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Unique presentation of retroperitoneal malignant perivascular epithelioid cell tumor (PEComa) in a young male

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ABSTRACT

Perivascular Epithelioid Cell tumors (PEComas) are rare mesenchymal tumors composed of epithelioid and spindle cells that can be found almost anywhere in the body with predominance for abdominopelvic locations. They are usually diagnosed in middle-aged females and are associated with tuberous sclerosis complex. This report describes an unusual presentation of a malignant retroperitoneal PEComa in an otherwise healthy, young male. Treatment included radical nephrectomy and adrenalectomy followed by medical oncology evaluation.

1. Introduction

Perivascular epithelioid cell tumors (PEComas) are a group of rare mesenchymal neoplasms with varying malignant potential. These tumors are often benign and have been described to occur in numerous locations in the body - both visceral and somatic soft tissue. PEComas have a distinct histologic appearance and immunohistochemical staining is used to differentiate and diagnose such tumors. Here, a case of a malignant retroperitoneal PEComa in an otherwise healthy, young male is presented.

2. Case presentation

A 35-year-old man presented to his primary care provider for evaluation of left upper abdominal pain and left flank pain. He denied any hematuria, palpitations, night sweats, headache, or history of hypertension. Physical examination was unremarkable with a soft, non-tender abdomen. Past medical history was significant for a renal contusion in 2008 after a dirt biking accident. He had no pertinent family history.

Abdominal ultrasonography was performed showing a structure in the left lower quadrant measuring 9.7x9.6 × 8.3cm with a slightly hypoechoic area surrounded by echogenic material. Computed Tomography (CT) of the abdomen and pelvis with contrast showed a complex fatty lesion involving the upper pole of the left kidney posterolaterally measuring 5x4x3cm consistent with an angiomyolipoma. The left adrenal gland was not clearly identified and there was a large mass measuring 10x9x8cm inferior to the tail of the pancreas and anterior to the left kidney that was suspicious for malignancy (Fig. 1).

The patient was referred to urology for further workup. Preoperative blood work including CBC, BMP, renin activity, plasma aldosterone, and AM cortisol, were all within normal limits. Levels of urinary homovanillate, vanillylmandelate, catecholamines, and metanephrines were unremarkable.

The patient underwent open radical left nephrectomy and left adrenalectomy. The retroperitoneal mass was discovered to be extending from the superior left kidney anteriorly and extending to the iliac vessels inferiorly which resulted in posterior displacement of the kidney. Pathology showed a 12x11 × 9.7cm malignant extrarenal PEComa with negative margins, no adrenal gland abnormalities, no lymph node involvement, and a 5cm intrarenal angiomyolipoma.

Histologically, the intrarenal angiomyolipoma was composed of small, bland spindle cells with pinpoint nucleoli and essentially no mitotic figures (Fig. 2A). The extrarenal PEComa consisted primarily of dyshesive epithelioid cells with similarly lightly eosinophilic-to-granular cytoplasm but larger nuclei, more atypia, and frequently prominent nucleoli (Fig. 2B). The PEComa had infrequent mitotic figures (~6/50 hpf). Extensive hemorrhage and areas of necrosis with scattered hemosiderin deposition was confirmed by an iron stain. The immunohistochemical (IHC) staining results are outlined in Table 1. The AJCC 8th edition TNM staging for the PEComa was pT3 pN0.

3. Discussion

PEComas are rare mesenchymal tumors that most commonly arise in the gastrointestinal tract, uterus, and abdominopelvic sites but can occur anywhere in the body including skin and bone.[1] Tumors that belong to

