

## CASE REPORT

### Primary uterine angiosarcoma with “rhabdoid morphology”: A case report

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#### Abstract

**Introduction:** Primary uterine angiosarcoma is a very rare tumour, with only 23 cases described till now. It is a malignant tumour with cells variably recapitulating the morphologic features of an endothelium and expressing immunohistochemical markers of endothelial cells. In general, it is a bulky neoplasm and frequently is at advance stage of disease at presentation. In general, patients with uterine angiosarcoma tend to have a poorer prognosis, mostly related to the aggressive nature and the metastatic potential of these tumours. **Case report:** We report a rare case of primary uterine angiosarcoma with unusual rhabdoid morphology in a 41-year-old female, who underwent radical hysterectomy and died of disease after 4 months of treatment. **Discussion:** We described the differential diagnosis of primary angiosarcoma of the uterus that can pose a diagnostic challenge.

**Keywords:** Angiosarcoma, uterus, rhabdoid

#### INTRODUCTION

Angiosarcoma is defined as malignant tumour of the endothelial cells and account for 2% of all soft tissue sarcomas. A primary origin in the uterus is extremely rare with only 23 cases reported in English literature. Generally, these tumours are bulky with advanced initial clinical stage at presentation.<sup>1</sup> Uterine angiosarcoma tends to exhibit a highly malignant behaviour and the overall survival of these patients is poor, with majority of women succumbed to the disease within one year after the initial diagnosis.<sup>2,3,4</sup>

#### CASE REPORT

A 41-year-old female presented with heavy uterine bleeding and back pain for two months duration with constitutional symptoms of tiredness and easy fatigability due to heavy bleeding per vaginum. The uterine bleeding had progressively increased. Endometrial curettage was done twice which was non-diagnostic. Ultrasonogram (USG) was done as an initial work but the only report by the ultrasonologist was a bulky uterus and the size was not mentioned. Considering the age and presentation of the patient, the initial impression of the gynaecologist was a leiomyosarcoma of the uterus and triggered further investigations. On computed tomography scan (CT) of abdomen, a hypodense lesion was identified within the uterus, indicative of a fibroid (Fig. 1A). Left

lower lobe of lung showed a well-defined soft tissue density lesion and an ill-defined lytic lesion at D9 vertebral body. Magnetic resonance imaging (MRI) scan of the whole spine showed a hyperintense signal at D9 vertebra suggesting a possibility of a bony metastasis. Bone scan also revealed similar osteoblastic lesion involving D9 vertebra.

Positron emission tomography (PET)-CT showed a metabolically active bulky uterus with a well-defined soft tissue density lesion in the left lower lobe of both lungs with bony lesions at D9 vertebra and 10<sup>th</sup> rib (Fig. 1B). In addition, hypermetabolic enlarged lymph nodes were also identified at the right internal iliac and precaval lymph nodes.

The patient underwent a debulking hysterectomy with bilateral tubes and ovaries since the initial endometrial curettage was

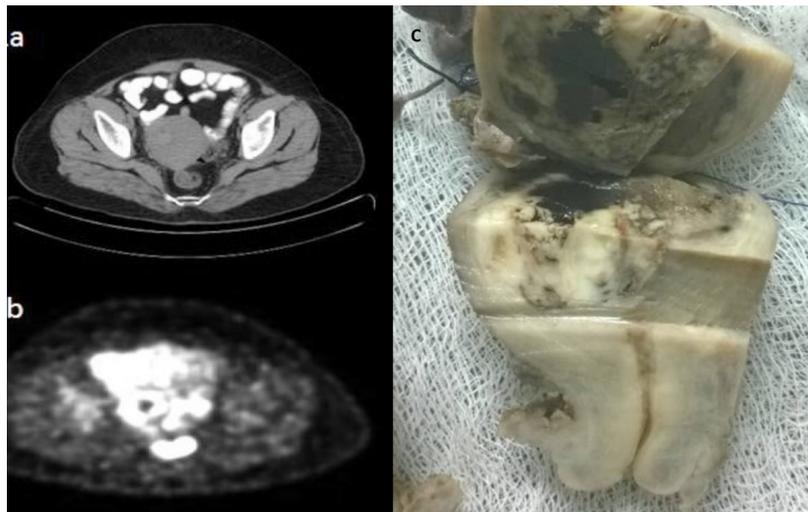


FIG. 1: CT scan (a) revealed uterine mass which was hypermetabolic on PET-CT (b). Cut surface of uterus, with myometrium showed an ill-defined, grey-white haemorrhagic tumour under the endometrium (c).

