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Perivascular epithelioid cell tumor of the uterus: Report of two cases and mini-review of the literature



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ABSTRACT

INTRODUCTION: Perivascular Epithelioid Cell tumor (PEComa) is a rare neoplasm of mesenchymal origin, with the uterus being the most common site of appearance, regarding the female genital tract.

CASE REPORT: We present two cases of PEComas of the uterus in patients aged 57 and 42-years-old, presented to our department with palpable abdominal masses and abnormal vaginal bleeding. During follow up period, both patients are free of recurrent disease one and two years after surgery, respectively, without receiving any adjuvant treatment.

CONCLUSIONS: PEComa of the female gynecological tract is a rare entity presenting with variable symptoms and different prognosis for each individual case. The diagnosis is based on histopathology and immunohistochemistry reports and the optimal treatment is the surgical resection of the tumor.

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1. Introduction

Perivascular epithelioid cell tumor is a rare mesenchymal neoplasm. It originates from the perivascular epithelioid cell (PEC) line and was first described in 1943 as an abnormal myoblast [1]. Several years later and through morphological and immunohistochemical studies, these tumors showed an unusual cell type with a perivascular distribution. Moreover, these cells are characterized immunoreactive for melanocytic markers, with an epithelioid appearance and a clear acidophilic cytoplasm, thus the term “perivascular epithelioid” was introduced [2]. Progressively, this family of tumors came to include angiomyolipoma, clear cell sugar tumors, lymphangiomyomatosis, clear cell myomelanocytic tumor of the falciiform ligament and other clear cell tumors [3]. According to World Health Organization (WHO), PEComas are now defined as mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells [4].

PEComas of the female gynecological tract account for nearly 25% of all the PEComa cases worldwide [5]. In most of the PEComa cases, the original site of appearance of the tumor was the uterine corpus, while there are a few reports in the literature where the

cervix is involved [6–8]. Most patients are in their 40s and the lack of non-specific clinical features makes the tumor hard to diagnose. In most of the cases, PEComa presents with abnormal vaginal or peritoneal bleeding, abdominal pain and uterine symptoms, such as rupture of the uterus and hemoperitoneum, while the radiological appearance is also a diagnostic challenge [7–9].

Uterine PEComas are classified as i. benign neoplasms, ii. tumors of uncertain malignant potential and iii. malignancies. Six high-risk criteria have been proposed for the classification of PEComas: tumor size ≥ 5 cm, infiltrative growth pattern, high nuclear grade cellularity, mitotic rate $> 1/50$ high power fields (HPF), necrosis and vascular invasion [10]. Tumors are classified as benign when they present with no features associated with malignancy. The term “uncertain malignant potential” refers to neoplasms that are characterized by a single histological feature, including nuclear pleomorphism or multinucleated giant cells or a size ≥ 5 cm. Malignant tumors are the ones that show 2 or more of the aforementioned criteria [11].

2. Case report 1

A 57-year-old Caucasian woman presented to our clinic with a palpable abdominal mass and symptoms of obstructive uropathy. Her past medical history included a total abdominal hysterectomy 15 years ago due to uterine fibromas and abnormal menstrual bleeding. Histopathology also reported a simple endometrial

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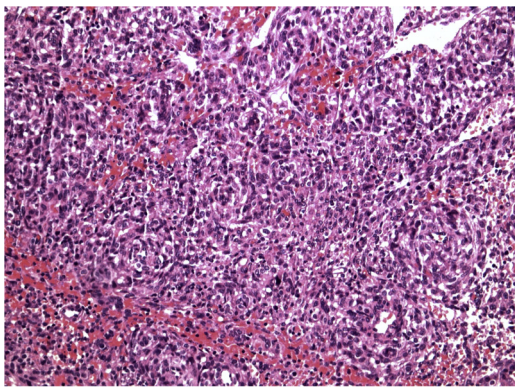


Fig. 1. Spindled and epithelioid cells with perivascular localisation.

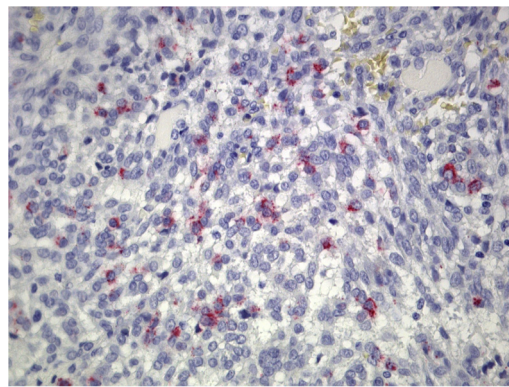


Fig. 2. Immunohistochemical stain HMB-45 positive.

hyperplasia without atypia. Four years later she underwent another surgery due to an abdominal mass located in the pouch of Douglas that was strictly attached to the sigmoid colon. The mass was removed and a radical omentectomy and bilateral salpingo-oophorectomy was conducted. Histopathology report stated that the mass was a fibroma with no malignant characteristics.