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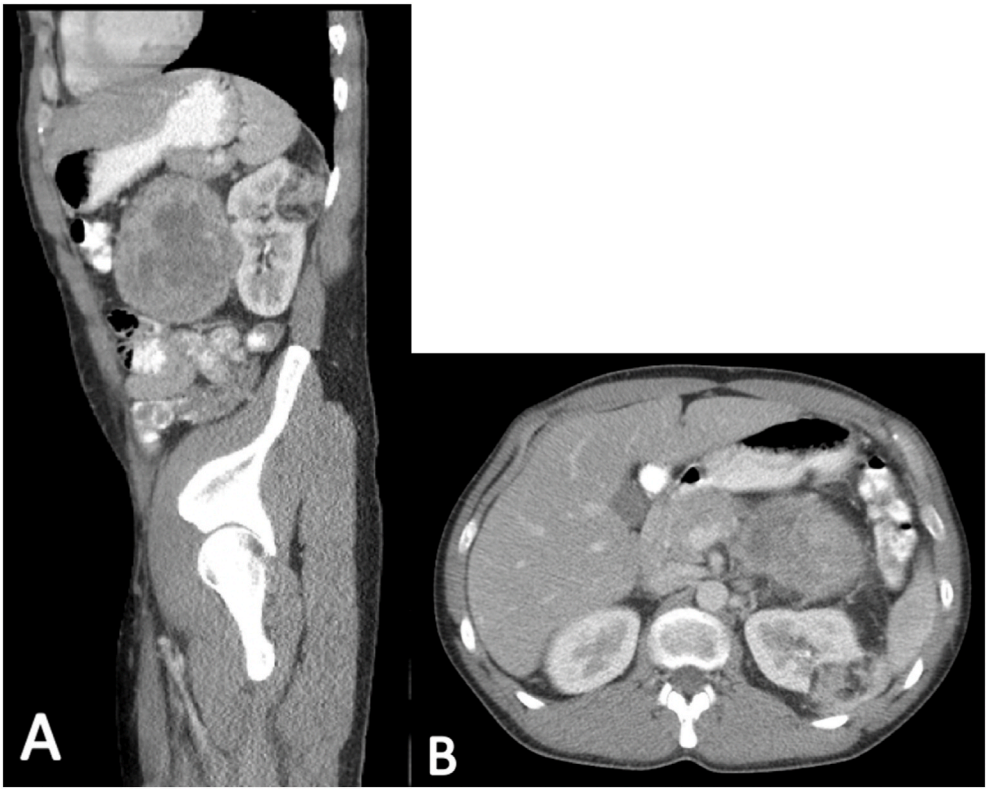

Fig. 1. A: Computed Tomography sagittal view of extrarenal PEComa anterior to left kidney with an intrarenal angiomyolipoma. **B:** Computed Tomography axial view of extrarenal PEComa anterior to the left kidney.

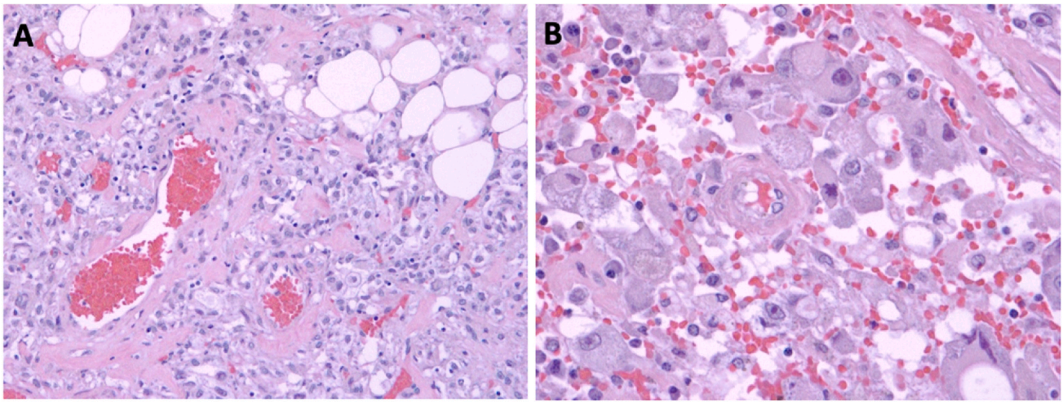

Fig. 2. A. H&E stain of intrarenal angiomyolipoma composed of triphasic neoplasm of fat, thick-walled blood vessels, and spindled-to-slightly epithelioid cells with lightly eosinophilic-to-granular cytoplasm. **B.** H&E stain of extrarenal malignant PEComa composed predominantly of dyshesive epithelioid cells with similar lightly eosinophilic-to-granular cytoplasm with larger nuclei, more atypia, and frequent prominent nucleoli.

