Case Reports
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EPITHELIOID ANGIOMYOLIPOMA: A RARE VARIANT OF RENAL ANGIOMYOLIPOMA

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Summary.- *OBJECTIVE: We present a case of primary renal epithelioid angiomyolipoma, its association with tuberous sclerosis and review the literature.*

METHODS: We present the case of a 12 year-old male with past medical history of tuberous sclerosis, characterized by developmental delay, tonic and clonic seizures, and cutaneous abnormalities. He presented with macroscopic hematuria and abdominal pain. CT scan of the abdomen

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showed the presence of a left renal tumor. He underwent left radical nephrectomy. Pathologic study of the specimen showed primary renal epithelioid angiomyolipoma, corroborated by immunohistochemistry staining. Review of the literature was performed for this rare variant and its malignant potential.

RESULTS: The presence of this epithelial variant is rare and must be taken into account because of its malignant potential and, thus, with different prognosis and follow up, compared to classical angiomyolipoma.

CONCLUSIONS: Renal angiomyolipoma is an uncommon benign tumor, representing a challenge for clinical and pathological diagnosis. Despite the big size they can reach, as well as bilaterality, multiplicity of lesions and/or lymphatic regional involvement, its malignant potential has not been established. Nevertheless, the epithelioid variant has been described recently, a rare entity with aggressive behavior, difficult histological characterization and poor prognosis.

Keywords: *Epithelioid angiomyolipoma. Kidney. Tuberous sclerosis.*

Resumen.- *OBJETIVO: Presentar un caso de angiomiolipoma (AML) variante epitelioide, primario renal, su asociación con Esclerosis Tuberosa (ET) y revisión de la literatura.*

MÉTODOS: Presentamos el caso de un paciente varón de 12 años con antecedente de retardo en el desarrollo psicomotor, crisis epilépticas tónico clónicas y estigmas cutáneos, todo esto compatible con ET. Debuta con hematuria macroscópica y dolor abdominal, encontrándose en la tomografía tumor que compromete dos tercios superiores del riñón izquierdo. Fue sometido a nefrectomía radical izquierda. La anatomía patológica, corroborada con estudios de inmunohistoquímica informó la presencia de AML, variante epiteliode.

Se reviso la bibliográfica existente sobre esta variante poco común y su comportamiento maligno.

RESULTADOS: La presencia de la variante epitelial es poco frecuente pero debe tenerse en cuenta por su comportamiento maligno y por lo tanto diferente pronóstico y seguimiento comparado al AML clásico.

CONCLUSIONES: El AML renal es un tumor benigno, poco común, que representa un reto para el diagnóstico clínico e histopatológico. A pesar del gran tamaño que puede alcanzar, la bilateralidad, la multiplicidad de las lesiones y/o el compromiso linfático regional, no se ha demostrado su potencial maligno. Sin embargo, en los últimos años se ha descrito la variante epitelioide, entidad rara de comportamiento agresivo, difícil caracterización histológica y pobre pronóstico.

Palabras clave: *Angiomiolipoma epiteliode. Riñón. Esclerosis tuberosa.*

INTRODUCTION

Angiomyolipoma (AML) of the kidney is a rare benign tumor, first described by Morgan in 1951. Histologically it is classified as typical (triphasic), with three components: mature fatty tissue, blood vessels and smooth muscle; and atypical (monophasic or epithelioid) (1,2). The epithelioid angiomyolipoma (AMLE), recently separated from the rest of angiomyolipomas, is a atypical histological variant, with aggressive behavior; associated in more than half of the cases to Tuberous Sclerosis (TSC), with mutations in the p53 gene and a high rate of distant metastases (3,4). We present the first case diagnosed in the institution.

CASE REPORT

A 12-years-old male patient with a history of delay in psychomotor development and tonic-clonic seizures treated with carbamazepine and phenytoin. Approximately 3 weeks before evaluation, the patient presented gross hematuria with clots and abdominal pain predominantly hypogastric. Computerized tomography of the abdomen and pelvis shoed a 80 x 64 x 56 mm heterogeneous mass involving two-thirds of the upper left kidney. Chest x-ray was normal and a brain computerized tomography showed a cortico-subcortical hypodense areas associated with multiple periventricular calcifications (Figure 1).

