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Malignant perivascular epithelioid cell neoplasm of uterus: A great mimic of fibroid

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Abstract

Perivascular epithelioid cell (PEC) neoplasms are an unusual group of mesenchymal tumors which arise from the perivascular epithelioid Cell that characteristically expresses melanocytic and muscle markers. These neoplasms show a wide range of morphologic spectrum and have been described in multiple anatomical locations which includes uterus. We report a 46-year-old patient diagnosed as uterine fibroid on ultrasonography in whom the hysterectomy specimen unveiled characteristic features of intramural PEComa consisting of small nests and sheets of clear epithelioid cells particularly present around the blood vessels in a background of loose oedematous stroma along with the foci of mature adipose tissue which exhibits myometrial infiltration. The correct diagnosis is crucial as there is an emerging role of mTOR inhibitors which can provide a ray of hope to the patients of PEComa.

Keywords: PEComa of uterus, Angiomyolipoma, Uterine epithelioid cell tumour.

Introduction

Perivascular epithelioid cell tumor (PEComa) is a collection of rare neoplasms defined by the World Health Organization as mesenchymal tumors which on histology and immune staining reveal distinctive melanocytic and smooth muscle differentiation. Hence thought to be derived from perivascular epithelioid cell.[(1)]The PEComa family of tumorincludes AML(angiomyolipoma), CCST(clear cell sugar tumor), LAM (lymphangiomyomatosis), and less well-defined PEComa of other anatomic locations called perivascular epithelioid cell tumor not otherwise specified (PEComa-NOS).[(2)] Most of the published literature on PEComa-NOS is as case reports and series, which emphasize on its presentation and morphology. Here we report a case of uterine PEComa misdiagnosed as fibroid clinico-radiologically. We will discuss this case to stratify it along the risk stratification criteria which may help to improve upon its management.

Case History

A 46-year-old married female visited hospital complaining of abnormal uterine bleeding of 5 months duration. Her past medical history was unremarkable. There was no history of contraceptives use or hormonal therapy. On clinical examination, the uterus was enlarged approx. 24 wks with moderate tenderness in lower abdomen. Ultrasonography showed 14 cm ×12 cm × 8 cm sized, hypoechoic lesion in the uterus with mild vascularity and necrotic changes suggestive of degenerative fibroid. Her hemoglobin level was 8.0gm%, rest all laboratory findings were within normal limits. She underwent total abdominal hysterectomy and bilateral salpingo-oopherectomy. On gross the uterus with cervix was of size 15 cm × 12 cm × 7cm. Endometrial cavity was distorted by the tumor of size 12 cm ×10 cm ×7 cm. It was well circumscribed; the cut surface was solid, greyish white and fleshy. There was also a cyst in the left ovary of size 5 cm × 4 cm × 1.5cm. On cut section, cyst contained sebaceous material and hair. On histology, the tumor revealed two cell types. There was admixture of epithelioid to spindled shaped tumor cells (Fig. 1).

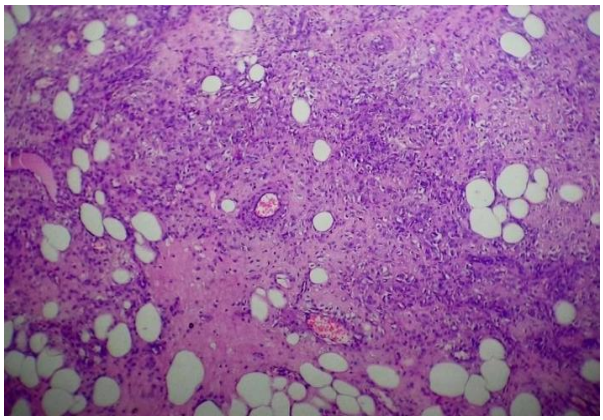

Fig. 1: Tumor composed of epithelioid, cells in diffuse sheets, groups of fat cells and thick walled blood vessels (10X)

The individual cells had eosinophilic to clear cytoplasm with central to eccentric, round to oval nuclei with fine chromatin and inconspicuous nucleoli (Fig. 1a).

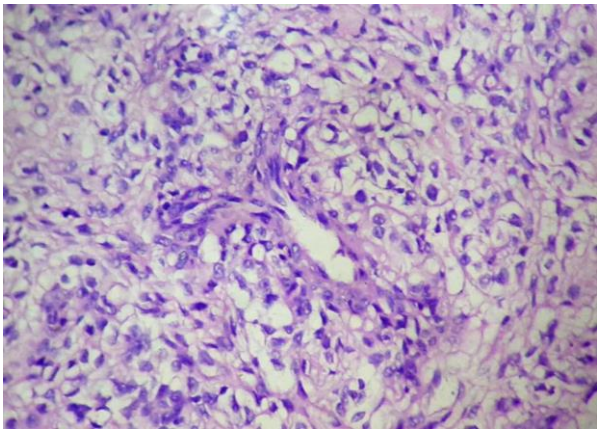

Fig. 1a: Tumor cells having clear cytoplasm, round to oval nuclei with minimal atypia and low mitosis (H&E stain, 40X)

Epithelioid cells were seen arranged around thick walled blood vessels in clusters and diffuse sheets (Fig. 1b).