the PEComa class include angiomyolipoma, lymphangioleiomyomatosis, pulmonary clear cell "sugar" tumor, and others with similar histologic features that are known as PEComa not otherwise specified (PEComa NOS). These tumors have a significant female predominance and a wide age range at initial diagnosis. Peak incidence is in young and middle-aged adults. Additionally, there is an association with tuberous sclerosis complex (TCS).[2]

Histologically, all PEComas share a distinct cell type known as the perivascular epithelioid cell (PEC) which does not have a normal tissue counterpart. PEComas are composed of epithelioid and spindle cells arranged in nests and/or sheets with clear to granular eosinophilic cytoplasm. Due to the close association with blood vessels, it has been hypothesized that PEC cells may originate directly from blood vessels.[2]

Further analysis for PEComas is done through IHC staining. The PECs stain positive for both smooth muscle (desmin and/or actin) and melanocytic (HMB-45 and/or melan-A) markers. Positive melanocytic staining was seen in the malignant PEComa in this patient. PEComas pose a unique diagnostic challenge as they can be mimicked immunohistochemically and morphologically by many other neoplasms including melanoma, clear cell sarcoma, gastrointestinal stromal tumors (GIST), and true smooth muscle cell tumors.[3] The differential diagnosis for PEComas must be broad and immunohistochemical staining is imperative for proper diagnosis of these rare tumors.

Furthermore, the degree of malignancy in PEComas is highly variable. Bleeker et al. published an update of the Folpe et al. classifications detailing a suggested risk stratification for PEComas based on histologic and morphologic features.[4] Malignant PEComas are tumors that contain two or more high-risk features including size >5cm, infiltrative growth

Table 1
Immunohistochemical staining results of the angiomyolipoma and PEComa.

Stain	Angiomyolipoma	PEComa
HMB45	(+)	(+)
MelanA	(+)	(+)
Calponin	(+)	(−)
Muscle Specific actin	(+)	(−)
CD117	Focally (+)	(−)
Desmin	Focally (+)	(−)
S100	Adipocytic component (+)	(−)
CD34	Blood vessel endothelium (+)	Endothelium (+)
CD 31		Endothelium (+)
SOX 10	(−)	(−)
ER	(−)	(−)
PR	(−)	(−)
SMA		(−)
CAM 5.2		(−)
Pancytokeratin		(−)

pattern, high nuclear grade and cellularity, mitotic rate >1/50 HPF, necrosis, and vascular invasion. With a size of 8cm, presence of mitotic figures at a rate of 6/50 HPF, and extensive necrosis, the tumor in our patient was classified as malignant. The size and mitotic rate in this tumor are the most significant factors indicating possible recurrence. Tumor recurrence up to five years following initial resection has been described.

Though no definitive treatment regimen has been effectively shown to treat malignant PEComas, studies show the potential utility for mTOR inhibitors such as nab-sirolimus for treatment.[4] Targeted approach with mTOR inhibitors has been proven to be more effective than traditional chemotherapy treatment used for soft tissue sarcomas.[4] Preliminary data suggest that complete response with mTOR inhibitors is possible.[5] Without a proven treatment option for recurrent PEComa, patients with high risk features can consider surveillance versus adjuvant chemotherapy or newly emerging mTOR inhibitors.

Follow-up MRI-brain was unremarkable; PET scan showed no metastases. Genetic testing was negative for TSC1/TSC2 and positive for a heterozygous p.G396D mutation of the MUTYH gene. Oncology did not recommend any adjuvant chemotherapy or radiation. The patient is scheduled for further follow-up with a national academic center for investigation of increased risk of other malignancies.

4. Conclusion

This case provides an overview of the clinical and histological characteristics of PEComas including a detailed explanation of the workup, immunohistochemical analysis, surgical treatment, and pathologic malignant classifications of a young patient's PEComa. Though there are no standard treatment options for PEComas, new studies have shown there may be potential benefits to using mTOR inhibitors for targeted treatment.

Section headings

Oncology.

Consent

Informed written consent was obtained from the patient for the publication of this article.

Declaration of competing interest

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