At physical examination, the patient is awake but does not obey orders, with severe disturbance of higher brain functions without motor deficit. Examination of the fondus oculi did not reveal retinal lesions. At the face, nose, and nasogenian folds multiple erythematous papules up to 2 mm were present. At abdominal palpation a nontender left flank tumor was present. Under the diagnosis of left kidney angiomyolipoma associated with tuberous sclerosis, the patients underwent a left radical nephrectomy and left para-aortic lymphadenectomy.

Macroscopically the specimen showed a 250 grams kidney, with a 8 x 7 x 2.3 cm brownish tumor replacing 90% of the renal parenchyma. Hemorrhagic and necrotic tissue was identified, infiltrating and destroying the pyelocalicial system (Figure 2).

Microscopically there is an infiltrating tumor with irregular edges, consisting mainly of polygonal epithelioid cells with clear cytoplasm, interspersed with granular eosinophilic and multinucleated cytoplasm similar to the ganglion cells. These cells presented nuclear atypia, prominent nucleoli and mitosis (0-5 mitosis / 10 high

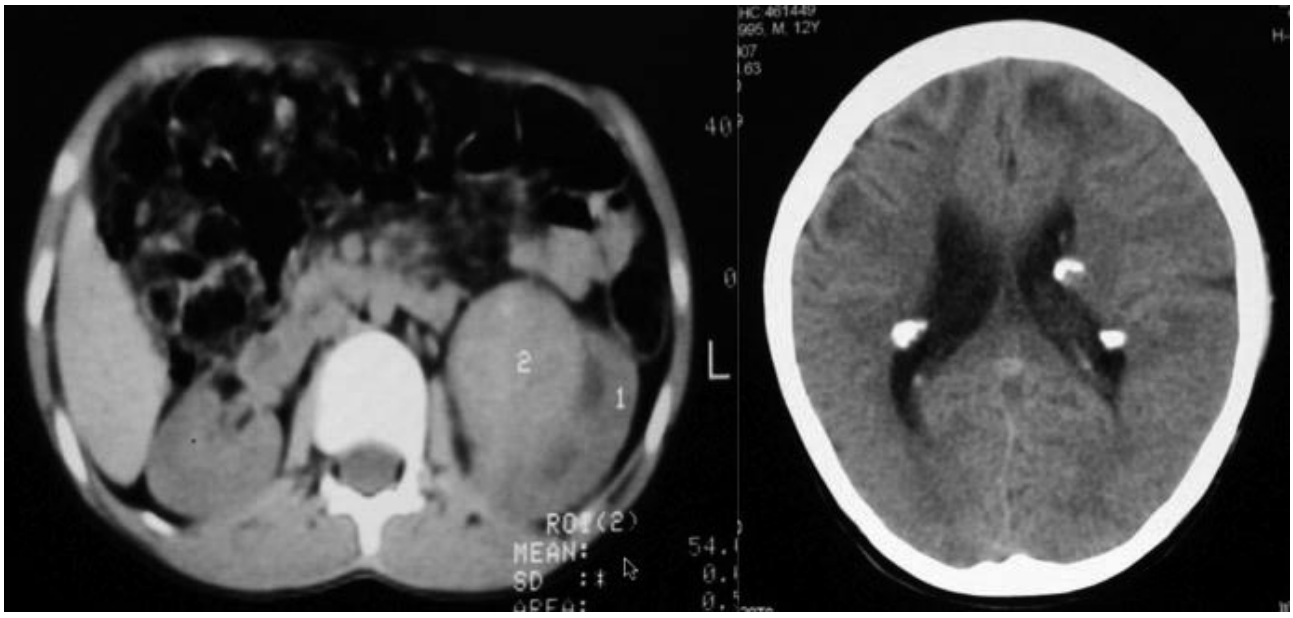

FIGURE 1. Contrast enhanced CT shows a mass heterogeneous that commits the two-thirds of the upper left kidney. Axial contrast enhanced CT demonstrates multiple calcifications periventriculars.

power fields); also present areas of hemorrhage and necrosis. There were no vascular or perineural invasion. The ureter, perirenal fat and surgical margins were free of malignancy.

This hystomorphology was consistent with epithelioid angiomyolipoma (Figure 3), which was confirmed by immunohistochemical tests, whose results are presented in Table I.