non-diagnostic and due to the deep-seated nature of the lesion, surgery was planned with a palliative intent to establish a diagnosis. On gross examination, the cut surface of myometrium showed a large globular tumour measuring 4.5 cm in maximum dimension, with intact overlying endometrium (Fig. 1C). The tumour was grey brown with large areas of haemorrhage and showed multiple satellite nodules on the overlying serosa of the fundus.

Microscopic examination revealed a normal endometrium with underlying myometrium occupied by a poorly differentiated tumour arranged in solid nests with areas of alveolar and vasoformative pattern. The neoplastic cells showed epithelioid morphology having eccentric nuclei with moderate amount of eosinophilic cytoplasm and hyaline globules within its cytoplasmic tummy, resembling rhabdoid cells (Fig. 2). Lymphovascular emboli

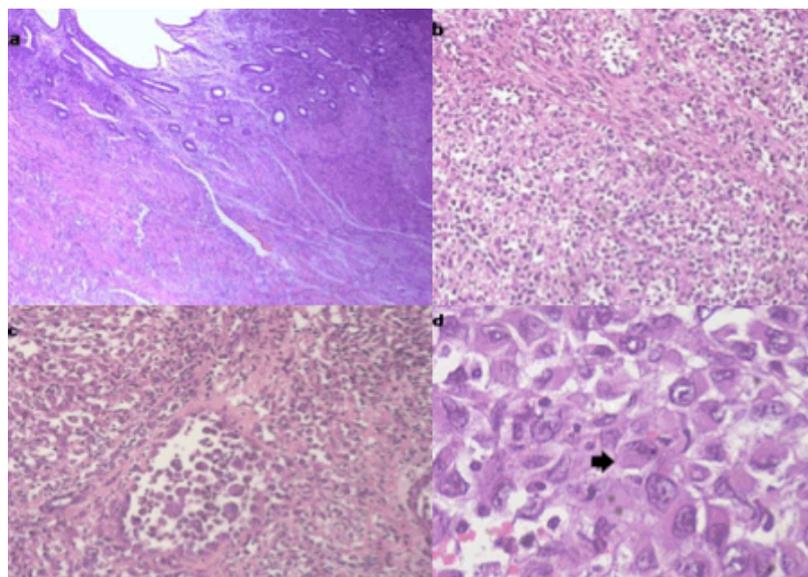


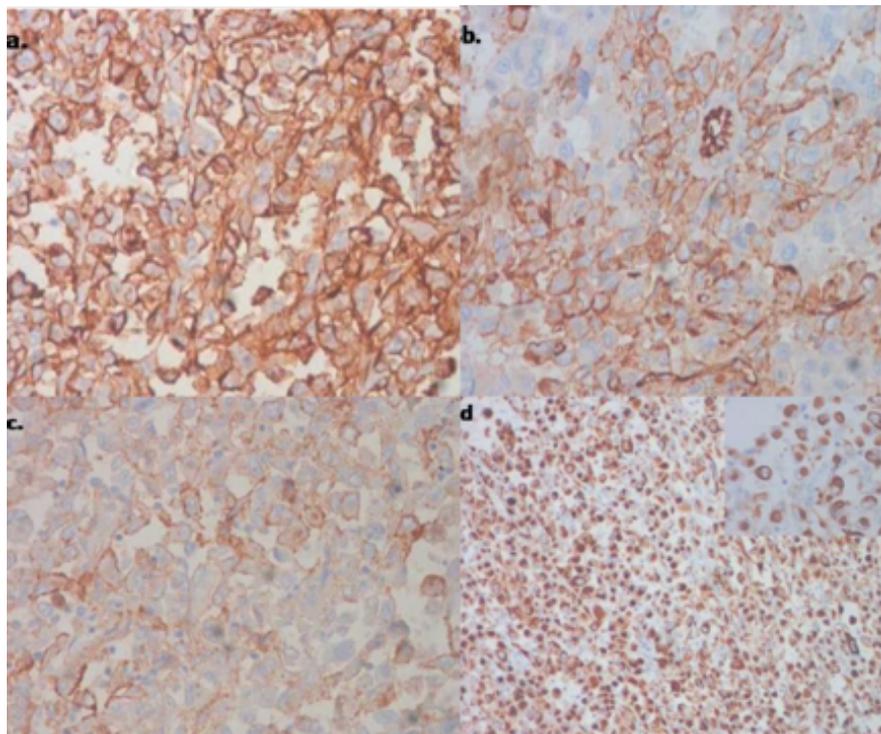
FIG. 2: (a) Normal endometrial glands with underlying myometrium occupied by a poorly differentiated tumour (H&E; x40). (b&c) A poorly differentiated tumour arranged in solid nodules as well as in vasoformative arrangement resembling alveolar pattern. (b. H&E; x100, c: H&E; x200). (d) The neoplastic cells showed epithelioid morphology with eccentric nuclei and moderate eosinophilic cytoplasm, and rhabdoid morphology with intracytoplasmic hyaline globules (arrow) (H&E; x400).

