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Case Report

Malignant retroperitoneal PEComa: A case report with emphasis on radiological findings ☆

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ABSTRACT

A perivascular epithelioid cell tumor (PEComa) is a rare mesenchymal neoplasm with distinctive perivascular epithelioid cells that usually demonstrates myomelanocytic differentiation. PEComas can arise in various organs and generally are benign. Uncommonly PEComas have been documented to be malignant with metastasis most frequently to the lung, liver, lymph nodes, and bone. Here, we present the case of a 59-year-old male with a malignant retroperitoneal PEComa with confirmed metastasis to the femur and suspected metastasis to the liver and lung. The purpose of this case study is to present the progression and findings of a metastatic malignant PEComa.

Introduction

Perivascular epithelioid cell tumors (PEComas) are uncommon mesenchymal tumors comprised of perivascular epithelioid cells (PECs), which have distinctive histological morphologies and immunohistochemical markers. These cells have "prominent cytoplasmic borders and clear to granular, eosinophilic cytoplasm" in a perivascular distribution [1]. The PEComa family has clinical subtypes either based on its origin or it is classified as PEComa-not otherwise specified (PEComa-NOS). While PEComas in general are rare, malignant PEComas, which have defined high-risk features, are even more uncommon and often diagnosed after metastasis to the lung, liver, lymph nodes, and bone. Radiological features have been poorly described due to variability and limited case numbers, so pathological analysis remains the standard for diagnosis as most research and focus has been on identifying the pathological and histological features of PEComas. Most recently, Tirumani et al. sought to gather the limited data on suggestive imaging findings of malignant PEComas to help bridge the gap between delayed diagnosis and initiating earlier treatment plans based on radiological findings [2]. This presentation is of a 59-year-old male presenting to the emergency department with complaints of abdominal pain and history of right hip pain who was discovered to have malignant PEComa of the retroperi-

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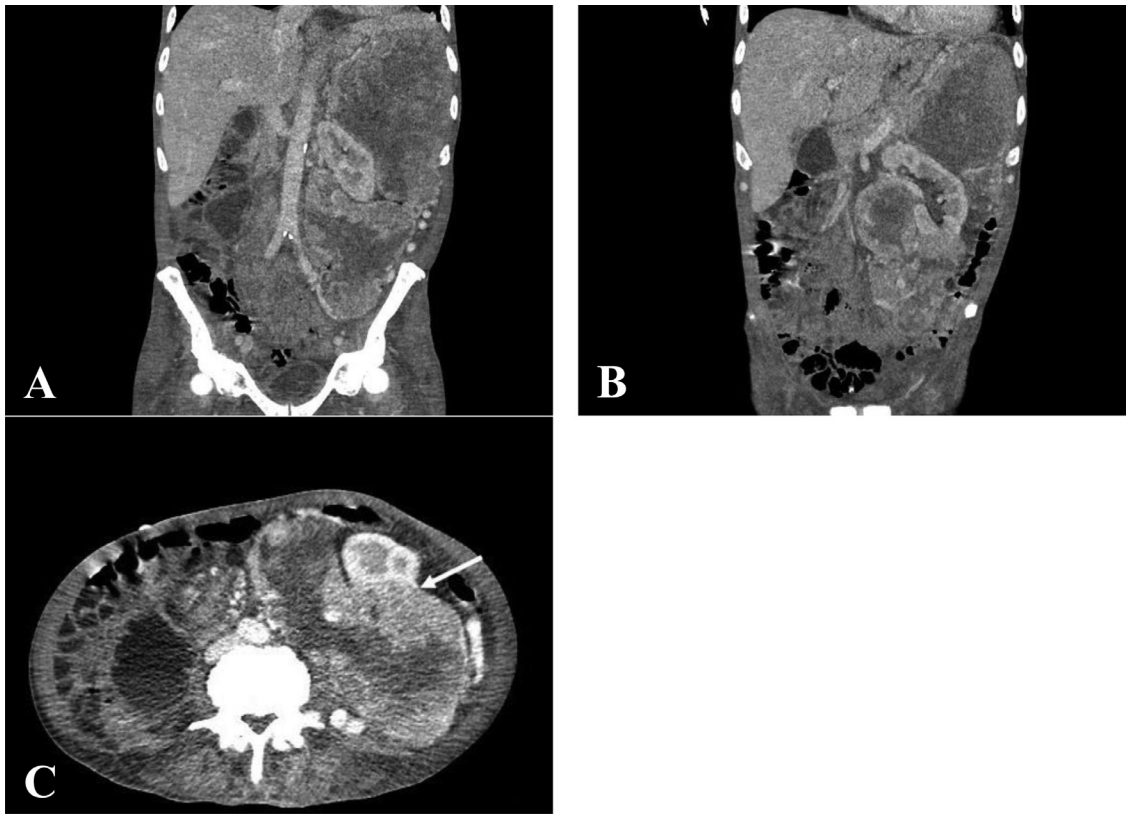

