

Primary Uterine Angiosarcoma

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Primary uterine angiosarcoma is a malignant tumor of the vascular endothelium that occurs predominately in peri and postmenopausal women with uterine bleeding and anemia.

We present a case of a 66-year-old woman with uterine angiosarcoma who underwent abdominal hysterectomy and bilateral salpingo-oophorectomy, showing the importance of immunohistochemical staining in making the final diagnose.

Histologically, the tumor has anastomosing vascular channels lined by highly atypical endothelial cells. Immunohistochemical staining was positive for endothelial markers CD31 and vimentin, supporting the diagnosis of uterine angiosarcoma.

Primary uterine angiosarcoma tend to demonstrate a highly malignant behavior. The major prognostic factors seems to be the size of the tumor at diagnosis and the presence of extra pelvic disease.

No consensus exist for best possible therapy given the few cases from which to draw conclusions.

Key-words: angiosarcoma; hemangioendothelioma; hemangiosarcoma.

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INTRODUCTION

Primary uterine angiosarcoma is extremely rare and has a poor prognosis.

Angiosarcoma (malignant hemangioendothelioma or hemangiosarcoma) is defined as a tumor of the endothelial cells that lined the blood vessels. It represents less than 1% of all soft tissue sarcomas (1). Although angiosarcomas can arise in any region of the body, most arise in the skin or superficial soft tissue of the elderly (1,2). The most common locations for angiosarcomas include skin, soft tissues, breast, spleen, liver and bone (1). Although rare, angiosarcomas have been reported to originate in the uterus, cervix, fallopian tube, ovary, parametrium, broad ligament and vagina. In the uterus, the vascular channels tend to infiltrate the myometrium and the tumor, if poorly differentiated, can display areas of solid growth (2).

Uterine angiosarcomas are very rare tumor, with only 20 cases valid cases or primary uterine angiosarcomas described.

Angiosarcomas of the uterus may be classified into primary and secondary cases. Predisposing factors for secondary angiosarcoma include ionizing radiation and chronic lymphedema after radical mastectomy (Stewart-Treves syndrome) (2).

CASE REPORT

A 66-year-old white woman presented to our department with a 30-day history of postmenopausal bleeding. The patient immediately sought care and had an outpatient hysteroscopic biopsy of an intra-uterine neof ormation which was interpreted as a uterine sarcoma.

The patient had a medical history significant for hypertension that was well controlled. She had no history of surgery, second malignancy, prior radiation therapy or chemical exposures. Her family history was irrelevant.

Her gynecologic and obstetrics history was resumed by: menarche at 15 years of age, regular menses, catamenia of 5 days, 3G3P (vaginal deliveries) and menopause at 52 years of age, without previous hormone therapies.

On physical examination, her height was 160 cm, weight 65 Kg, 36.2°C, pulse 101 bpm and regular, and blood pressure 145/84 mmHg. Her heart and respiratory sounds were normal. The bimanual examination revealed an enlarged 13-week-size uterus, with adnexa not palpable. Papanicolaou smears of the cervix revealed no atypical findings.

On routine laboratory studies a slight microcytic anemia was diagnosed (Hb: 10.3 g/dl)

A transverse contrast-enhanced CT image showed a strongly enhanced central area in the uterine cavity (Figure 1).

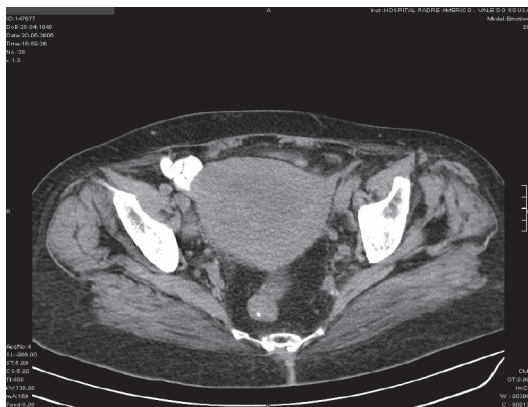


Fig. 1 - Transverse section of contrast-enhanced CT image.

Approximately 2 weeks after her biopsy, she underwent an exploratory laparotomy, with total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy. The ovaries and fallopian tubes were atrophic in size, the uterus weighed 660 g and measured 12x13x7.5 cm. The macroscopic appearance of the uterine cavity was spongy hemorrhagic tumor with necrotic tissue (Figure 2).