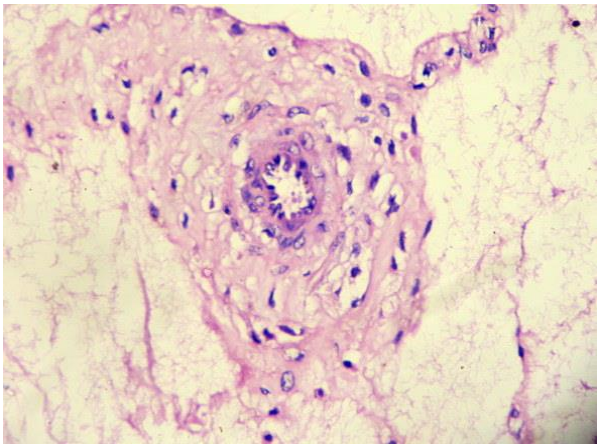

Fig. 1b: Classical perivascular distribution of clear cells (H&E stain, 20X)

Focally the tumor cells were infiltrating into the myometrium. The spindle cell component consisted of short fascicles and bundles having oval to plump nuclei with uniform chromatin. The mature adipocytes were seen in the groups and sheets. Foci of extensive hyalinization and hydropic degeneration were seen. Occasional mitotic figures were noted. There was no evidence of tumor necrosis. The neoplastic epithelioid cells were positive for HMB-45 (Fig. 2).

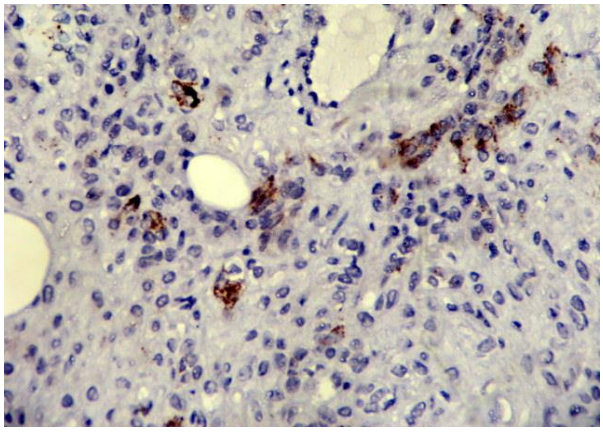

Fig. 2: Tumor cells showing cytoplasmic positivity (IHC- HMB45, 40X)

Considering the above features, the diagnosis of Uterine Perivascular epithelioid tumour (PEComa) was made. Given the size of primary mass and the presence of myometrial infiltration, the high risk features proposed by Folpe et al,[3] we classified it as malignant or high risk PEComa. Endometrium showed combination of hypersecretory and cystically dilated glands with abundant secretion in the lumen. The lining cells showed stratification and at places there was lining of single layer of columnar to cuboidal cells. At places glands showed mucinous metaplasia. The stroma was loose edematous, abundant and showed pseudodecidualization with prominent spiral arterioles. In addition to the above findings there was presence of a mature cystic Teratoma (Dermoid cyst) in the contralateral ovary.

Discussion

In 1994, Bonetti et al[4] forwarded the concept of a family of tumor which comprised of angiomyolipoma, clear cell sugar tumors and lymphagiomyomatosis. It was observed that these three lesions shared a common morphological and immunophenotypical cell type which was previously designated as "perivascular epithelioid cell".[5] Detailed study of these tumors in the different anatomic locations of these cell types suggested the name PEComa, first proposed by Zamboni et alin 1996.These tumors are known for a myomelanocytic phenotype and show immune reactivity for both melanocytic (HMB-45/melan-A) and smooth muscle (actin /desmin) markers.[6] The most common primary sites for PEComa-NOS is female genital tract and more specifically the uterus.[7] Some PEComa are seen in patients with tuberous sclerosis complex.[8] Patients with uterine PEComa show symptoms such as abnormal uterine bleeding, lower abdominal pain and palpable mass, which is similar to other uterine tumors particularly fibroid.[1] Thus, uterine PEComa are often misdiagnosed as uterine leiomyomas before surgery. Therefore the correct diagnosis totally depends on pathologist high index of suspicion.

PEComa are usually composed of epithelioid cells having clear to granular eosinophilic cytoplasm with focal perivascular accentuation and spindled cell component.[1] In our case, tumor cell predominantly consist of epithelioid cells with clear to eosinophilic cytoplasm mainly seen around the blood vessels. In addition there is a component of numerous thick walled blood vessels, bundles of spindle shaped cells and adipocytes. The mitosis was a rare phenomenon. The tumor showed myometrial infiltration at places. The epithelioid cells showed cytoplasmic positivity for HMB45. School Meester et al reported HMB-45 in PEComa as the most sensitive (16/16 positive, 100%) marker. Desmin was positive in 15 out of 15 cases (100%) and SMA in 14 of 15 (93%).[9] The diagnosis of uterine PEComa is challenging as it shares a distinct clinic-morphologic and immuno-phenotypic overlap with some myometrial smooth muscle neoplasm. Amongst this category are epithelioid smooth muscle tumours (ESM) which exhibit cells in nests or diffuse sheets displaying eosinophilic cytoplasm, although a clear appearance may be seen.[10] These tumours generally do not reveal vascular network that is characteristic of PEComa. Extracellular myxoid material has been described in ESM. Uterine PEComa definitely display at least focal immunoreactivity for melanocytic markers in almost all cases (100%), while ESM is rarely positive for HMB-45. PEComa need also to be differentiated from endometrial stromal sarcoma (ESS). Dominant spindle cell component seen as short fascicles and present around thin walled blood vessels is a classical feature of ESS. It is negative for HMB-45, SMA and Desmin.[6,8] PEComa-NOS even though rare has become an increasingly recognized entity. The evaluation of adverse risk factors like tumor size and infiltration of myometrium predicts the recurrence after surgical resection and help in postoperative counseling.[3] Because both these adverse risk factors were evident in our case, we classified PEComa into high risk category.

To conclude, the knowledge of morphological features are of great help in differentiating PEComa from epithelioid smooth muscle tumors and its mimics which is further established by immunohistochemistry. The correct diagnosis is indispensable for the reason that mTOR inhibitors now can provide a ray of hope in the treatment of patients of PEComa.

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