Fig. 1 – CTs showing retroperitoneal mass. (A) Coronal image from contrast-enhanced CT scan of the abdomen and pelvis demonstrating extent of large, heterogeneously enhancing, retroperitoneal mass extending from the level of the diaphragm to the left hemipelvis. Mass effect on the left kidney with anterior, inferior, and rightward displacement. Rightward displacement of the aorta and varices of the left hemiabdomen are apparent. (B) Coronal image from contrast-enhanced CT scan of the abdomen and pelvis demonstrating the inseparable interface between the inferior pole of the left kidney and the large left retroperitoneal mass. (C) Transaxial image from contrast-enhanced CT scan of the abdomen and pelvis demonstrating the inseparable interface between the inferior pole of the left kidney and the large left retroperitoneal mass (white arrow).

toneum with confirmed metastasis to the femur, and suspected metastasis to the lungs and liver.

Case presentation

A 59-year-old man presented to the emergency department with a 3-month history of frequent hospital visits due to right hip pain. He was being treated for arthritis with no relief, and had developed a new complaint of abdominal pain for 1 month. He noticed a palpable left-sided abdominal mass and complained of weight loss, low appetite, night sweats, and chills. A bedside ultrasound diagnosed a left-sided retroperitoneal mass that appeared contiguous with the kidney. Computed tomography (CT) identified a large heterogeneous mass in the left hemiabdomen appearing inseparable from the inferior pole of the left kidney (Fig. 1), multiple pulmonary parenchymal nodules in the left lower lung (Fig. 8), and possible metastasis in the right gluteal muscle. CT imaging from 2012 showed that there was a notable mass in the left kidney pole, but it was unclear if that mass was related to the presentation of today's mass, and a formal read was unavailable (Fig. 2).

Magnetic resonance imaging (MRI) showed a heterogeneous left abdominal mass extending from the diaphragm level down to the iliac crest measuring at least 25 cm with prominent surrounding venous collaterals, as well as a mass in the right femur (Fig. 3).

Surgical excision was not recommended unless metastatic cancer was ruled out so an ultrasound-guided left retroperitoneal mass core biopsy was performed. The histological core biopsy results are shown in Fig. 4 and consistent with a PEComa. Immunohistochemical staining results are shown in Fig. 5. The morphology and immunostaining results combined are consistent with a malignant PEComa.

The genomic profile showed a low tumor mutation burden with a TP53 Y234C mutation, NTRK1 low level gain/amplification, CDKN2A and CDKN2B gene loss (suggestive of 9p21 deletion), BRCA2 gene loss, low tumor mutation burden, and one variant of unknown significance in the EP300 gene.

Another MRI was obtained due to increasing complaints of right hip pain. The results are shown in Figs. 6 and 7

