Case Report

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Pathology Section

Behind the Peritoneum: A Case Report of Rare Retroperitoneal PEComa

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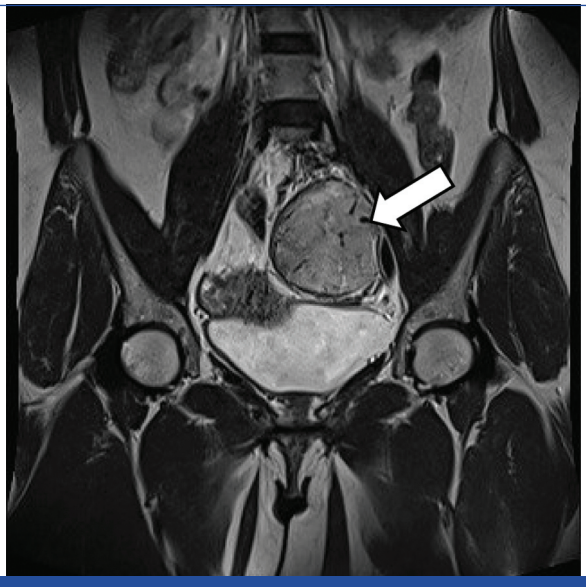
ABSTRACT

The Perivascular Epithelioid Cell tumours (PEComas) are exceptionally infrequent tumours arising from mesenchyme, distinguished by epithelioid appearance and myomelanocytic markers' expression of the proliferating perivascular cells. These tumours can be found in various locations including the lungs, gastrointestinal tract, kidneys, liver, uterus and retroperitoneum. Documented retroperitoneal PEComas are less than 50 in number. Fewer than five cases have been reported in last eight years. Authors hereby report a case involving 28-year-old female patient who experienced abdominal pain which was intermittent and was subsequently diagnosed with retroperitoneal mass measuring 7×6×5.5 cm. The Magnetic Resonance Imaging (MRI) of abdomen and pelvis revealed a well-defined hyperintense mass present on left side of the pelvis, distinct from the separately visualised uterus and ovaries. Surgical resection of the mass was performed during which it was identified as retroperitoneal mass, and histopathological analysis confirmed the diagnosis of PEComa, with immunohistochemical markers positive for Human melanoma Black-45 (HMB-45) and Vimentin, while Smooth Muscle Actin (SMA), Desmin, SOX10, S100 and Cluster Differentiation 34 (CD34) were negative. Surveillance with routine imaging was advised for the patient. She has been under follow-up for the past four months without any symptoms and continues to be actively monitored. This emphasises importance of PEComa to be considered for differential diagnosis for retroperitoneal masses in young women. It also underscores the critical role of histopathology and Immunohistochemistry (IHC) in reaching an accurate diagnosis. The present case contributes to the limited number of reported retroperitoneal PEComa cases in literature.

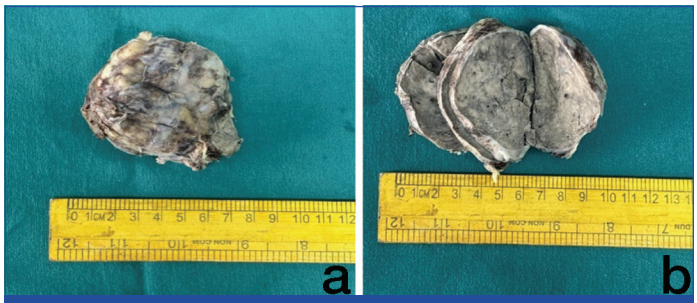
Keywords: Immunohistochemistry, Neoplasm, Perivascular epithelioid cell tumours, Tuberous sclerosis complex

CASE REPORT

A 28-year-old female with one live child and no history of abortion {Para one, Live one and no Abortion (P1L1A0)}, presented to Outpatient Department (OPD) of the hospital with complaints of on and off abdominal pain for past six months. She was a known case of broad ligament fibroid on secondary infertility treatment for the past two years. She had no other co-morbidities and her menstrual cycles were regular. She underwent MRI of abdomen and pelvis, which revealed a well-defined mass which was measuring 6.8×6.1×6.2 cm in left side of pelvis, while the uterus and ovaries were visualised separately. The radiological impression was given as suspicious of paraganglioma or neurogenic tumours [Table/Fig-1]. She underwent surgery to remove the mass. It was only recognised as retroperitoneal mass during surgery. The mass was sent for histopathological examination with provisional diagnosis of paraganglioma. Gross examination revealed a globular grey white to grey brown mass measuring 7×6×5.5 cm, external surface was capsulated and glistening. Cut surface was solid and soft in consistency with few tiny cystic areas [Table/Fig-2a,b]. Grossly, the differentials of fibrosarcoma and smooth muscle tumour were considered.



