

An Aggressive Case of Malignant Renal Pecoma Non-Responsive to Motor Inhibition: A Case Report

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Abstract

Perivascular epithelioid cell tumors (PEComas) are made up of cells with distinctive morphologic, immunohistochemical, ultrastructural and genetic features. They may arise in various locations and are usually benign. Malignant PEComas are rare and associated with an aggressive clinical course and metastatic spread. We present a case of a 56 years old healthy patient who presented with right flank pain and a large mass located at the medial aspect of the right kidney. The mass ruptured during laparoscopic removal. The tumor was eventually labeled as an epithelioid malignant neoplasm most suggestive of malignant PEComa. The patient demonstrated during follow up both local and systemic metastasis that are unresponsive to this point to mTOR inhibition with various agents.

Keywords: Everolimus; mTOR; Pecoma; Renal; Votrient

Introduction

Perivascular epithelioid cell tumors (PEComas) are made up of cells with distinctive morphologic, immunohistochemical, ultrastructural and genetic features. They may arise in various locations and are usually benign. Malignant PEComas are rare and associated with an aggressive clinical course and metastastatic spread.

We present such a case with bone, skin and retroperitoneal metastasis, non-responsive to surgical and adjuvant mTOR inhibition.

Case Report

A 56-year-old, generally healthy caucasian male with no significant past medical history started complaining of continuous right flank pain starting April 2013. The patient had no urinary complaints of any sort. Physical examination was normal and blood work and urine analysis were within normal limits. An abdominal ultrasound revealed a hypoechogenic mass adjacent to the right kidney causing hydronephrosis of an intermediate degree, and a widened proximal right ureter. The mass was irregular and 7*8 cm in size with many anechoic centers and displayed no blood flow. The urinary bladder was of normal thickness with no stones or residual urine.

CT urography performed demonstrated the mass as a well circumscribed one, 11 cm in diameter located at the medial aspect of the lower pole of the right kidney (Figure 1). The mass had nodular thickenings that showed enhancement with contrast. The mass was pressing on the right collecting system, the duodenum and the head of the pancreas. The urinary bladder was normal in appearance and there



Figure 1: Abdominal CT demonstrating a well circumscribed 11 cm mass located at the medial aspect of the left pole of the right kidney. The mass has nodular thickenings that show enhancement. The mass is pressing on the right collecting system, the duodenum and the head of the pancreas.

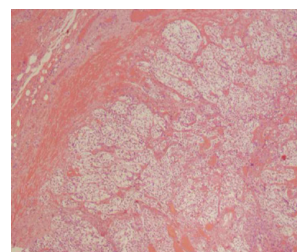


Figure 2: Pathological view demonstrates large atypical cells with eosinophilic and clear cytoplasm, organized in diffuse pattern, trabecular, ribbon like and nesting pattern.

was no lymphadenopathy. The patient underwent open resection of the mass. A flank incision was performed between the 11th and the 12th rib including removal of the 12th rib. The mass was located at the area of the right pedicle causing rotation the kidney upwards while pressing the right ureter. During the separation of the mass it ruptured releasing fluid and clots. The tumor involved the right upper ureter requiring resection of the ureter followed by closure over a ureteral stent. The patient was discharged 4 days later with no complications and the ureteral stent was withdrawn 6 weeks later.

Microscopic examination revealed a cystic tumor measuring 8 cm in diameter, composed of large atypical cells with eosinophilic and clear cytoplasm, oval nuclei and visible nucleoli, with foci of giant cells with bizarre hyperchromatic nuclei (Nuclear grade 3-4). The cells were organized in a diffuse pattern, trabecular, ribbon like and nesting pattern (Figure 2). Scattered mitotic figures were present (3/50 HPF). Foci of tumoral necrosis was also present. Ki-67 proliferation index was about 5% to 6%. Capsular invasion was identified but no vascular invasion was seen. Focally the tumor was present less than 0.1 cm from the surgical margin.

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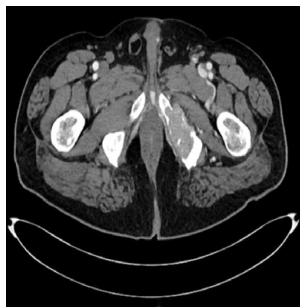


Figure 3: Abdominal CT 18 months' post-surgery shows tissue like lesions surrounding the right kidney, the largest one causing mild hydronephrosis. There is also a subcutaneous lesion near the surgical scar.

