

Oncology

Retroperitoneal PEComa: Case report and review of literature

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Introduction

Perivascular epithelioid cell tumors (PEComas) are uncommon mesenchymal tumors composed of perivascular epithelioid tissue. They can occur anywhere in the body, but their most common forms are renal angiomyolipoma (AML) and pulmonary lymphoangioleiomyomatosis (LAM). Only 160 cases of AML PEComa have been reported to date. The histological characteristics of a malignant PEComa are not well defined and often rely on the presence or absence of metastatic spread. Additionally, their clinical presentation and radiographic appearance can often mimic that of soft tissue sarcomas. Naturally, malignant PEComas display a far more aggressive clinical course than benign variants, such as renal AML, with approximately 50% of cases demonstrating disease progression.¹ Although many large PEComas undergo surgical resection for fear of malignancy, there are not well-established preoperative characteristics that can adequately risk-stratify patients. (see [Figs. 1 and 2](#))

Case presentation

The patient in this case is a 70-year-old Caucasian woman in her normal state of health when she checked into an emergency room with a chief complaint of tingling in all extremities. A chest x-ray showed multiple pulmonary nodules, prompting a CT scan; the scan showed a solid, heterogeneous retroperitoneal mass with lobulated external contours, approximately 21 × 18 × 24cm.² The scan also captured multiple pulmonary and liver nodules. An outside biopsy of the abdominal mass was performed and diagnosed as a malignant neoplasm without further delineation. The specimen was positive for MART-1 and HMB-45 and negative for pancytokeratin, CD117, CK7, antigen BCL-2, calretinin, synaptophysin, S100, actin, and desmin.³

Approximately one month following her initial presentation, she underwent resection of the mass, which was presumptively palliative to alleviate her abdominal discomfort associated with bowel obstruction. The mass was adherent to the kidney, requiring radical nephrectomy. The liver masses were easily palpable and biopsied. Another mesenteric mass was identified and excised. The final pathology was a 33cm PEComa within 1mm of the inked margin. It was unclear whether this tumor originated from the kidney or the retroperitoneum. Immunohistochemistry was positive for Melan-A, cathepsin K, and

HMB-45. It was negative for S100, Sox10, and Sox16 toxie as well as the keratin markers. The TFE3 FISH was negative. Extensive necrosis and unusual mitotic figures lead to the PEComa's malignant classification. The hepatic specimen showed no signs of neoplasm and was determined to be the result of chronic inflammation. The mesenteric mass specimen was fibroadipose tissue with fat necrosis. One month after the procedure, an F-18 FDG PET CT scan showed no FDG avidity in the hepatic and pulmonary nodules, and there was no evidence of recurrence in the retroperitoneum.

Discussion

While the majority of all PEComa cases are AML or LAM, malignant PEComa are a rare finding. Both AML and LAM are highly correlated with a prior presentation of tuberous sclerosis. This disease, caused by mutations in the TSC1 or TSC2 genes, which regulate cell division and differentiation, often involves cognitive delays or cutaneous findings. Despite the correlation between AML and LAM with tuberous sclerosis process, this correlation does not exist between tuberous sclerosis process and the other forms of PEComas. Imaging studies have not been effective, to date, in accurately differentiating between PEComa of malignant potential, benign potential, or other soft tissue malignancy. Instead, PEComa diagnoses rely on the utilization of histological examinations of cells and immunohistochemical markers, post-excision. PEComas can be diagnosed during a histological review using some key attributes seen in these cells. The epithelioid cells' cytoplasm are clear and granular, and their nuclei are center-oriented, round, and do not have prominent nucleoli. They can also be diagnosed using immunohistochemical markers. PEComas typically stain for myogenic markers (actin, myosin, calponin) and melanocytic markers (HMB-45, Melan A (Mart 1), Mitf). Although not specific, expression of cathepsin K has been identified as a sensitive marker for PEComa. In this case the diagnosis of a malignant PEComa was made upon the discovery of the unusual mitotic figures and extensive necrosis in the specimens resected during the patient's operation at Johns Hopkins. These figures and characteristics were noted upon a histological exam of the specimens by the hospital's pathology. Though a malignant denotation's criteria may be unclear, it is evident that PEComas can be malignant in nature and develop into metastatic disease.

Treatment for PEComas typically entails surgical excision of the

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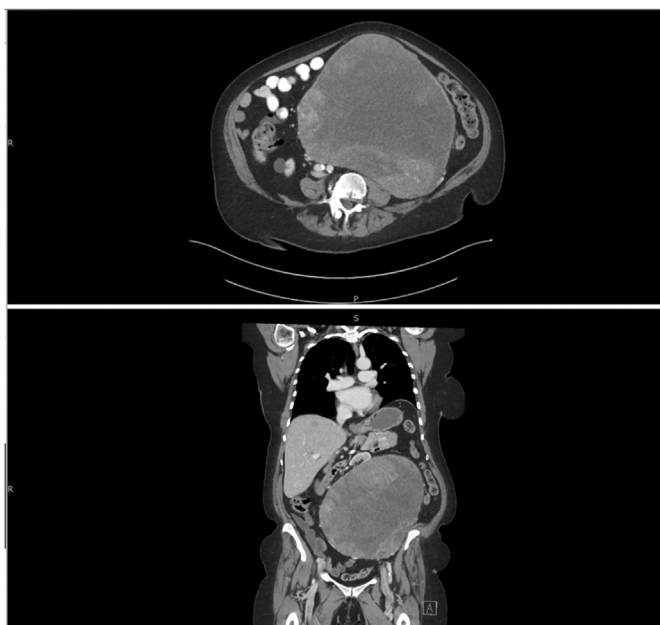


Fig. 1. CT scan reveals a solid, heterogeneous retroperitoneal mass with lobulated external contours, approximately 21 × 18 × 24cm.