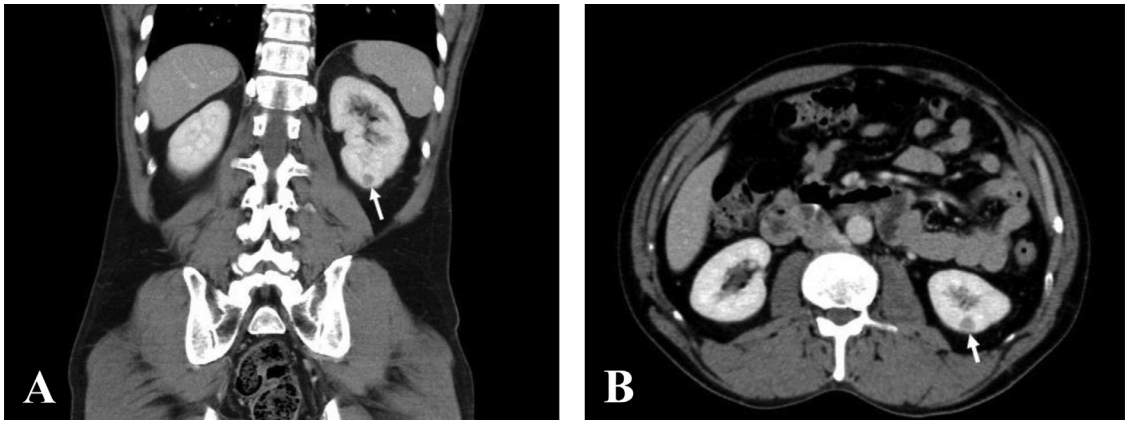

Fig. 2 – 2012 CT. Coronal image (A) and transaxial image (B) from contrast-enhanced CT scan of the abdomen and pelvis almost 9 years prior demonstrates an indeterminate density lesion at the inferior, posterior cortex of the left kidney (white arrows).

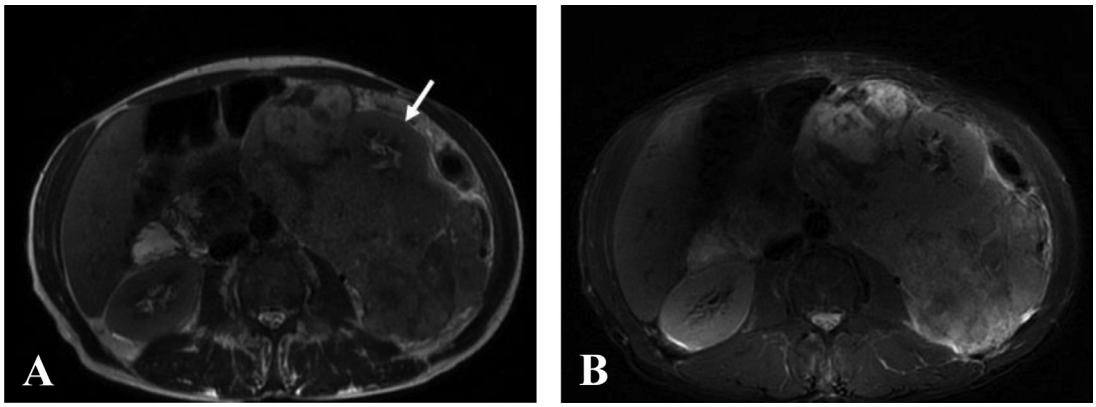

Fig. 3 – MRIs showing retroperitoneal mass. (A) Transaxial T1-weighted non-contrast MR image demonstrates a heterogeneous mass inseparable from the inferior pole of the left kidney, demonstrating signal intensities hypointense, isointense, and hyperintense compared to skeletal muscle. Note anterior displacement of the left kidney (white arrow). (B) Transaxial T2-weighted image demonstrates a heterogeneous mass inseparable from the inferior pole of the left kidney, demonstrating signal intensities generally isointense and hyperintense compared to skeletal muscle.

