Case Report

# Sclerosing Perivascular Epithelioid Cell Tumor of the Uterus: A Rare Entity Posing Diagnostic Challenge

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**Abstract**

Perivascular epithelioid cell tumor (PEComa) is a rare mesenchymal uterine tumor and the histological variant, sclerosing PEComa is exceedingly rare. Sclerosing PEComas preferentially occur in the retroperitoneum and occurrence in the uterine corpus is seldom seen. These tumors pose a diagnostic challenge and need distinction from morphological mimickers such as epithelioid smooth muscle tumors, endometrial stromal sarcoma, and metastatic carcinoma. Accurate diagnosis can be established coupling histomorphology with immunostaining. The distinction from other entities is of prime importance considering the therapeutic and prognostic implications. Herein, we describe a case of uterine sclerosing variant of PEComa with diagnostic difficulties and key to diagnose this entity.

**Keywords:** *Mesenchymal, perivascular epithelioid cell tumor, sclerosing, tumor, uterine*

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## Introduction

The nomenclature of Perivascular epithelioid cell tumour (PEComa) was first given by Bonetti *et al*[1] in 1992. These are a rare family of tumors encompassing angiomyolipoma, clear cell sugar tumor, lymphangioleiomyomatosis, clear cell myomelanocytic tumor of the falciform ligament, etc.[2] They are known to occur at various anatomic locations with nearly a quarter of them occurring in the female genital tract.[3] In the female genital tract, the uterine corpus is involved in most of cases with the cervix, adnexa, vagina/vulva, and broad/round ligament being rare sites.

PEComas are mesenchymal tumors composed of perivascular epithelioid cells which characteristically have a dualistic myomelanocytic immunophenotype.[1,4] They are composed of epithelioid or spindled cells surrounded by delicate thin-walled vasculature. Variable amount of stromal hyalinization can be seen. Stromal hyalinization exceeding 50% gives rise to an exceedingly rare morphological variant called the sclerosing variant of PEComa.[5] Herein, we describe a case of uterine sclerosing variant of PEComa with its morphological differentials and approach to an accurate diagnosis of this rare entity.

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## Case Report

A 29-year-old female with one live issue presented with abdominal distension, heavy menstrual bleeding for 2 years with pain abdomen, and passage of clots. She complained of awareness of mass per abdomen, early satiety, and weight loss. Ultrasound abdomen done outside revealed a large uterine mass with increased vascularity for which fine-needle aspiration cytology was done which was nondiagnostic. Subsequently, biopsy done outside revealed a morphological diagnosis of malignant neoplasm. Clinical and radiological findings were consistent with sarcoma. The patient gave a history of a rapid progression of abdominal mass over the last 4 months. Per the abdomen, the uterine mass was hard and 24 weeks in size. Per vaginum, the mass was fixed and hard with the cervix pushed anteriorly. Magnetic resonance imaging revealed a huge uterine mass (9.3 cm × 19.1 cm × 24 cm) with increased vascularity, internal cystic areas, and obliterating the entire endometrial cavity. With a radiological and

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preoperative biopsy diagnosis of uterine sarcoma, hysterectomy was done. Intraoperatively, the uterus was enlarged (~25 cm × 20 cm) with a degenerating mass occupying the pouch of Douglas and the cervix was pushed up. The mass was densely adhered to the urinary bladder and the bowel wall. The adhesions were released by sharp dissection. Bilateral fallopian tubes were stretched over the mass and appeared edematous. Both ovaries appeared healthy and were preserved.

On gross examination, the uterus was enlarged and bosselated, measuring 25 cm × 20 cm × 12 cm. On bivalving the uterus, 21 cm × 19 cm × 12 cm solid gray-white circumscribed tumor was seen replacing the myometrium and compressing the endometrial cavity [Figure 1a]. The tumor was firm in consistency. Bilateral ovaries and fallopian tubes were unremarkable.

Histopathologic sections showed a relatively well-circumscribed tumor in cords, trabeculae, and focally as nests in an extensively sclerotic stroma [Figure 1b]. Tumor cells showed were round-to-oval nuclei, with vesicular chromatin, nucleoli, and moderate amount of clear to slightly eosinophilic cytoplasm. Stromal hyalinization was striking [Figure 1c and d]. Mitotic count was <1/50 HPF. Lymphovascular invasion was not identified. Findings were of a mesenchymal uterine neoplasm.

On immunohistochemistry, tumor cells were positive for HMB-45 [Figure 2a], desmin, and vimentin [Figure 2b]. Patchy positivity for h-caldesmon was seen [Figure 2c]. The tumor cells were negative for CD10, progesterone receptor, cyclin D1, pan-cytokeratin, calretinin, and inhibin [Figure 2d]. The case was reported as PEComa of uncertain malignant potential. The patient was managed surgically without any chemotherapy, 1-year postsurgery is doing well and is on follow-up.

## Discussion

The variants of PEComa described in the uterus include sclerosing PEComa, PEComatosis, lymphangioleiomyomatoses such as PEComa, PEComa with transcription factor E3 (TFE3) rearrangement, and PEComa with RAD51B rearrangement.[6] Sclerosing PEComa is seen preferentially in females from 34 to 73 years, with a mean of 49 years with retroperitoneal location.[5] The patient can present with abnormal vaginal bleeding and/or abdominal pain. Occasional rupture of the uterus and hemoperitoneum has also been reported.[7] Several hypotheses have been proposed for the histogenesis of PEComas which remains an enigma. Nevertheless, the association between PEComas and the tuberous sclerosis complex has been well established.[8] Translocations of TFE3 which is a member of the microphthalmia transcription factor (MiTF) gene family have been reported.

