Renal epithelioid angiomyolipoma: Successfully Treated With Chemotherapy

Introduction
Renal epithelioid angiomyolipoma (REA) is a relatively rare mesenchymal tumor. It is composed of muscle, blood vessels and adipose tissue and is commonly considered to be a benign tumor [1, 2]. These lesions are usually detected incidentally. But in some patients, it may be presented with flank pain, hematuria or a tender renal mass [3]. REA may be sporadic or a part of tuberous sclerosis complex (TSC). When it is a part of TSC, the disease is seen earlier, tends to be multiple, larger and have a high rate of acute hemorrhage [1].

Internal abdominal imaging is appropriate for asymptomatic and <4cm REA [4, 5]. Partial nephrectomy or angiographic embolization is recommended for symptomatic and/or lesions greater than 4cm [6]. When REA causes uncontrolled hypertension, local invasion or evidence of malignancy, the treatment of choice is total nephrectomy [4]. But in some cases, REA can metastasize and have an aggressive clinical behavior. There is no a consensus about the treatment of these aggressive forms of REA. Although some cases followed without evidence of recurrence postoperatively, many cases have recurrence of the disease. So some authors suggest adjuvant therapy for REA [1, 7].

Although there is not a controlled study, doxorubicin, dacarbazine, ifosfamide, cyclophosphamide and cisplatin were shown to be effective in case reports [7]. Here, we present a case of REA, successfully treated with chemotherapy.

Case Report
A 36-year-old man, with a history of abdominal swelling, anorexia, nausea and vomiting, was investigated at another center at February 2010. A 7x7 cm cystic mass was detected by abdominal ultrasound at the...
upper pole of the left kidney. Then left nephrectomy had been performed. The gross specimen was a fragile, 7x7cm, solid tumor. The tumor had a high mitotic activity and had invaded perirenal adipotic tissue and there were tumor cells in the medullary vessels. With the immunohistochemical study HMB-45 and melan-A were positive and S-100, HMWCK, EMA, CK-7 and cytokeratin were negative. The diagnosis was renal epithelioid angiomyolipoma after the histopathological evaluation.

After four months, the patient had been admitted to hospital with the left abdominal swelling. In the radiological evaluation, there were solid lesions with the greatest size of 60mm, in the left iliac fossa, a 32mm solid lesion at the left hypochondrium and multiple intraabdominal lymphadenopathies. Thus, three cycles of doxorubicine 60mg/m², every 3-week had been administered to the patient. After cytotoxic therapy a radiologic evaluation was made. It was seen that the masses in the left iliac fossa and in the left hypochondrium progressed.

The patient had been referred to our hospital at October 2010. We planned to administer cisplatin and dacarbazine therapy. After three cycles of therapy the lesions were stable and there was subjective response. Therefore the therapy had been complemented to six courses. After the sixth course, radiologic evaluation had been done. But both the left iliac and the left hypochondriac masses had progressed again.

Discussion

REA is a newly recognized entity. Before the identification of this entity some patients had been misdiagnosed as renal cell carcinomas. Unlike renal cell carcinoma, REA's do not contain epithelial membrane antigens and cytokeratins. REA's are often positive for melanoma markers such as HMB-45, HMB-50 and melan-A and may also be focally positive for smooth muscle antigens as SMA [1]. In the study of Pea et al. they reexamined the five patients' blocks that were previously classified as renal cell carcinoma and associated with tuberous sclerosis. Three of the tumors were HMB-45 positive and were reclassified as REA. In our case, HMB-45 and melan-A were positive and cytokeratin, CK-7, EMA, S-100 were negative [8].

Classical renal angiomyolipomas usually have benign behaviours. They may have locoregional and multicentric involvement and metastasis of classic angiomyolipomas also behave in a benign manner. Unlike classical renal angiomyolipoma, REAs show more aggressive behaviours [1]. Although there is no randomized study about REA because of the rarity of this entity, there are case reports. L’Hostis had reported 46 cases of renal angiomyolipoma [9]. Only one of them was epitheloid type and at the end of the follow up, this was the only one fatal case. Cibas et al. had reported another case that metastasized to liver 3 years after partial nephrectomy [7]. Varma et al. had reported another aggressive case of REA [10]. Nine years after total nephrectomy, multiple liver metastasis and vena cava involvement had been detected. Despite of this aggressive behavior, there was no evidence of malign transformation in any of the biopsy specimens from the metastatic sites. Our patient’s disease had recurred four months after the nephrectomy. He had a solid mass in the left iliac fossa and multiple intraabdominal lymphadenopathies.

Previously it has been believed that the surgical treatment is sufficient. But after the case reports of REA that had recurred after surgery, adjuvant treatments had been considered. There is no consensus about the treatment of REA. Unlike renal cell carcinomas, REA's are chemosensitive [1]. Doxorubicine, dacarbazine, ifosfamide and cisplatin are the most frequently used agents [7]. Cibas et al. had obtained 50% reduction at the tumor size with doxorubicine therapy. Because of the tuberous sclerosis complex gene 2 mutations and mammalian target of rapamycin (mTOR) pathway are both active in angiomyolipomas, some authors suggest mTOR inhibitors in the REA therapy. But in the study of Higa et al. there had been no response to sirolimus therapy [2]. In our case, there was no response to doxorubicine therapy in the first line. In the second line we treated our patient with cisplatin and dacarbazine combination. But we had no response again.

REA's are relatively rare tumors. They must be distinguished from renal cell carcinoma with immunohistochemical study. First choice of therapy is surgery but they can metastasize after surgery. There is no known effective therapy in this situation. Doxorubicine, cisplatin, dacarbazine are the mostly used agents. But they are not effective for all patients. Therefore, we need new agents or new methods for treating these patients.