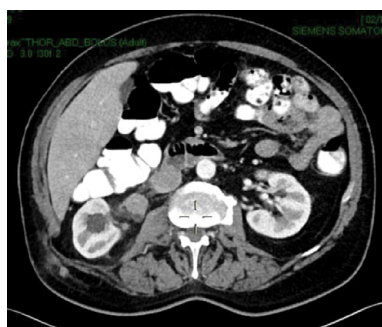


Figure 4: Additional lesion that appeared was a 6 cm lesion in the left lower ramus pubis.

Immunohistochemically, the neoplastic cells were positive for CD99, NSE, CD56, E-cadherin, Vimentin, HMB-45, Calretinin, and P-53, and Negative for Pankeratin, CK7, CK20, EMA, P-63, Inhibin, Synaptophysin, Chromogranin, PAX-8, CD20, CD34, S-100 and Desmin.

The diagnosis of adrenocortical carcinoma was considered, but Inhibin and Melan-A were negative, making the possibility quite unlikely. The H&E appearance corresponded with PEComa with weak positivity for HMB45 and diffuse nuclear positivity for MITF while SMA and desmin were negative. The tumor was eventually labeled as an epithelioid malignant neoplasm most suggestive of malignant PEComa.

The patient began clinical and radiological follow up in our oncological service. An abdominal CT performed on November 2014, a year and a half post-surgery, demonstrated tissue like lesions surrounding the right kidney measuring up to 2 cm, and the largest one causing mild hydronephrosis (Figure 3). Additional lesions that appeared were a subcutaneous lesion near the surgical scar (Figure 3A) and a 6 cm lesion in the left lower ramus pubis (Figure 4).

The patient was started on Everolimus and was referred for drainage of the right kidney. An antegrade pyelography showed complete obstruction at the level of the upper ureter and a nephrostomy tube was inserted. A biopsy of the subcutaneous lesion demonstrated fibrofatty tissue infiltrated by epithelial polygonal cells with a clear cytoplasm, identical morphologically and Immunohistochemically to the original tumor.

The patient continued the biological treatment and on the follow up abdominal CT, only 2 months later, all the hypodense lesions grew larger, except for the subcutaneous lesion that was taken out in the biopsy. The treatment was changed to Votrient which kept the

metastasis foci stable in size and location for only 6 months. Since then the patient has changed several regimens of treatment including Palbociclib and Aredia, Adriamycin and currently Gemzar without durable effect.

Discussion

Epithelioid Angiomyolipoma (Perivascular epithelioid cell tumor [PEComa]) of the kidney is a mesenchymal lesion very closely related to the classic angiomyolipoma. A couple of hundred cases are published, with mean age group of approximately 40 years and male to female ratio of 1:1 [1,2]. The perivascular epithelioid cell, or PEC, appears in a certain group of tumors and has its typical morphological, Immunohistochemical and genetical characteristics [3,4]. It has been speculated that the PEComa can modulate its morphology and immunophenotype and appear in a spectrum of forms [4,5], making the diagnosis, as in our case, somewhat challenging. PEComas of the kidney include several entities among them the renal epithelioid angiomyolipoma (or renal PEComa) recognized by the WHO in the 2004 classification of kidney tumors [6]. Peri-renal PEComas as in our case are extremely rare making the differential diagnosis even more difficult [7]. Prior to the recognition of this variant many cases were wrongfully labeled as renal cell carcinoma. This entity is recognized by a unique Immunohistochemical staining for melanocytic markers like HMB45 and smooth muscle markers and not for epithelial markers. Most PEComas are benign and surgical resection with an adequate margin remains the standard treatment of PEComa. But, looking at the literature there have been several reports of distant metastases after surgical resection of renal PEComas with poor prognosis [4,8]. Even though there was spillage during the initial open surgery, one can't ignore the poor prognostic characteristics of the tumor of size and necrosis [1] and the rapid clinical progression. Although it has been proven that PEComas respond to mTOR inhibition [9,10], it seems that our patient shows no such response and we continue to look for a solution on his behalf.

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Conflicts of Interest

There are no conflicts of interest to disclose.

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