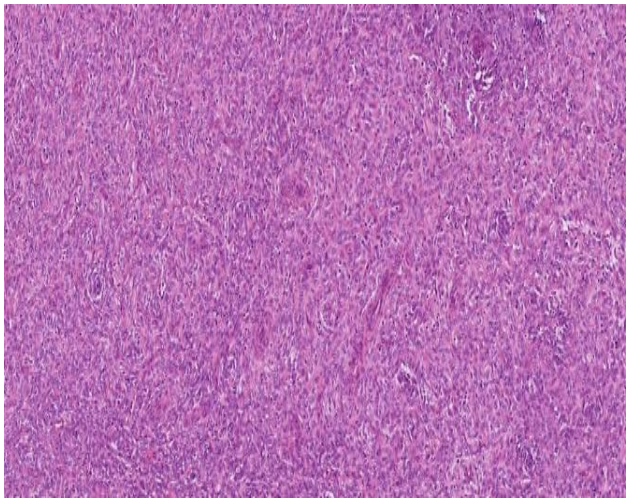

Figure 5: Displaying high power histology slide of hysterectomy with obvious tumour cells` atypia with prominent thin wall vessels, loss of interstitial differentiated cells with high mitotic figures.

DISCUSSION

This case was both complex and confounding, making the ESS diagnosis difficult to achieve, reinforcing the challenges of diagnosing uterine sarcomas, and the need for suspicion of malignancy at first presentation. Many factors are considered to contribute to the delayed identification of the malignancies such as this one. The abundance of non-specific symptoms, including vaginal bleeding and pelvic pain, overlap with a multitude of possible conditions, particularly in premenopausal women, and the imaging techniques that are readily available, including ultrasound and MRI, are unable to rule out a malignancy.[7] The use of the usually diagnostic biopsies are often unable to detect uterine malignancies, due to the inaccessibility of the tissue, deep in the muscle layer of the uterus.[8] Perhaps the most important factor that contributes to the lack of early diagnosis, is the rarity of the malignancies-sarcomas are thought to make up only 3-4% of the total number of gynaecological malignancies in England.[9] Fibroids are common causes of heavy menstrual bleeding in premenopausal women and mostly this what directed the clinicians towards in this case.[10]

A 2016 publication discussed a 36-year-old nulliparous female presenting with progressive symptoms, including abdominal pain, pelvic pain, hypermenorrhoea.[11] Following multiple hospital presentations, with recurrent symptoms despite various attempts to treat, over a few years, a uterine fibroid embolization was performed. The diagnosis of ESS was missed. Not only did both patients, despite persistent symptoms, only receive a biopsy after multiple hospital presentations, but both biopsies missed an underlying malignancy. With both women being pre-menopausal, the consideration of a malignant cause as a differential was clearly not discussed until later. This emphasises the importance of considering malignancy, especially with factors such a failure to respond to medical

treatment, particularly following the missed diagnoses in two similar cases, after biopsies. Additionally, a 2018 case report discusses a 79-year-old patient, presenting with a septic -like picture after experiencing symptoms including postmenopausal bleeding and abdominal pain with raised inflammatory markers secondary to tumour break down.[12] Similarly, to our case, this patient had experienced a deep venous thrombosis of her left leg, and as a result was also taking anticoagulation medications, further complicating the diagnosis and subsequent treatment. A case from 2012, of a premenopausal woman, presenting with heavy vaginal bleeding, and an abdominal mass which was found to be a fibroid.[13] Post operatively, the patient was found to also have extensive pelvic thrombosis and was later diagnosed with endometrial stromal sarcoma, following a similar pattern to this case.

We believe that the case we are presenting is the first case of a premenopausal woman presenting with heavy vaginal bleeding, extensive pelvic thrombosis who presented with sepsis- like picture and a large fibroid uterus diagnosed with ESS.

Many elements of this case made care challenging. The first being the raised BMI. A 2018 study found that intra-operative complications were five times more common in extremely obese patients compared to patients with a healthy BMI, with post operative complications increasing by over 17 times in obese patients.[14] The difficulties expected because of the patient's BMI had to be balanced against the emergent situations that the clinicians were presented with. Several clinicians completed examinations on separate occasions, with no outlying findings apart from the large fibroid uterus and the clinicians were reassured by the normal endometrial biopsy and imaging. The biggest challenge was the presence of pelvic thrombosis. It was very difficult to follow the treatment protocol when paired with heavy bleeding. This was very difficult to manage, as clinicians attempted to balance anticoagulation and the bleeding.

Improved outcomes for the patient could have been achieved, had several factors been considered together and in depth. The only biopsy taken had an extensive report, discussing the findings that were suggestive of menstrual type breakdown, with the specimen being described as 'scanty'. Despite this markedly insufficient result, a repeat biopsy or hysteroscopy was never completed, which could have still missed the diagnosis especially final histology of the removed uterus showed menstrual phase endometrium only with no evidence of atypical hyperplasia or malignancy. Hence although the endometrial biopsy was not repeated, it did not contribute to the patient`s outcome having the tumour already infiltrating the uterine muscle and serosa. This indicates that endometrial biopsy may not be able to direct towards ESS diagnosis as a normal biopsy can falsely be reassuring.[11]

Furthermore, early in the patient's care, a raised LDH level was identified which was not considered or commented on. Although non-specific, the protein biomarker has been reported to be elevated in uterine sarcomas, compared with benign leiomyomas-this finding should have provided further diagnostic direction in this case as a result. The incidental finding of a 12 mm pelvic lymph node on pelvic MRI scan which could be associated with malignancy, was conflicting with the CT findings of no pelvic lymphadenopathy hence was not considered during the management pathway.[15] Another consideration was that the patient did not seem to be responding to any medical treatment for the heavy vaginal bleeding, which should have raised the suspicion of possible malignancy together with the extensive pelvic thrombosis. The raised BMI with a large pelvic fibroid mass did not explain the extensive pelvic thrombosis, and therefore should have been considered as a 'red flag' for potential malignancy. The increased expression of tissue factor with malignancy is thought to contribute to the hypercoagulable state.[16]

CONCLUSION

Gynaecological malignancy in the form of ESS needs to be considered in premenopausal women presenting with extensive pelvic thrombosis, heavy vaginal bleeding not responding to any medical treatment and uterine fibroids. They could present with sepsis like picture due to tumour necrosis. Other factors such as raised LDH, presence of pelvic lymphadenopathy, should lead to a larger scope for considering malignancy in premenopausal women.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Howford M, Matthews N, Gudipati M, Al-Inizi S. Endometrial stromal sarcoma in a large fibroid uterus presenting with sepsis-like picture, extensive pelvic thrombosis and severe menorrhagia. Int J Reprod Contracept Obstet Gynecol 2026;15:2766-70.