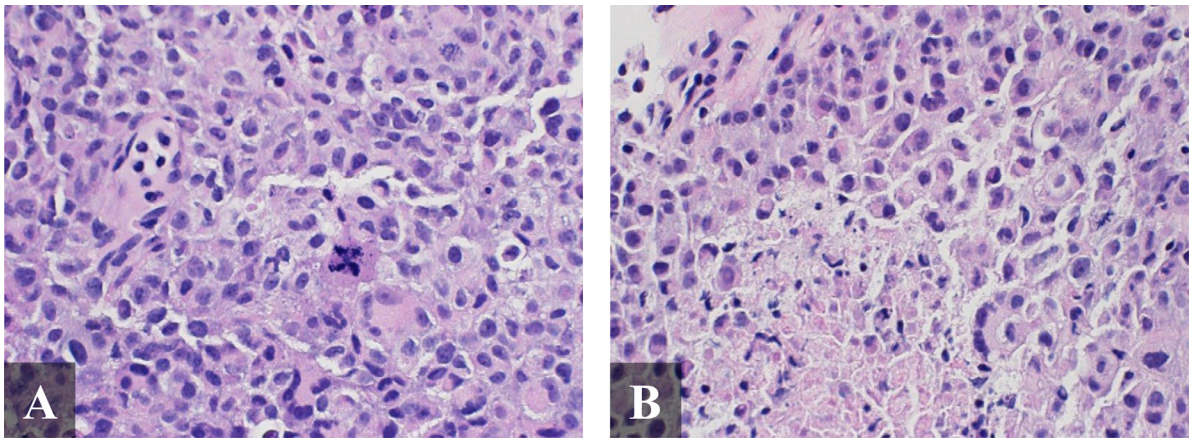

Fig. 4 – Histological profile of neoplasm. (A) Hematoxylin and eosin (H&E) slide of the neoplasm demonstrating nests of cells with clear-to-granular and eosinophilic cytoplasm and round-to-oval nuclei with occasional nucleoli and pleomorphism. An atypical mitotic figure is present near the center of the image (×400). (B) H&E slide showing the neoplasm with associated pink amorphous necrosis in the middle to lower half of the image (×400).

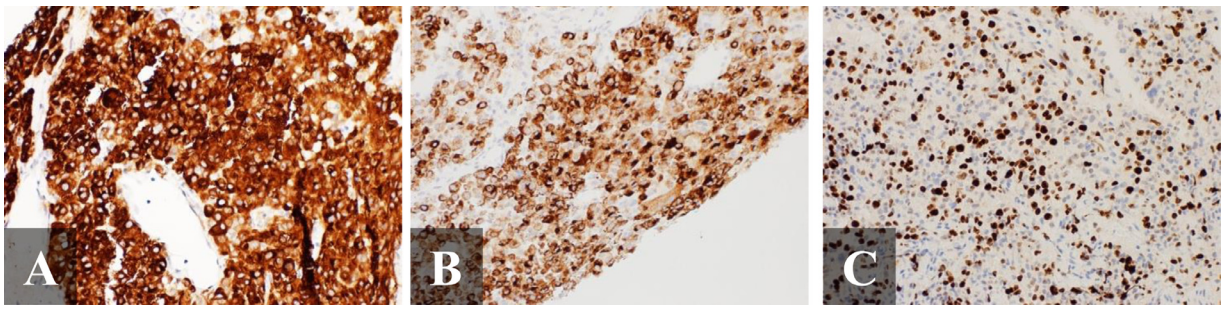

Fig. 5 – Immunohistochemical profile.

