



Case Report:

Epitheloid Variant of Angiomyolipoma in a Patient with Tuberous Sclerosis.

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Abstract: Epitheloid angiomyolipoma of kidney is a type of Perivascular endothelial cell derived tumor with an aggressive behaviour with specific pathological, immunohistochemical and genetic characteristics. They can occur in a pure form or in association with classical angiomyolipoma. It can be associated with tuberous sclerosis in 50% of cases. Our case is a possible case of tuberous sclerosis with epitheloid angiomyolipoma, hepatic angiomyolipoma and lymphangioleiomyomatosis with normal MRI brain and no cutaneous features. Radical nephrectomy with biopsy of hepatic lesion was performed. Histopathological examination revealed epitheloid variant with features of angiomyolipoma. It is six months post surgery and patient is doing well with no evidence of recurrence. Epitheloid angiomyolipoma is a rare malignancy with only 120 cases reported in literature.

Key Words: Epitheloid angiomyolipoma; Tuberous sclerosis; Hepatic angiomyolipoma; Pulmonary lymphangioleiomyomatosis.

Introduction

Epitheloid angiomyolipoma (AML) of kidney is a type of PEComas included in the new WHO classification of renal tumours. Perivascular endothelial cell is the cell of origin for a group of tumours like clear-cell "sugar" tumor (CCST) of the lung and extrapulmonary sites, lymphangioleiomyomatosis, clear-cell myomelanocytic tumor of the falciiform ligament/ligamentum teres and rare clear-cell tumors of other anatomical sites including Angiomyolipomas.[1] Epitheloid AMLS were associated with tuberous sclerosis in more than 50% of cases. These tumours are related to loss of tuberous sclerosis complex genes TSC1 (9q34) or TSC2 (16p13.3) which seem to have a role in the regulation of Rheb/mTOR/p70S6K pathway.[1]

Tuberous sclerosis complex is an autosomal dominant disorder characterised by features described in Table 1.[2]

Major features	Minor features
Facial angiofibromas	"Confetti" skin lesions
Hypomelanotic macules	Gingival fibromas
Shagreen patches	Pits in dental enamel
Cortical tubers	Cerebral white matter radial migration lines
Subependymal nodules	Retinal achromatic patches
Subependymal giant cell tumors	Bone cysts
Retinal hamartomas	Hamartomatous rectal polyps
Cardiac Rhabdomyomas	
Renal Angiomyolipoma	
Pulmonary Lymphangioleiomyomatosis	

Definitive diagnosis: 2 major features or one major and one minor feature
Probable diagnosis: One major and one minor feature
Possible diagnosis: One major or two or more minor features
Note: Cortical tubers together with cerebral white matter radial migration lines are counted as one feature. In patients with LAM or renal AML, other features are required for diagnosis.

Nearly only 120 cases of epitheloid angiomyolipoma were reported in literature.[1]

Case Report:

A 22 years old female presented with dull aching pain over right side of abdomen with no other associated symptoms. On general examination, patient was normal. On abdominal

examination, there was mass abdomen located in right hypochondrium extending to lumbar region of size 10 cms below the costal margin and was bimanually palpable. A contrast enhanced computer tomography showed a 12.8 x14.2x17.2 cms heterogeneously enhancing lesion arising from upper pole of kidney, with large packets of fatty density[-35 to -20 HU] and an aneurysm [Fig.1 a & b]. The lesion was abutting liver with no obvious infiltration. Renal

Vein and Inferior vena cava were normal without any significant lymphadenopathy. Liver showed multiple hypodense non enhancing areas involving both lobes of liver and these lesions were hyperechoic in ultrasonography.[Fig.1c] Lung showed multiple cysts characteristic of lymphangioleiomyomatosis [Fig.1e & f]. A MRI scan was performed to rule out any central nervous system lesions and was found to be normal.