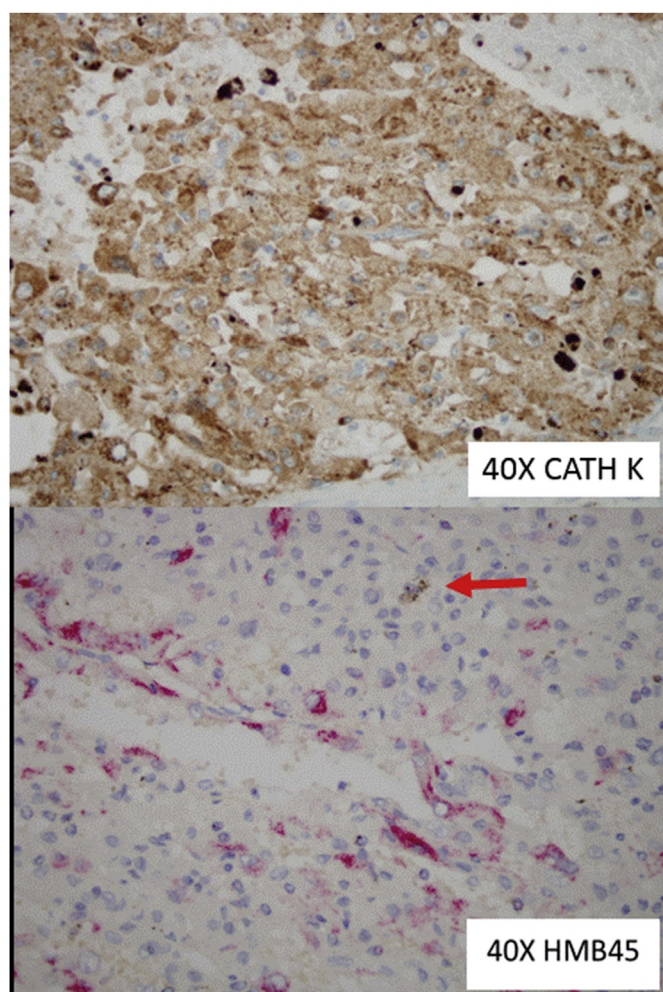


Fig. 2. Histological confirmation of PEComa with immunoreactivity to Cathepsin K and HMB45.

diseased tissue. In a study published in 2010 by Brimo et al.,⁴ it was noted that 9 of the 40 patients showed local recurrence or widespread metastatic growth. Of these 9 patients, 4 died of disease. The authors noted common disease and demographic characteristics in these patients. These characteristics include “older age, larger tumor size, higher percentage of epithelioid component, severe atypia, higher percentage of atypical cells, higher mitotic count, atypical mitotic figures, necrosis, lymphovascular invasion, and renal vein invasion”.⁴ These characteristics were used to create a list of features that predicts the likelihood of malignant behavior. The features are as follows: “(1) > or = 70% atypical epithelioid cells, (2) > or = 2 mitotic figures per 10 hpf, (3) atypical mitotic figures, and (4) necrosis”.⁴ An increased number of features present correlates to a higher likelihood of malignant behavior.⁴ In patients who may have increased likelihood for disease recurrence or progression, regular surveillance with routine imaging is critical.

Conclusion

Perivascular epithelioid cell tumors are rare soft tissue tumors in the retroperitoneum, with variable malignant potentials. As a result, there are very few clear guidelines for determining the malignant and metastatic potential of PEComas, and in many cases the determination is made on a case-to-case basis. In this report, we highlight the case of a large PEComa with presumptive metastatic spread, which was diagnosed as malignant but, to date, has only had a negative metastatic workup.

Due to the finite number of PEComa cases recorded, there are not established guidelines for diagnosis, treatment, or surveillance. When evaluating a patient that presents with PEComa, it can be useful to use the predictive model devised by Brimo et al.⁴ It accurately categorized 78% of malignant and 100% of benign epithelioid AMLs with atypia.⁴ This model could become an invaluable tool for post-surgical treatment determinations. As this is a rare tumor with poorly understood treatment strategies, categorizing patients based on likelihood of metastasis and recurrence with this model can help patients and physicians make appropriate decisions about surveillance vs. adjuvant treatment. Patients at higher risk may want to seek adjuvant treatment and therapies, as there are not well-established treatment guidelines. These patients may be considered for adjuvant chemotherapy or radiation courses to prevent metastasis or recurrence. Through data collection, this model could provide us with the information needed to develop a more sophisticated course of treatment and adjuvant therapy for patients presenting with malignant PEComa.

References

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- Figure 1. CT Scan of the Retroperitoneal Mass. Obtained from Johns Hopkins Brady Urological Center, February 1, 2018.
- Figure 2. Pathology Slide Reveals PEComa Cells in the Mass. Obtained from Johns Hopkins Brady Urological Center, January 25, 2018.
- Brimo F, Robinson B, Guo C, Zhou M, Latour M, Epstein JI. Renal epithelioid angiomyolipoma with atypia: a series of 40 cases with emphasis on clinicopathologic prognostic indicators of malignancy. *Am J Surg Pathol*. 2010;34(3):715–722.