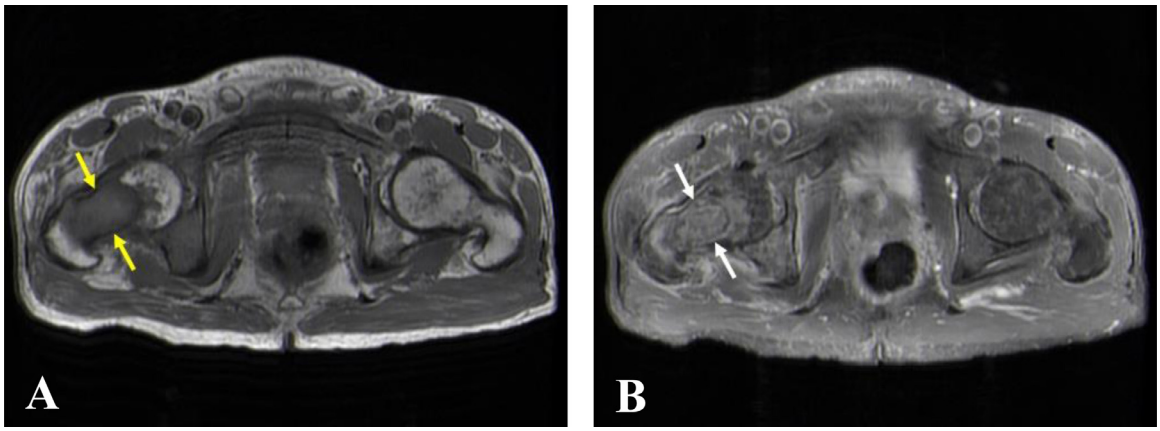

Fig. 6 – Transaxial T1-weighted pre-contrast and post-contrast (A and B, respectively) images of the bilateral proximal femora. Pre-contrast images demonstrate replacement of normal fatty marrow by a metastatic focus (yellow arrows). Post-contrast images demonstrate avid contrast enhancement of this metastatic focus (white arrows). Subsequent CT-guided biopsy proved PEComa.

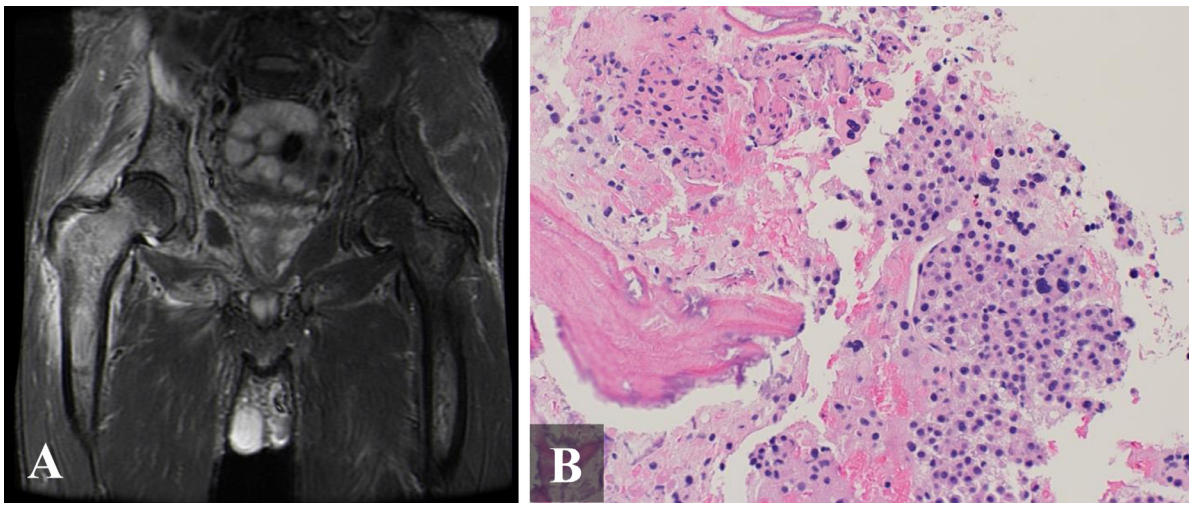

Fig. 7 – (A) Coronal STIR image of the proximal femora demonstrating asymmetric edema of the proximal right femur and surrounding soft tissues, reflecting metastatic disease. (B) H&E stain showing metastatic PEComa to the right femoral bone with nests of cells with eosinophilic cytoplasm and round/oval nucleus (x100).