**TABLE 1: Immunostains used with clones and dilutions**

| IHC marker     | Clone (Manufacturer)     | Dilution |
|----------------|--------------------------|----------|
| CK             | AE1/AE3 (Dako)           | 1:100    |
| Vimentin       | V9 (Dako)                | 1:50     |
| LCA            | 2B11 + PD7/26 (Dako)     | 1:200    |
| CD31           | JC70A (Dako)             | 1:70     |
| CD34           | QBEnd10 (Dako)           | 1:50     |
| Thrombomodulin | 1009 (Dako)              | 1:50     |
| S-100          | Polyclonal Rabbit (Dako) | 1:1200   |
| FLI-1          | MRQ-1 (Cell Marque)      | 1:25     |
| Desmin         | D33 (Dako)               | 1:100    |
| SMA            | 1A4 (Dako)               | 1:50     |
| Myogenin       | F5D (Dako)               | 1:25     |
| HMB-45         | HMB45 (Dako)             | 1:50     |
| INI-1          | MRQ-27(Dako)             | RTU      |

and perineural invasion was also observed. Multiple satellite tumour nodules were present within the myometrium, on the fundic serosal surface, endocervical crypts and vaginal cuff cut ends. Tumour showed large areas of necrosis

(40%). Immunohistochemical (IHC) staining was performed on Ventana platform with clones and dilutions of antibodies as shown in Table 1. On IHC (Fig. 3), the tumour cells expressed CK and vimentin (intracytoplasmic tummy like



**FIG. 3:** (a) Immunostaining for CD34 with strong positive membranous staining in tumour cells (x200). (b) Immunostaining for CD31 with positive membranous staining in tumour cells (x200). (c) Immunostaining for thrombomodulin with positive membranous staining in tumour cells (x200). (d) Immunostaining for cytokeratin with strong positive membranous and cytoplasmic staining in tumour cells (x200), with tummy like globular positivity (inset) (x400).

inclusions), CD34, CD31, thrombomodulin and FLI-1. Stains for LCA (CD45), HMB45, S-100, Desmin, SMA, and myogenin were negative. INI-1 immunostains were also done which did not reveal any loss. Thus, a diagnosis of primary uterine epithelioid angiosarcoma with rhabdoid morphology was rendered. Patient was started on paclitaxel-based chemotherapy regimen, however after 4 months of initial diagnosis she succumbed to the disease.

## DISCUSSION

A variety of mesenchymal tumours, both malignant and benign, can occur within the uterus including endometrial stromal tumours, uterine tumours resembling sex cord stromal tumours, smooth and skeletal muscle tumours.<sup>1</sup> Angiosarcoma is a malignant tumour of endothelial cells, mostly arising in the skin or superficial soft tissues of the breast, spleen, liver and bone. Angiosarcomas are rarely reported to originate in the uterus, cervix, fallopian tube, ovary, parametrium, broad ligament and vagina.<sup>2,3</sup>