Physical examination during her last visit showed a large abdominal mass. CT scans revealed two more of reducible size, located at the parametria, that were adjacent to both ureters. The masses were surgically removed and small parts of both ureters had to be excised while ureteral catheters (pig-tails) were placed in order to resume the synechiae of the urinary tract.

Macroscopic analysis showed a pelvic mass sized $13 \times 13 \times 7$ cm and two smaller ones at the right and the left parametrium, sized 4 cm and 8 cm, respectively. Histopathology report showed that all the tumors removed were of mesenchymal origin with epithelioid and necrotic characteristics (Fig. 1). The tumor cells had a mitotic rate of 10/50 HPF and immunohistochemistry report came back positive for HMB-45, SMA, h-Caldesmon and p53 while negative for p16 and S100. The report concluded that the morphological and immunophenotypical characteristics of the tumor were compliant with a Perivascular Epithelioid Cell tumor.

3. Case report 2

A 42-year-old Caucasian woman presented to our clinic with pelvic tenderness upon physical examination and abnormal menstrual bleeding. CT scans showed a mass at the uterine wall sized 8 cm with no other pathology. She had a free medical history with no prior surgeries. The patient underwent a dilation and curettage prior to abdominal myomectomy. Histopathology report showed a neoplasm of mesenchymal origin, with immunophenotypical characteristics compliant with Perivascular Epithelioid Cell tumor. The cells showed a mitotic rate $< 1/50$ HPF. Immunohistochemistry report was positive for the melanocytic marker HMB-45 (Fig. 2) and the smooth muscle markers SMA and desmin, while h-caldesmon marker was negative.

4. Discussion

In this study, we report two cases of uterine PEComas in patients with variable symptoms and different medical history. In both cases, an abdominal mass was found by CT scan.

In the first case, the patient had recurrent surgeries due to abdominal masses and her latest symptoms included obstructive uropathy. Uterine PEComa was diagnosed after the third surgery, with the two prior histopathology reports stating uterine fibromas. This constitutes a case of primary uterine PEComa in the basis of a history of a fibromatous uterus. The recurrence of the abdom-

inal masses could raise the hypothesis of a correlation between benign fibromas and tumors of mesenchymal origin, such as PEComas. The tumor was characterized by epithelioid cell morphology, with cells presenting variability in size and shape. Immunohistochemistry revealed expression of the melanocytic marker HMB-45 and the smooth muscle marker h-Caldesmon. The morphologic features and the immunohistochemical staining pattern supported a diagnosis of PEComa.

In the second case, the patient had a clear medical history with no prior surgeries or admissions to a hospital. She presented with abdominal pain and abnormal menstrual bleeding. After the patient's desire to retain her uterus, an abdominal myomectomy was performed. Histopathology report stated that the tumor cells had exhibited no atypia and no prominent nuclei. However, immunohistochemistry report showed that the tumor expressed the melanocytic marker HMB-45 and the smooth muscle markers SMA and desmin, suggesting a case of uterine PEComa.

Bonetti et al. introduced first the term Perivascular Epithelioid Cell tumor in 1992 [2]. Ten years later, the World Health Organization defined PEComas as mesenchymal tumors composed of perivascular epithelioid cells that express both melanocytic and smooth muscle markers [4]. The origin of PEComas remains yet unknown but studies suggest that they arise from neural stem cells that present with the ability to differentiate into both myoid and melanocytic cells [12,13]. Apart from our two, there have been 78 reported cases of uterine PEComas in the literature, the most common site being the female genital tract [14].

PEComas express both melanocytic marker HMB-45 and smooth muscle marker SMA [12]. In our study, these melanocytic and smooth muscle markers were expressed in both cases. In patients with mesenchymal tumors of the uterus, apart from leiomyosarcomas and endometrial stromal sarcomas, PEComas should be considered in the differential diagnosis, despite the fact that distinguishing these mesenchymal neoplasms could be very difficult. Even though PEComas are usually positive for melanocytic markers, there have been reports in the literature of leiomyosarcomas and ESS tumors expressing HMB-45 [15,16].

Regarding PEComas, it seems that the optimal treatment is surgical resection of the tumor. For non-aggressive PEComas, surgery is the treatment of choice, while it has been demonstrated that, in cases of high-risk patients with underlying morbidity, preoperative or neoadjuvant treatment seems beneficial [17]. In both our cases, patients are free of recurrent disease one and two years after surgery, respectively, without receiving any adjuvant treatment. However, the fact that PEComas are extremely rare, makes it hard to conduct randomized controlled trials, in order to assess the outcome of each therapeutic approach.

5. Conclusions

PEComas of the female gynecological tract are a rare entity that presents with variable symptoms and different prognosis for each individual case. The diagnosis is based on histopathology and immunohistochemistry reports and the optimal treatment should be individualized for each patient. However, it seems that surgical resection of the disease is the ideal approach and a close follow-up is obligatory in order to assess the need of adjuvant therapy. Patients should be thoroughly examined with a detailed history, while molecular genetic studies seem to be the future in understanding the nature of these tumors.

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