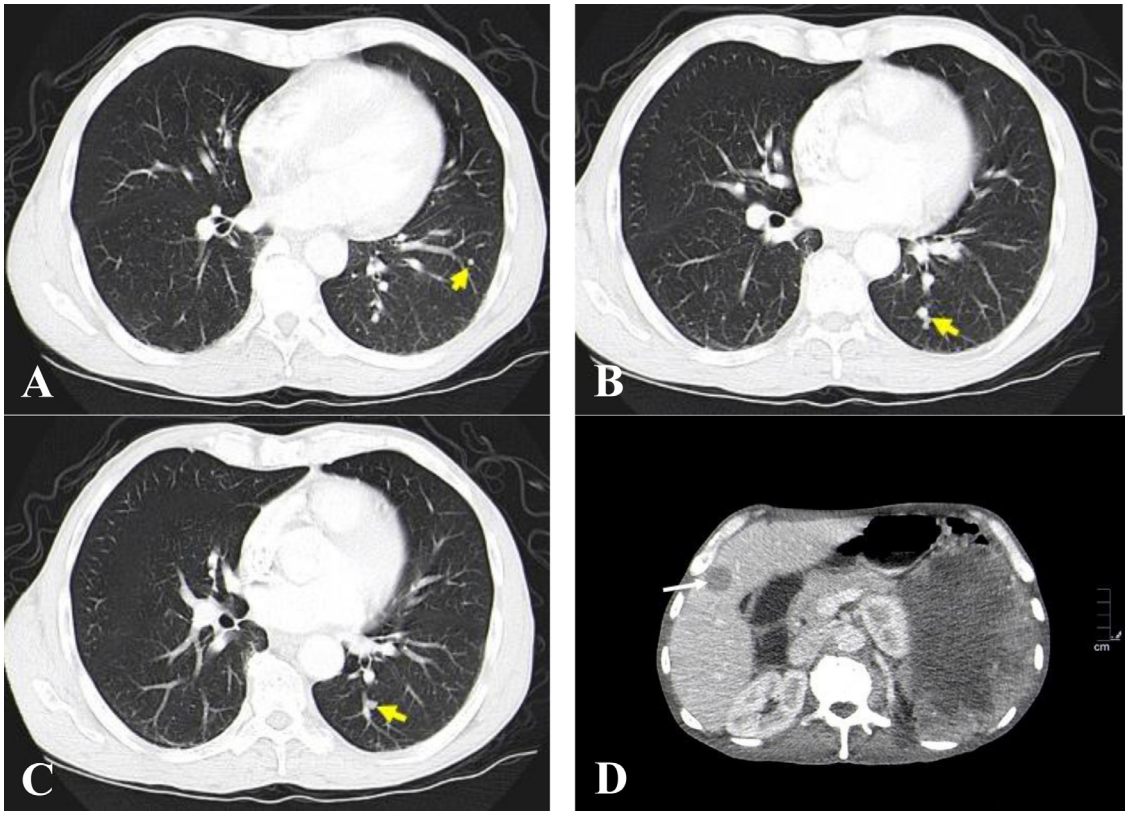

Fig. 8 – Suspected metastasis. (A-C) Transaxial images from contrast-enhanced CT scan of the chest demonstrating multiple left lower lobe parenchymal nodules (yellow arrows), some suggesting peripheral calcifications, measuring on the order of 4-5 mm. These nodules are not seen on prior studies and are suspicious for metastatic disease. (D) Transaxial image from contrast-enhanced CT scan of the abdomen and pelvis demonstrates a 2.2 cm x 2.0 cm hypoattenuating lesion of the right lobe of the liver (yellow arrow). This lesion is not seen on prior studies and is suspicious for metastatic disease.

which were concerning for malignancy or metastatic disease in the right proximal femur. An interventional radiology-guided bone biopsy of the lesion confirmed metastatic malignant PEComa (Fig. 6).

Surgical removal of the primary PEComa would involve multivisceral resection including the distal pancreas, left kidney, descending colon, spleen, and possibly part of the stomach, making him a poor surgical candidate associated with high risk for morbidity as well as postoperative mortality. It was decided to treat with chemotherapy in the hopes of decreasing the tumor to a resectable size. With conventional chemotherapy having little activity in PEComas, he was started on sirolimus. Initially, he was started on a therapeutic 2 mg/d dose of sirolimus that was confirmed with a blood level of 6.1 (ref range 3-18), but after 2 weeks, the medication was stopped because of poor tolerance due to excessive nausea and vomiting. During this time, new CT images also showed a lesion in the liver suspected to be metastasis (Fig. 8), so he was restarted on sirolimus at a lower dose of 1 mg/d. The patient deteriorated further, requiring crutches to walk due to his severe right hip pain, and had significant right leg weakness with inability to move his right foot. Orthopedic surgery did not feel he was a candidate for an operation for the right femur lesion. The patient was seeing palliative care for pain management, he required frequent blood transfusions due to anemia, and his mobility continued to decrease. Four months after his presentation and 3 months after his diagnosis, the patient passed away.