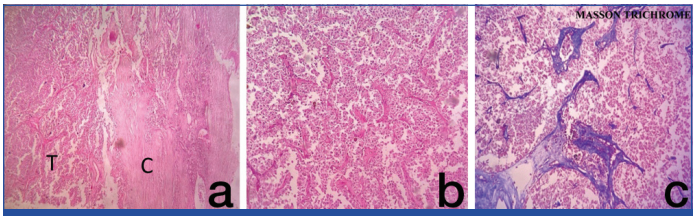
[Table/Fig-1]: MRI abdomen and pelvis revealed a well-defined T2/T1 isotense to hyperintense mass lesion in left-side of pelvis (white arrow).



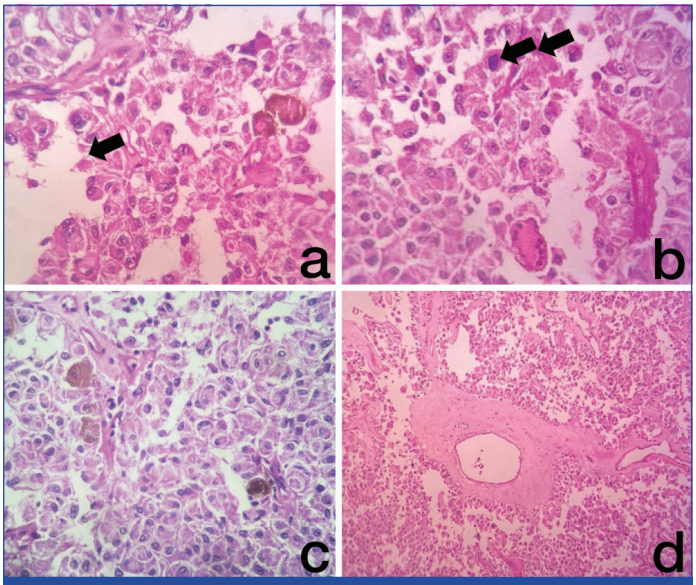
[Table/Fig-2]: Gross features of retroperitoneal mass: a) External surface showing capsule and glistening surface; b) Cut surface shows solid mass with tiny cystic areas.

Microscopy showed partly encapsulated malignant tumour arranged predominantly in alveolar pattern, incompletely separated by sclerosed fibrous septa containing good number of blood vessels [Table/Fig-3a-c]. The individual cells were polygonal, featuring central to eccentric, round nuclei having vesicular appearance, coarse chromatin and conspicuous nucleoli. They also had abundant eosinophilic and granular cytoplasm. Cells with rhabdoid morphology, intracytoplasmic melanin, binucleation and multinucleation, with bizarre hyperchromatic nuclei, perivascular pseudorosettes are noted [Table/Fig-4a-d]. Nesting and dyscohesive pattern also noted along with 3-4 mitotic figures per 10 High Power Field (HPF). Special stains such as Masson Fontana (MF) and Periodic Acid Schiff (PAS) highlighted melanin pigment and glycogen in cytoplasm,

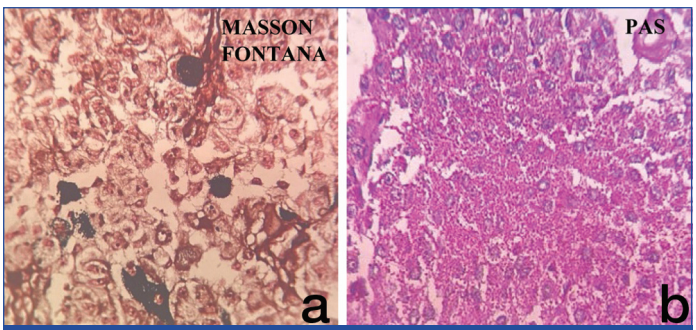
respectively [Table/Fig-5a,b]. Based on these histopathological findings, the differential diagnosis of alveolar rhabdomyosarcoma, PEComa and clear cell sarcoma were considered. IHC with Human Melanoma Black 45 (HMB45) showed strong cytoplasmic and membranous positivity in tumour cells while vimentin showed scattered strong positivity in tumour cells and strong positivity in background blood vessels. SMA and desmin were negative in tumour cells and positive in background blood vessels which act as internal control [Table/Fig-6a-d]. S100, SOX10 and CD34 were negative in tumour cells [Table/Fig-7a-c]. Ki67 proliferative index was 4%. Positive and negative control used for each IHC marker is given in table [Table/Fig-8].



[Table/Fig-3]: Retroperitoneal mass histology: a) Tumour (T) is partially capsulated (C) (H&E, 40x); b) Alveolar pattern of arrangement, incompletely separated by sclerosed fibrous septa containing good number of blood vessels (H&E, 100x); c) Masson trichome stain highlights sclerosed septa (MT stain, 100x).