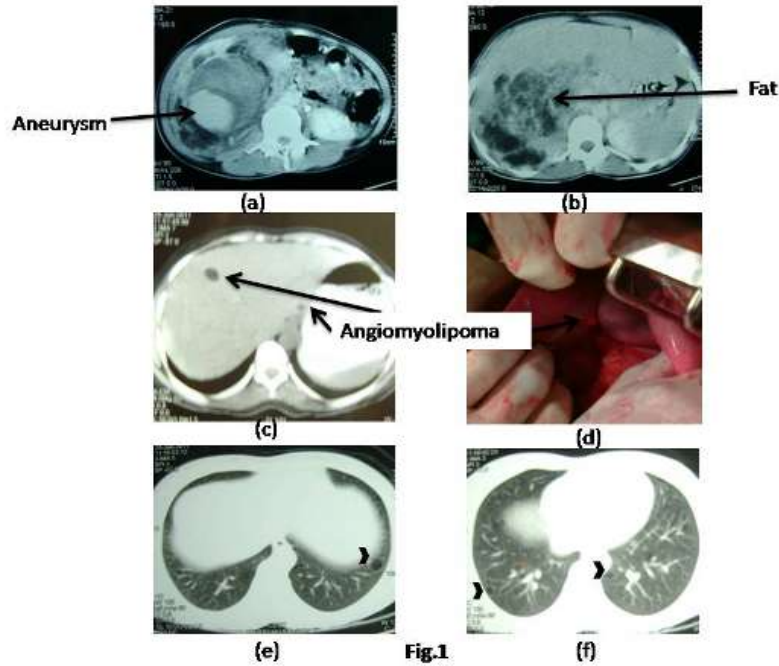


Fig. 1: (a,b,c,e,f) CT image showing Angiomyolipoma of kidney with characteristic fat content, aneurysm formation, multiple Angiomyolipomas of Liver and multiple cavitary lesions in Lung- Lymphangioleiomyomatosis; (d)Intraoperative image showing Angiomyolipoma of Liver

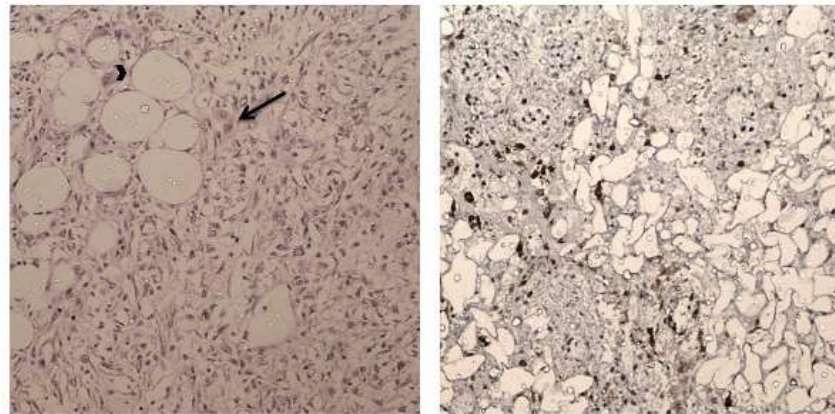


Fig. 2(a)

Fig.2(b)

Fig.2: Triphasic and epithelioid AML photomicrographs (a) Hematoxylin-eosin staining (x40) of an epithelioid AML with epithelioid cells (arrows) adjacent to a typical AML demonstrating fat (arrowheads). (b) HMB-45 immunostaining (x40) of the epithelioid cells (arrows) with the HMB-45 stain.

With a diagnosis of angiomyolipoma of right kidney, a right nephrectomy had been performed. Liver had multiple angiomyolipomas [Fig. 1d]. Grossly there was 12.5x9x7 cms sized tumor involving upper pole with areas of necrosis and hemorrhage. Microscopically the tumor showed fat cells, mixed with spindle shaped epithelioid cells with nuclear atypia, pleomorphism, and hyperchromatism. Epithelioid component was less than 10% of tumor. Four perihilar lymph nodes were resected which were free of tumor. Immunohistochemistry revealed HMB45 positivity, focally c-kit positive and negative for cytokeratin. Hence a diagnosis of angiomyolipoma with an epithelioid component.