Primary uterine angiosarcoma is a rare tumour with only 23 documented cases in the English literature. Grossly, these tumours are large, haemorrhagic, and often extensively necrotic that grow within the myometrium.<sup>5</sup> Angiosarcomas are tumours of the endothelial cells that line the blood vessels.<sup>2</sup> The first case of primary uterine angiosarcoma was reported in 1902 by Silberberg *et al.*<sup>6</sup> They occur predominantly in peri and postmenopausal women.<sup>2</sup> In a review of first 19 cases, 74% (14 of 19) were perimenopausal with a mean age of 55 years.<sup>3</sup> A case occurring in the premenopausal age of 35 years has been described with extensive extrauterine spread.<sup>7</sup>

Uterine angiosarcomas commonly present with uterine bleeding, anaemia, pelvic masses and weight loss.<sup>2,3</sup> The macroscopic appearance of an angiosarcoma is similar to that in other sites forming a haemorrhagic, partially cystic or necrotic mass.<sup>1</sup> Similar appearance was evident in our case of myometrial tumour with presence of overlying uninvolved endometrium. Diagnosis on endometrial curettage is usually not possible as in most cases the myometrial tissue is generally not reachable.

The current case, apart from having vasoformative pattern, it also had peculiar rhabdoid morphology. The tumour cells lining the vascular structure exhibited large cells with moderate N/C ratio, eccentric nuclei and cells with dense pale pink cytoplasm with a

hyaline globoid like cytoplasmic inclusions. The dense cytoplasm, in most instances stains with intermediate filaments such as pan-cytokeratin, had an intracytoplasmic blob like appearance.

The neoplastic cells in angiosarcomas are generally immunoreactive for low molecular cytokeratin and also vascular differentiation markers such as CD31, CD34, ERG1, FLI1, thrombomodulin, GLUT1 and factor VIII-related antigen.<sup>1,5</sup> Muscle markers such as actin and desmin, ER/PgR (oestrogen and progesterone receptors), S-100, LCA and HMB-45 are all negative.<sup>2</sup> The major differential diagnosis include sarcomatous overgrowth in a carcinosarcoma (malignant mixed mullerian tumour) and adenosarcoma.<sup>1</sup> Other possible differential diagnosis which could raise diagnostic dilemma in descending order of frequency include a high grade leiomyosarcoma, malignant melanoma and an alveolar rhabdomyosarcoma.<sup>2</sup> All these tumours have a characteristic histomorphology. However, in the event of overlapping morphological features, immunohistochemistry can play a vital role in distinguishing all of the above mentioned differential diagnosis.

Endometrial curetting in some myometrial based tumours are difficult to sample and possess a substantial risk of an iatrogenic perforation. Even if curetting is successful they can still pose a great diagnostic challenge by expression of pan cytokeratin. Hence, one should be aware of this entity as their behaviour and progression are quite different from other epithelial tumours of mullerian origin. The unusual morphological finding in our case was the presence of "rhabdoid" morphology which on cytomorphology showed the presence of hyaline cytoplasmic inclusions. These inclusions were even more enhanced via pan-CK immunostain which were highlighted as tummy like inclusions. Epithelioid angiosarcomas can exhibit rhabdoid morphology.<sup>8</sup> Rhabdoid morphology can also be seen in various other tumours for example renal epithelial tumours and anaplastic thyroid tumour. Rhabdoid morphology is considered a progression of tumours of diverse tissue histotype to a higher grade, more aggressive neoplasms.<sup>9</sup>

Angiosarcomas have a tendency for both local recurrence and early distant metastasis despite aggressive multimodality therapy.<sup>2</sup> The predominant prognostic factor seems to be the size of the tumour at diagnosis and the presence of extra pelvic disease.<sup>3</sup> Generally, the median survival of a patient diagnosed with uterine

angiosarcoma is known to be rather short, in the range of 1 to 2 years, and the reported 5-year survival rate is 10-35%. Recurrence occurs on an average at 8.2 months.<sup>3</sup> Although radiation and chemotherapy are options being utilised, no consensus exists for an optimal therapy.<sup>3</sup> Paclitaxel is currently the most commonly used drug for angiosarcoma.<sup>2</sup>

## CONCLUSION

In conclusion, primary angiosarcomas of the uterus are rare tumours. They not only pose a diagnostic challenge to the clinician due to the deep myometrial localisation but also to the pathologist, in mimicking a carcinosarcoma.

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