Atypical epithelioid renal angiomyolipoma

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ABSTRACT

A very rare case of atypical bilateral giant epithelioid renal angiomyolipoma in a twenty-six-year old woman is presented. Patient was asymptomatic. Imaging studies detected large masses in both kidneys and there was no evidence of hereditary diseases such as tuberous sclerosis or Von Hippel-Landau disease. Left total nephrectomy and right partial nephrectomy were performed. Pathological report described various large non-encapsulated nodular tumors with local fat and adjacent renal parenchyma invasion. The largest tumor was in the left lower pole and measured ten by six centimeters in diameter. Histological report stated small vein invasion by malignant cells near the renal hilum with no evidence of renal carcinoma. There has been no distant metastasis at three-year follow-up.

Keywords: Giant renal masses, atypical epithelioid angiomyolipoma, malignant invasion of small renal veins, Costa Rica.

RESUMEN

Se presenta un caso muy raro de angioliomipoma (AML) renal atípico epitelioide gigante bilateral, en una mujer de 26 años, asintomática, en quién los estudios de imágenes detectaron grandes masas en ambos riñones y en la que no se encontró evidencia de enfermedades hereditarias como la esclerosis tuberosa (ET) o la Enfermedad de von Hippel-Lindau. Se hizo una nefrectomía total izquierda y una nefrectomía parcial derecha. El patólogo describió varias tumoraciones nodulares grandes, no encapsuladas, con invasión local de la grasa y del parénquima renal adyacente, con la tumoración más grande en el polo inferior izquierdo de 10 por seis centímetros de diámetro y en la histología se encontró invasión de venas pequeñas por células malignas cerca del hilio renal, sin encontrar evidencia de carcinoma renal. No se ha demostrado la presencia de metástasis a distancia en tres años de seguimiento.

Palabras clave: Masas renales gigantes, angioliomipoma epitelioide atípico, invasión maligna de venas renales pequeñas, Costa Rica.
INTRODUCTION

Angiomyolipomas (AMLs) are rare benign mesenchymal tumors that present in 0.2% of the population. They are composed of blood vessels, smooth muscle cells, and mature adipose tissue that in addition to being of renal origin can present in other sites such as liver, spleen, abdominal cavity, retroperitoneum, uterus, spermatic cord, Fallopian tubes, vagina, skin, and lungs. Approximately 80% occur sporadically and 20% in patients with tuberous sclerosis (TS). They are the most frequent renal mesenchymal tumors. The large majority of AMLs are benign (such as hamartomas), mixed, non-encapsulated, locally infiltrating tumors. They are composed of variable proportions of thick walled, haphazard blood vessels, mature adipose tissue, and fusiform cells similar to smooth muscle. Histologically they are classified as triphasic, monophasic, and epithelioid according to the proportions of the above-mentioned components they contain. They are considered to be just one or epithelioid when they contain epithelioid cells and granular cytoplasm making up 5% of tumor volume, with round nuclei and occasional disperse multinucleated giant cells, and when their component is 100% epithelioid. Epithelioid angiomyolipomas have a tendency toward malignant transformation involving perirenal fat, extension to the renal sinus, the renal vein, lymph nodes, and adrenal gland. Only a few cases of distant metastasis have been reported. More than 20 cases extending into the vena cava and more than 40 with positive periaortic lymph nodes have been described. It has been said that the disease of multiple organs including the liver, in synchronous or metachronous form, does not necessarily imply the presence of metastasis. A low percentage of fat is characteristic of this type of AML and makes its diagnosis with CT or magnetic resonance difficult.

Mean age of presentation of isolated cases is 43 years and AML is 4 times more frequent in women than in men. Interestingly 80% of cases affect the right kidney. Although AMLs tend to grow slowly, accelerated growth is seen in large masses or multiple tumors and also during pregnancy, suggesting the possibility of hormonal influence.

Approximately 77% of tumors under 4 cm are asymptomatic but 82% of tumors larger than 4 cm produce symptoms that include fever, nausea, vomiting, palpable mass, hematuria, high blood pressure, anemia, and shock. Retroperitoneal hemorrhage (Wunderlich syndrome) occurs in 50% of tumors larger than 4 cm. Kidney failure presents in 15% of multiple AMLs.