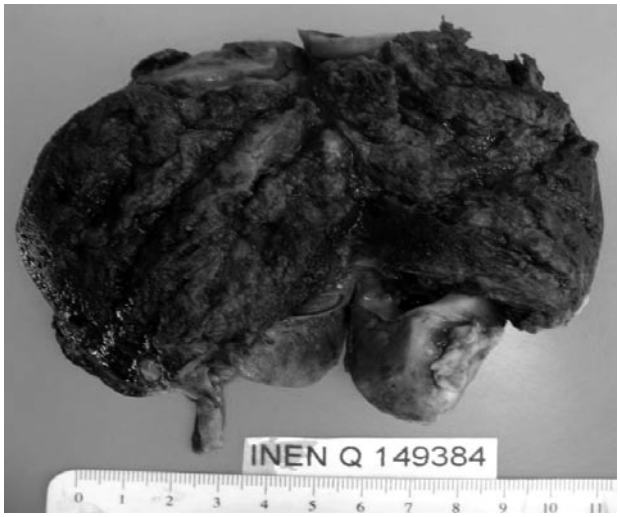

FIGURE 2. Macroscopic image. Note the hemorrhagic aspect of the tumor mass.

DISCUSSION

Renal AML, also known as hamartoma, is a relatively rare benign tumor that appears in 0.3% of the general population and accounts for 3% of solid renal masses. It belongs to the family of lesions characterized by epithelioid perivascular proliferation cells and consists, in varying proportions, of three cell lines: mature fatty tissue, smooth muscle and irregular blood vessels (1,2). Usually presents under two clinical forms: as a single large tumor in women of middle age, or associated with Bourneville disease or tuberous sclerosis, which is usually bilateral, multiple, and with the highest incidence in young men, representing between 15 and 20% of cases (3-5).

Tuberous Sclerosis (TSC) is a hereditary disease whose diagnosis can be made at different stages of life. The infant starts with bending spasms, hipsiarrithmia and hypomelanotic spots on the skin. In older children and adolescents, as our patient, they present with epilepsy, facial angiofibromas, and intracranial calcifications in the region of the ventricular walls (6,7). It also involves other organs such as kidneys, liver, brain, heart, eyes, lungs and bones (8-11). The association of AML and RCC is an unusual finding. Lane et al. reported 28 cases of coexistence of AML and RCC including ipsilateral (18), contralateral (6) and bilateral (3) tumors (9). Given the paucity of published cases, it is not yet possible to tell to what extend this coexistence of AML and RCC influences the prognosis (12).

AML is present in 50 to 80% of cases of TSC, and their partnership is more close with epithelioid variant of renal AML, an entity of relatively recent description, with

TABLE I. INMUNOHISTOCHEMISTRY PANEL.

	HMB45	CD117	Vimentin	α Actin	Keratin
ANGIOMYOLIPOMA	+	+	+	+	+

few reports in the literature, which is characterized by its aggressiveness. It is known that more than half of patients with AMLE have ET (2,6).

AMLE affects both sexes equally, with an average age at diagnosis of 38 years. Patients are symptomatic, complaining of flank pain, palpable mass, and less than 15% will present renal failure due to compression and replacement of renal parenchyma. Is a tumor that brings a diagnostic problem, often being interpreted as a renal cell carcinoma, or high-grade sarcoma. The imaging studies simulate clear cell carcinoma scanty fatty tissue (7,8).

Macroscopically, tumors are medium to large size, yellowish-orange with large areas of hemorrhage and necrosis. There may be extrarenal tumor extension or involvement of the vena cava or renal vein. Microscopically, is an infiltrating tumor, very cellular, consisting mainly of polygonal cells with vacuolate cytoplasm, eosinophilic granular or clear, with plenty of glycogen, and other multinucleated similar to the ganglion cells. Can also be found a small proportion of fusiform cells. Cells samples nuclear anaplasia, mitotic activity with presence of atypical figures, vascular invasion, necrosis and inflammatory response. The bleeding is prominent. Few cases show focal areas of classic AML. Most cases, as in the present case, lack the typical elements of AML (9).