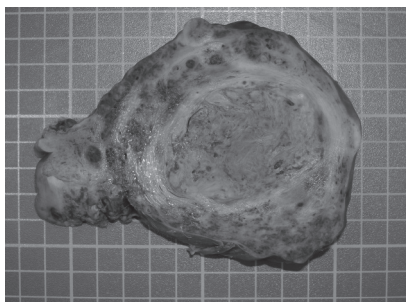
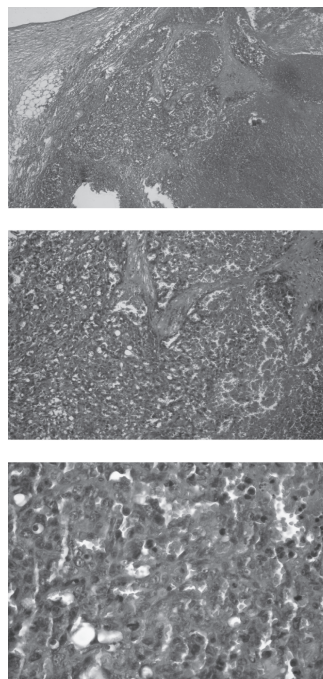


Fig. 2 - Gross view of the surgical specimen. Central submucosal neoformation with 7 cm (leiomyoma). Hemorrhagic and thickness of the endometrium. Hemorrhagic round neoformations in the surrounding myometrium.

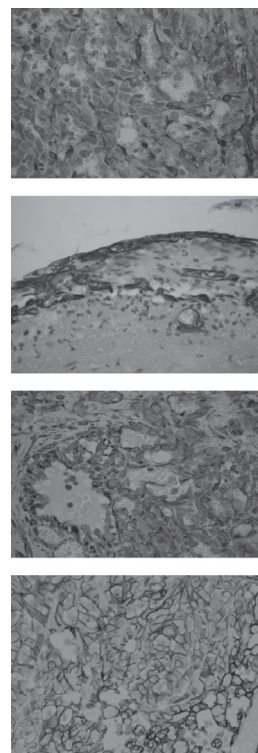
Final pathology was interpreted as a high-grade endometrial stromal sarcoma with pathologically positive lymph nodes (Figures 3-5).

The immunohistological examination confirm the vascular origin of the tumor, staining positive for CD31 and vimentin (Figures 6-9).

Postoperatively, the patient was referred to the Oncology Institute (Porto) and six courses of adjuvant chemotherapy (paclitaxel) were administered. The patient has been on a 15 months follow-up with metastatic lesions in bone, liver, adrenal glands and inguinal lymph nodes diagnosed 9 months after surgery; it was decided to perform palliative chemotherapy of second line with doxorubicin.



Figs. 3-5 - Microscopic findings. The tumor was composed of vascular channels of irregular size and shape. Vascular channels lined with neoplastic endothelial cells with mitotic figures (hematoxylin and eosin). 3 - (4x10); 4 - Myometrial invasion by angiosarcoma (10x10); 5 - (x400).



Figs. 6-9 - Immunohistochemical findings. 6 - Actin strains positive in muscle cells and negative in malignant cells (x400); 7 - Keratin strains focally positive in epithelial cells and negative in malignant cells (x400); 8 - Vimentin strains strongly positive in malignant cells (x400); 9 - CD31 strains strongly positive in malignant cells (x400).

DISCUSSION

Soft tissue sarcomas account for less than 1% of all malignancies (1), and angiosarcomas comprises just 2% of all soft tissue sarcomas. Pathologically, it appears that two criteria must be met to demonstrate convincingly that a neoplasm is a primary vascular neoplasm. One must show that the cells composing the tumor are of vascular origin and that the lesion in question is not a more common uterine neoplasm with extensive vascularity, such as a vascular leiomyoma (2,3). Anastomosing vascular channels lined by highly atypical endothelial cells should be seen.

Higher grade lesions have a tendency for both local recurrence and early distant metastasis despite aggressive multimodality therapy (1,4).

Immunohistochemical is the preferred method for diagnosis today. Muscle markers such as actin and desmin, ER/PR (estrogen and progesterone receptors), S-100, Kermix, LCA and HMB-45 are usually all negative. CD31, factor VIII, vimentin and Q bend, all endothelial cell markers are usually positive (2,3).

The differential diagnosis of angiosarcomas of the uterus can include carcinosarcoma (malignant mixed Mullarian tumor), leiomyosarcoma, adenosarcoma and hemangiopericytoma (2). Witkin et al point out that a clear distinction must be made between an angiosarcoma and a highly vascular smooth muscle tumor such as a leiomyoma.

Generally, the median survival of a patient with uterine angiosarcoma is known to be rather short, in the range of 1 to 2 years (2), and the reported 5-year survival rate is 10-35% (1). In general, patients with uterine angiosarcomas tend to have poor prognosis mostly related to the aggressive nature and the metastatic potential of these tumors.

The rarity of this tumor has meant that optimal management protocols have not been established. Nevertheless, surgical resection is the only potentially curative approach for this disease. Having said that, following surgical resection of angiosarcoma local and distant recurrence is common. Although several authors have tried combination chemotherapy, only limited success has been reported. Paclitaxel is currently the most commonly used drug for angiosarcoma. The role of adjuvant chemotherapy is unknown (1).

In conclusion, despite its rarity, primary uterine angiosarcoma should be considered in the differential diagnosis of uterine tumors.

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