Largest series on sclerosing PEComas by Hornick and Fletcher[5] had tumor size varying from 4.5 to 28 cm. The index case had a large tumor measuring 21 cm in maximum dimension. Sclerosing PEComas are grossly well-circumscribed, solid, firm, or rubbery in consistency with a tan, gray, or white appearance. Sections show a well-circumscribed tumor, rarely with infiltrative margins with cells arranged as cords and trabeculae, embedded in an extensively sclerotic stroma as seen in our case. Sclerosing PEComas are a diagnostic challenge lacking almost pathognomonic morphological feature of conventional PEComas, i.e., the delicate framework of blood vessels imparting a nested or alveolar appearance.

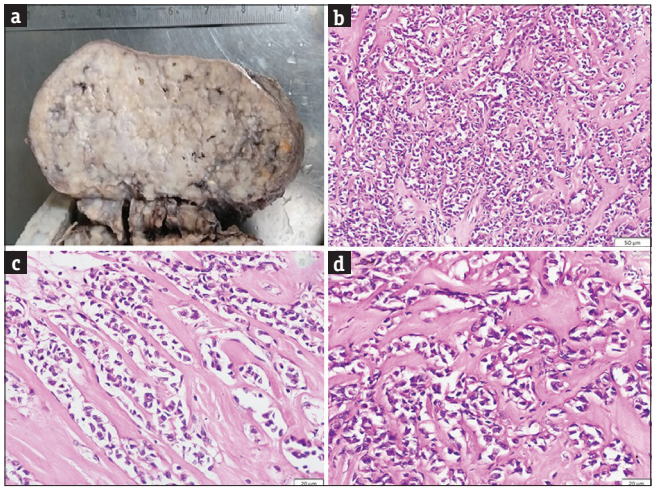


**Figure 1:** (a) Gross photograph showing cut section of the tumor (b) Tumor cells arranged in small nests and cords (H and E, ×200) (c) Cords of tumor cells separated by thick hyalinized stromal tissue (H and E, ×400) (d) Bands of thick hyalinized tissue (H and E, ×400)

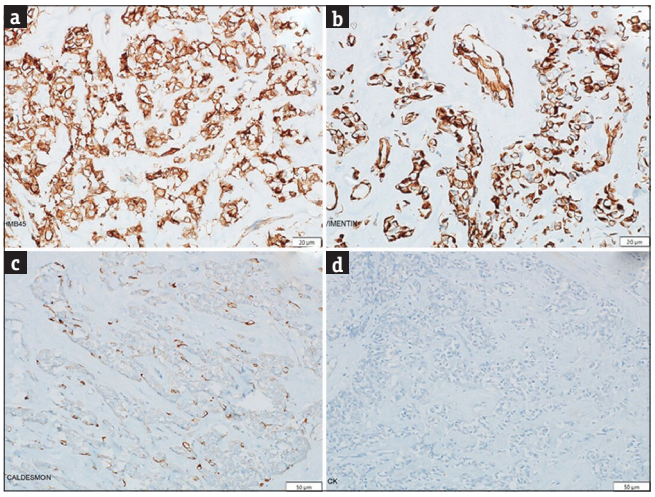


**Figure 2:** (a) Tumor cells with diffuse and strong positivity for HMB45 (IHC, ×200) (b) Tumor cells strongly positive for vimentin (IHC, ×200) (c) Occasional cells positive for caldesmon (IHC, ×200) (d) Cells are negative for pan-cytokeratin (IHC, ×200)

These are histomorphological differences among the broad group of sarcoma variants including epithelioid leiomyosarcoma and endometrial stromal sarcoma.[5,9]

To clinch an accurate diagnosis, a panel of immunostains needs to be employed. PEComas are immunoreactive for at least one melanocytic marker (HMB-45, melan-A, tyrosinase, and MiTF) and one smooth muscle marker (smooth muscle actin, pan-muscle actin, desmin, h-caldesmon, calponin, and muscle myosin).[2,10] Leiomyosarcoma shows positivity only for smooth muscle markers. Pan-cytokeratin and epithelial membrane antigen help in distinguishing between a metastatic carcinoma and PEComa, being positive in carcinoma.[5] CD10 and cyclin D1 are markers for endometrial stromal sarcoma.

Ascertaining the malignant behavior of PEComas is of paramount importance in planning further management. The latest edition of the World Health Organization blue book provides proposed algorithms for stratifying the behavior of uterine PEComas.[11] According to the modified gynecology-specific criteria, tumors with uncertain malignant potential have <3 of the following features; ≥5 cm, high nuclear grade, necrosis, vascular invasion, and mitosis >1/50 HPF, while malignant ones have 3 or more of these features. The current case as per these criteria falls into PEComas with uncertain malignant potential warranting a close follow-up of the patient. No optimal management strategy or treatment algorithms exist for uterine PEComas as these are rare tumors limiting the scope of randomized controlled trials.[3] Surgical management is the standard of care for the want of an accurate primary preoperative diagnosis which is not established on imaging.[12] PEComas generally have a favorable prognosis, but recurrence and distant metastasis are well-known phenomena which mandate a long-term surveillance program.[3] In the era of personalized medicine, targeted therapies with mammalian target of rapamycin (mTOR) inhibitors have shown promising results in patients with recurrence and those with metastasis.

## Conclusion

Sclerosing PEComas of the uterus are exceedingly rare tumors which pose a diagnostic challenge. Morphological mimics can be distinguished by employing a panel of immunostains. The distinction from other entities is of prime importance considering the therapeutic and prognostic implications.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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