Post operative recovery was uneventful and patient was discharged on postoperative day six. Patient was in followup for 6 months and there was no features of recurrence.

Discussion:

Renal AMLs are present in 50-75% of cases with tuberous sclerosis and 20% of patients with AML have TS.[3] Bonetti et al in 1992 [4] described a special type of cells called perivascular endothelial cell and later in 1996 Zamboni et al [5] described "PEComas" which constitutes group of related mesenchymal tumors with cell of origin as PEC. These tumors are similar in morphology and immunohistochemistry and are positive for HMB 45.

Angiomyolipomas can be classified as classical AML and epithelioid AML. Epithelioid AML can be further classified as Atypical AML or Malignant Epithelioid AML (MEAML). Classical AML is a triphasic tumor with abnormal blood vessels, fat and smooth muscles. Atypical AML have little fat content and have less probability of having abnormal tortuous vessels which are characteristically seen in classical AML. Malignant epithelioid AML was first reported by Pea et al in 1998, following only few cases had been reported in literature. The distinguishing features of MEAML are its size, relatively less or absent fat and blood vessels, high mitotic index, and the only confirmatory sign is presence of metastases. Epithelioid AML can occur in a pure form or along with classical AML as in our case. The aggressiveness of the epithelioid variant depends on the percentage of epithelioid component in the tumor. A new classification had been described taking this into account for AMLs a) Classical/ typical AML b) Pure/Predominant Epithelioid histology with >95% of epithelioid component c) Angiomyolipoma with component of epithelioid histology < 95% - need to specify the amount of epithelioid component. Of 120 cases of epithelioid AML reported in literature 47% had progressive disease.[1]

Pulmonary lymphangiomyomatosis is a progressive disorder affecting lungs occurs in 1-3% of patients with tuberculosis and estrogen hormone was thought to play a role in LAM as they are rare in men, unusual before menarche and after menopause in women. They can manifest acute onset of breathlessness, chest pain, cough, pneumothorax, chylous effusions, etc., and later progressively leading to respiratory failure. These lesions need to be identified before surgery for kidney as they may develop spontaneous pneumothorax in 60-70% of patients.

Hepatic AMLs are rare with nearly 120 cases reported in literature and most of them are sporadic. Only 5.8% cases have been found to be associated with tuberous sclerosis. When both hepatic and renal AMLs are present, tuberous sclerosis may be a possible diagnosis.

Conclusion:

Epithelioid variant of AML can occur in pure form or in cases with AML. These patients require close followup as they have

aggressive behaviour. Renal AMLs can be associated with Hepatic AML and Pulmonary LAM which needs evaluation to rule out TS complex.

References:

1. Nese N, Martignoni G, Fletcher CD, Gupta R, Pan CC, et al Pure epithelioid PEComas (so-called epithelioid angiomyolipoma) of the kidney: A clinicopathologic study of 41 cases: detailed assessment of morphology and risk stratification. *Am J Surg Pathol.* 2011 Feb;35(2):161-176.
2. Roach ES, Gomez MR, Northrup H. Tuberous sclerosis complex consensus conference: Revised clinical diagnostic criteria. *J Child Neurol.* 1998;13:624-628.
3. Logue LG, Acker RE, Sienko AE. Best cases from the AFIP: Angiomyolipomas in tuberous sclerosis. *Radiographics.* 2003;23:241-246.
4. Bonetti F, Pea M, Martignoni G, Zamboni G. PEC and sugar. *Am J Surg Pathol* 1992;16:307-308.
5. Zamboni G, Pea M, Martignoni G et al. Clear cell 'sugar' tumour of the pancreas. A novel member of the family of lesions characterised by the presence of perivascular epithelioid cells. *Am J Surg Pathol* 1996;20:722-730.