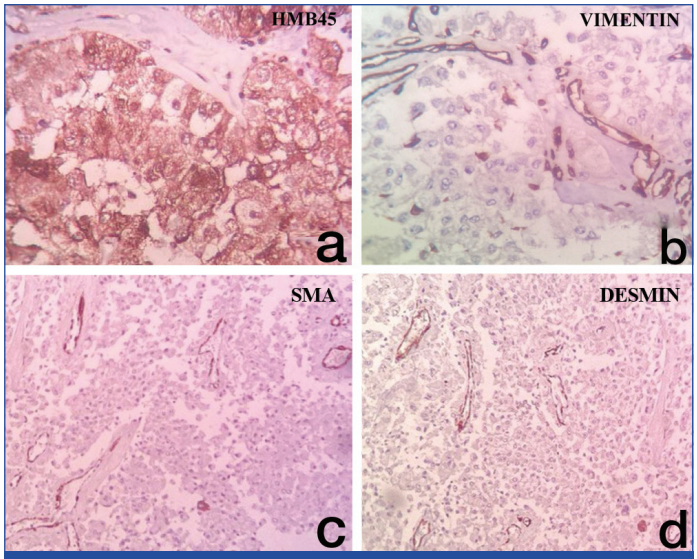


[Table/Fig-4]: Retroperitoneal mass histology: a) Individual cells were polygonal with central to eccentric round vesicular nuclei, coarse chromatin and conspicuous nucleoli with abundant eosinophilic and granular cytoplasm (H&E, 400x); b) Tumour cells with binucleation and multinucleation (arrow below) and with bizarre hyperchromatic nuclei (top arrow) seen (H&E, 400x); c) Intracytoplasmic melanin (arrow) (H&E, 400x); d) Perivascular pseudorosettes are noted (H&E, 400x).

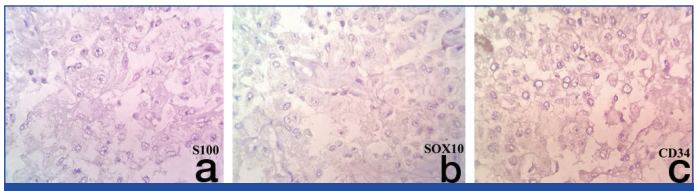


[Table/Fig-5]: a) Masson Fontana (MF) highlighting melanin pigments (MF stain, 400x); b) PAS highlighting glycogen in cytoplasm of tumor cells (PAS stain, 400x).

Based on HMB45 positivity and desmin negativity, alveolar rhabdomyosarcoma differential was excluded. While, S100 and SOX10 negativity excluded the differential of clear cell sarcoma. Based on the above-mentioned histopathological and IHC findings, the diagnosis of PEComa of retroperitoneum was confirmed. Since a radical resection of the mass had already been performed, only routine imaging for surveillance was advised for the patient. She came for a follow-up after three months, during which an MRI was done, and the findings were unremarkable. She has been under follow-up for the past four months without any symptoms and continues to be actively monitored.



[Table/Fig-6]: Immunohistochemical studies: a) HMB45 showed strong cytoplasmic and membranous positivity in tumour cells (HMB45 stain, 400x); b) Vimentin showed scattered strong positivity in tumour cells and strong positivity in background blood vessels (vimentin stain, 400x); c) SMA is negative in tumour cells and positive in background blood vessels which acts as internal control (SMA stain, 100x); d) Desmin is negative in tumour cells and positive in background blood vessels which acts as internal control (desmin stain, 100x).



[Table/Fig-7]: a) S100 negative in tumour cells (S100 stain, 400x); b) SOX10 negative in tumour cells (SOX10 stain, 400x); c) CD34 negative in tumour cells (CD34 stain, 400x).

IHC marker	Positive control used	Negative control used
HMB45	Benign nevus tissue	Liver tissue (hepatocytes)
S100	Schwannoma tissue	Liver tissue (hepatocytes)
SOX10	Schwannoma tissue	Liver tissue (hepatocytes)
CD34	Background blood vessel (internal control)	Liver tissue (hepatocytes)
SMA	Background blood vessel (internal control)	Liver tissue (hepatocytes)
Desmin	Background blood vessel (internal control)	Liver tissue (hepatocytes)
Vimentin	Background blood vessel (internal control)	Liver tissue (hepatocytes)

[Table/Fig-8]: Positive and negative controls used for various IHC markers.