Discussion

PEComas are rare mesenchymal tumors that were first described by Apitz et al. in 1943 as containing an abnormal myoblast in a case of a renal angiomyolipoma [3]. It wasn't until 49 years later Bonetti introduced the concept of PECs, a cell type that morphologically have an epithelioid appearance with a clear to granular cytoplasm with a round/oval central nucleus and they express myogenic and melanocytic markers, such as HMB45 and Melan A/Mart-1 [4]. The etiology of PEComas remains unclear, but 3 recent hypotheses have been proposed by Martignoni et al. One hypothesis is PECs derive from undifferentiated cells of the neural crest that can express dual smooth muscle and melanocytic phenotype. The second is they have a myoblastic and smooth muscle origin that contains a molecular alteration leading to melanogenesis and melanocytic markers (such as Melan-A/Mart-1). The last is that they have a pericytic origin [5].

PEComas typically follow a benign course with a nonspecific clinical presentation, making timely diagnoses difficult. Imaging techniques are not conclusive or diagnostic, so biopsy or surgery with immunohistochemical analysis is still the mainstay for confirmation [6]. This delayed diagnosis has led to reported cases of PEComas already being locally disseminated or metastasized by the time of diagnosis. As with our patient, there was suspected evidence of metastasis to the left lower lung and right gluteal muscle when he was first diagnosed.

While imaging techniques are not confirmatory, there are some common features proposed by Tirumani et al. that would lead to earlier consideration of a PEComa as a differential. His research analyzed 26 malignant PEComas and noted that on imaging they were all large (4.5–25 cm) well circumscribed tumors with no infiltration or local invasion, had metastatic patterns most commonly arising first in the lungs followed by the liver and bones, showed points of calcification and/or hemorrhage, were hypo- to isointense when compared to skeletal muscle on T1-weighted imaging, and were heterogeneously hyperintense on T2-weighted imaging [2]. The radiological findings in this paper's case aligned with these findings, showing a large 25-cm mass in the retroperitoneum with no infiltration or invasion, with confirmed metastasis to the femur and suspected metastasis first to the lung, and later to the liver. Differing from Tirumani's findings is that this PEComa showed more variability on contrast MRIs with T1-weighted imaging being hypo-, iso-, and hyperintense to surrounding muscle and T2-weighted imaging being iso- to hyperintense.

Radical resection is the mainstay of PEComa treatment, for both local tumors and metastasis because these tumors are characterized by resistance to chemotherapy and radiotherapy [7,8]. The treatment for advanced or unresectable disease is still controversial, with more research going into successful treatment options [9]. One promising option is using sirolimus, an immunosuppressive drug that inhibits activation of the mammalian target of rapamycin (mTOR) complex. The mTOR complex promotes cellular survival, cellular growth, and catabolic processes. Limited clinical studies have showed hopeful radiographic responses when taking oral mTOR inhibitors due to PEComas mechanistically being linked to activation of the mTOR signaling pathway [10].

Considering the increasing knowledge on PEComas, the aggressive nature of malignant PEComas, and the promising treatment with mTOR inhibitors, it has become important to notice subtle imaging features and the metastatic patterns that would suggest these rare tumors into consideration as a differential diagnosis.

Conclusion

PEComas are rare tumors with unpredictable behavior. Our case represented a malignant PEComa with extensive mass effect from the primary lesion in the left retroperitoneum, with metastasis to the right femur, and suspected metastasis to the liver and lung. Despite surgical resection being the usual first line of treatment, the extensive nature of this PEComa precluded surgical resection of the primary lesion as a viable option, whereas earlier identification might have included this as an option. With an increasing awareness of radiological findings, this could lead to earlier suspicion of PEComas, adding them to the differential diagnosis of large well-circumscribed tumors. Treatment with sirolimus was trialed but ultimately intolerable by the patient at therapeutic doses. In this patient's case, the evolution of this aggressive disease and late diagnosis surpassed treatment options and resulted in a fatal outcome 3 months after diagnosis.

Patient consent

Informed consent has been obtained from the patients next of kin to which this case report is based upon. The patient was deceased at the time of this case report being written.

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