Immunohistochemistry is important to characterize this tumor. The presence of immunoreactivity positive for HMB45, HMB50, CD117, CD63, and the negativity to epithelial markers and cytokeratins confirm the diagnosis (2). It has also been described an expression variable markers for smooth muscle (smooth muscle actin and actin specific muscle). Genetically, it shares the same alteration than the classic AML; that is, the loss of allelic short arm of chromosome 16p (TS2). Furthermore, mutations in the p53 gene in the epithelioid variant have been identified, suggesting an important role in their malignant behavior. In approximately one third of cases metastases of AMLE have been described to lymph nodes,

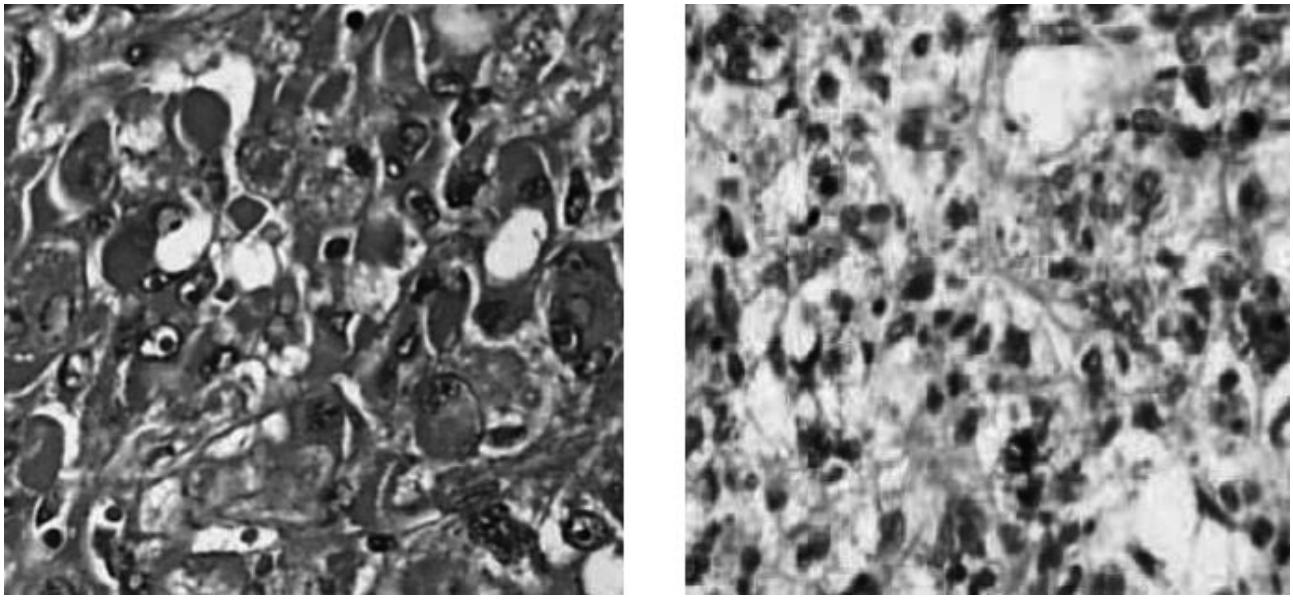

FIGURE 3. Microscopic image. Cells polygonal of epithelioid aspect, and other multinucleated similar to the ganglion cells. Epithelioid AML with many HMB-45 positive cells.

liver, lung, bone and marrow. To date, no pathological parameters have been identified which directly correlates with survival. However, tumors with necrosis, mitotic activity and nuclear anaplasia, have a more aggressive behavior (1,2).

The management of renal AMLs is widely discussed in the literature (9,13-15). The most widely accepted is the therapeutic algorithm of Oesterling et al, based on clinical presentation, the size of the tumor and bilaterality. Thus, in asymptomatic tumors, evaluation with abdominal ultrasound and/or CT-scan every six or twelve months, depending on the size of the tumor, greater or less than 4 cm., respectively, is necessary. In symptomatic and/or bilateral tumors, artery embolization, selective kidney or conservative surgery (nephron sparing) are the treatments of choice. Radical nephrectomy is reserved for those cases with hemodynamic instability due to massive bleeding, large tumors, or coexistence with carcinoma in the same kidney, criteria considered in the clinical management of the present case (14,15).

CONCLUSIONS

Renal angiomyolipoma is an uncommon benign tumor, representing a challenge for clinical and pathological diagnosis. Despite the big size they can reach, as well as bilaterality, multiplicity of lesions and/or lymphatic regional involvement, its malignant potential has not been established. Nevertheless, the epithelioid variant has been described recently, a rare entity with aggressive behavior, difficult histological characterization and poor prognosis.

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