DISCUSSION

In the present case of retroperitoneal mass, grossly fibrosarcoma and smooth muscle tumours were considered as differentials. But the histological findings revealed a sarcoma with epithelioid morphology and melanin pigment. Hence, the differential at this point was alveolar rhabdomyosarcoma, PEComa and clear cell sarcoma. HMB45 positivity with desmin negativity in tumour cells ruled out the diagnosis of alveolar rhabdomyosarcoma, while the absence of SOX10 and S100 expression excluded clear cell sarcoma. Ultimately, the diagnosis of PEComa was confirmed based on histopathological and IHC findings.

The PEComa was identified first, by Bonetti et al., in the year 1992 [1]. These infrequent and distinctive tumours from the mesenchyme

are characterised by epithelioid cells typically organised around blood vessels. PEComas are unique in that they express both melanocytic and smooth muscle markers, setting them apart from other soft-tissue tumours [2]. Tumours with perivascular epithelioid cell differentiation exhibit distinct morphological, immunohistochemical and ultrastructural features [3]. These tumours can appear in various anatomical locations, such as the lungs, gastrointestinal tract, kidneys, liver, uterus and retroperitoneum [4]. PEComas primarily affect young adults, with a higher incidence in females compared to males [5]. The family of PEComa comprises of Angiomyolipomas, Lymphangioleiomyomatosis, clear cell sugar tumour of lung, clear cell myomelanocytic tumour and PEComas classified as Not Otherwise Specified (NOS). The biological behaviour of PEComas is unpredictable [6]. Clinical presentation, pelvic examination and radiological findings are often non specific, which can lead to confusion with benign tumours or other malignancies. The non specific nature of these findings complicates the clinical diagnosis of PEComa, making radical surgical resection the preferred treatment. Diagnosis is typically confirmed post-surgery [5,7-10].

Fewer than 50 cases of retroperitoneal PEComa have been documented in the English literature [10]. The pathogenesis of PEComa remains poorly understood, with one theory suggesting a connection to tuberous sclerosis complex [11]. One hypothesis proposes that PEComas arise from undifferentiated neural crest cells due to their expression of melanocytic markers, while another suggests origin from muscle (smooth) and subsequent changes in molecular pathways which eventually leads to melanocytic marker expression [12]. A third theory posits that the melanocytic marker expression is acquired through chromosomal translocations or mutations that impact melanosome protein expression during tumour development [13]. Recent theories indicate that PEComas, as well as, gastrointestinal stromal tumours may originate from telocytes, as PEComas express markers associated with telocytes, such as S100, SMA and Vascular Endothelial Growth Factor (VEGF) [14].

The histogenesis and physiological counterparts of PEComa are not yet fully understood [15]. PEComas can alter their morphology and immunophenotype based on their microenvironment. Under some conditions, they display pronounced muscle features, while in other scenarios, they show more epithelioid characteristics with strong positivity for HMB45 and weak or focal expression of SMA, as observed in the present case [5].

Folpe AL and Kwiatkowski DJ have proposed a criterion for assessing PEComas' biological behaviour. In case of malignancy, risk factors such as size of tumour greater than 5 cm, a mitotic rate exceeding 1 per 50 HPF, nuclear grade, as well as, cellularity is high, presence of the necrosis, invasion into vessels and infiltrative growth pattern are noted. According to their classification, PEComas are categorised as benign (those tumours under 5 cm with only one risk factor), or with uncertain malignant potential (those tumours over 5 cm without other risk factors), or malignant (those tumours with either two or more risk factors) [13]. Based on these criteria, the present case patient falls into the malignant PEComa category. Following the radical resection of the mass, the patient was recommended to undergo routine imaging for surveillance, and she has been symptom-free for the past four months. She remains under active surveillance.

Finally, Touloumis Z et al., recommended following sarcoma guidelines for patient follow-up, as no standard follow-up protocol for PEComa has been established [10]. Fewer than 5 cases have been reported as retroperitoneal PEComa in last eight years cases and it has been compiled in a table [Table/Fig-9] [1,10,16,17].

Author	Year	Age (years)/ Gender	Maximum diameter of tumour (cm)
Siddiqi S and Mesropyan L, [16]	2022	40s/male	7.1
Yim H et al., [1]	2021	46/female	7.4
Touloumis Z et al., [10]	2019	37/female	8.5
Singer E et al., [17]	2018	70/female	33

[Table/Fig-9]: Retroperitoneal PEComa cases reported between 2016 to 2024 [1,10,16,17].

This discussion underscores the rarity of retroperitoneal PEComas in secondary infertility, highlighting the importance of integrating clinical suspicion with histopathological analysis for accurate diagnosis and tailored management.

CONCLUSION(S)

The PEComas are rare mesenchymal tumours with distinctive histological features. Since they can resemble other soft-tissue tumours on imaging studies, differentiating PEComa from other types of soft-tissue tumours is crucial. Accurate diagnosis relies on a combination of histopathological examination and IHC. This emphasises importance of PEComa to be considered for differential diagnosis for retroperitoneal masses in young women.

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