Clinically, hyperprolactinemia and galactorrhea in cases of epithelioid AML have been reported, without finding abnormalities in the pituitary gland. Cases of AML associated with coexisting clear cell renal carcinoma or with carcinoma foci inside an AML have also been reported. 2,4

CASE PRESENTATION

Patient is a 26-year-old asymptomatic woman with bilateral renal masses diagnosed by US and CT who was seen in the Urology Service in December of 2006. There was a 70 x 40 cm mass in the lower pole of the right kidney and a 45 x 35 cm mass in the midsection of the left kidney. Kidney function was normal and patient had creatinine of 0.9 mg/dL and microcytic anemia. No hepatic metastases or indication of TS or Von Hippel-Lindau disease were found and no AML was found in a study carried out on patient’s relatives, including her daughter. Left total nephrectomy and right partial nephrectomy were carried out on January 10, 2007. Abundant residual tumor remained in the upper pole. Histological study reported malignant focal invasion of the blood vessels, sarcomatoid degeneration, and atypical epithelioid AML (Figure 1). Three years later patient had creatinine of 1.4 mg/dL, normal hemoglobin of 15 g, and no evidence of metastatic disease. CT showed residual tumor in right kidney with no signs of local extension and no lymph nodes. There was no evidence of metastasis in chest radiograph and in central nervous system CT (Figure 2). Patient had dengue fever in December of 2007 and currently is in good health with no evidence of metastatic extension 3 years after surgery.

DISCUSSION

En 1991 an epithelial variant of AML 5 was described after the discovery of the reaction of certain AMLs to the melanosome-associated HMB-45 protein. In this variant, cells similar to smooth muscle cells show a predominantly epithelioid morphology. 5 Currently the majority of authors believe that these AML cells similar to smooth muscle cells originate in perivascular epithelioid cells (PEC). Tumors with predominant PEC are known as PEC tumors, or PEComas, and include lymphangioleiomyomatosis, clear cell lung tumor (“sugar” tumor), clear cell myomelanocytic tumors of the ligamentum teres and falciiform ligament, and uterine PEComas. Coexpression of the myogenic (smooth muscle actin or desmin) and melanocytic (HMB-45) tumor markers constitute a distinctive feature of PEComas. 6

The first case of malignant AML was reported by Lowe et al. in 1992 when they described a sarcomatous
transformation (leiomyosarcoma) in a previously benign AML. However it is possible that many of the renal adenocarcinomas associated with TS reported before were actually malignant epithelioid AMLs as demonstrated by Pea et al. in 4 of their 5 cases. In addition to cellular atypia, many other disturbing findings have been observed in these tumors such as necrosis, sarcomatoid transformation, numerous atypical mitoses, renal vein and vena cava invasion, regional lymph node disease, and local recurrence, but these findings may not be equivalent to malignancy. Currently the only acceptable malignancy criterion in AML is the presence of distant metastasis, principally to the lung and liver. Up to 2008 nearly 120 cases of malignant AML have been reported in the English language medical literature.

Recent studies have investigated the genetic and immunohistochemical differences between aggressive and non-aggressive AML. Various mutations of p53 have been reported in malignant tumors and are considered important for tumorigenesis and tumor progression. In 2002 Kawaguchi et al. showed diffuse immunoreactivity for p53 and p53 mutation in atypical epithelioid cells. Despite this, in a similar case, Linglei et al. found only non-specific focal areas immunopositive for p53 and p53 mutation in aggressive AML and p53 abnormalities. In 2004 Islam et al. studied the immunohistological differences among 3 cases of aggressive AML and 9 cases of benign AML using a troponin similar to T with actin that is expressed in smooth muscle cells as an antibody specific for calponin. All the non-aggressive AML cases showed strong immunoreactions. In contrast, aggressive myomatous tumor cells showed no reaction to the antibody specific for calponin h1, but showed strong immunoreactions with the smooth muscle actin. They concluded that there is a potential molecular difference between these two forms of AML. Calponin h1 loss in the tumor cells of the aggressive type could be related to invasive pathological findings and this aggressive type could be categorized as an intermediate type between the benign and malignant varieties.

**BIBLIOGRAPHY**