

Case Report

Cytology of Renal Angiomyolipoma with Predominant Epithelioid Cell Component - A Report of Two Cases with Review of Literature

Sood N*, Batra R**

Abstract

Renal Angiomyolipoma (AML) is a benign lesion with a variable admixture of fat cells, thick walled blood vessels, smooth muscle and polygonal epithelioid cells. The lesion can be diagnosed with certainty in the presence of all the components on fine needle aspiration, supported by CT findings. However the presence of predominant population of epithelioid cells with paucity or absence of other components can be particularly worrisome, especially if radiological findings are noncontributory. These large cells with low N:C ratio and frothy cytoplasm and anisonucleosis require detailed evaluation and careful search for typical background cytology. Two such cases of AML with a predominant population of epithelioid cells are being described with their cytological and histological findings with a review of literature to highlight the diagnostic dilemma and emphasize the utility of HMB-45 immunostaining in such cases.

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Introduction

Renal angiomyolipoma (AML) is an uncommon benign lesion accounting for less than 1% of renal tumours¹ and an incidence of 13/10000 adults.¹ It is characterized by a variable admixture of blood vessels, fat, smooth muscle and perivascular epithelioid cells (PEC).¹ There are two distinct clinical patterns in AML. Those associated with tuberous sclerosis vary in size, are bilateral and multifocal with no sex predilection.¹ Sporadic cases however are large in size, unilateral and unifocal.¹

Fine needle aspiration cytology (FNAC) and computed tomography (CT) have been of help in diagnosis in typical cases showing sheets of endothelial cells, clusters of smooth muscle cells and groups of mature fat cells but the diagnostic dilemma arises in cases showing a large population of polygonal epithelioid cells, pleomorphism and mitosis.² Epithelioid cell variant of renal angiomyolipoma (EAML), conventional renal cell carcinoma (RCC) and

chromophobe RCC have to be considered in such cases.² Immunomarkers like smooth muscle actin, S-100 and HMB-45 are additional corroborative markers for confirmative diagnosis. HMB-45 positivity in epithelioid and spindle cells is the mainstay of diagnosis of renal AML.

Two cases one each of solitary and bifocal renal AML are being described with special emphasis on the epithelioid cell component.

Case Reports

Case 1

A 30-year-old male presented to the surgical OPD with pain in the right lumbar region. CT abdomen showed a hypodense well defined exophytic lesion 45x25 mm with predominant fat density present in mid-lower pole of right kidney with splaying of calyces and streaky hyper-densities within the lesion suggestive of a vascular component. A presumptive diagnosis of angiomyolipoma was rendered and CT guided FNAC was performed.

The aspirates were haemorrhagic and markedly cellular consisting of islands and small aggregates of polygonal epithelioid cells with low N:C ratio with central, round or oval nucleus with fine

*Senior Pathologist and Head, **Senior Resident, Department of Pathology, D.D.U. Hospital, Hari Nagar, New Delhi-110064.

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Corresponding Author: Dr. Neelam Sood, B-3/337, (G.F.), Paschim Vihar, New Delhi-110063.

E-mail: neesu123@yahoo.co.in; rashmiscin@yahoo.com

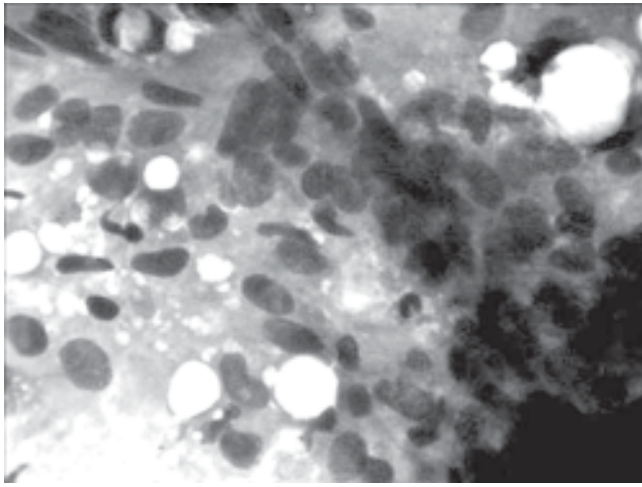


Fig. 1 : FNAC of Case 1, showing predominant population of epithelioid cells admixed with few spindle cells, endothelial cells and few fat droplets (MGG, x 1000).

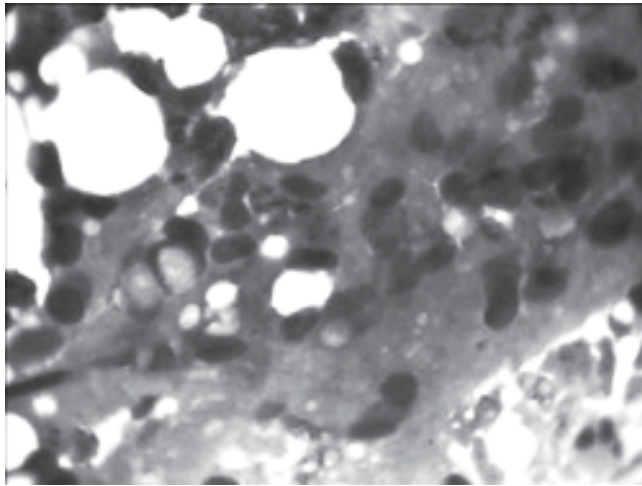


Fig. 2 : FNAC of Case 1, showing admixture of spindle cells and fat cells (MGG, x 1000).

nuclear chromatin admixed with few endothelial cells and spindle cells with oval nuclei (Figs. 1,2). Dissociated epithelioid cells were seen either as naked nuclei or with finely granular and vacuolated cytoplasm giving it a frothy appearance. Large fat vacuoles were seen associated with these cells. A FNAC diagnosis of renal angiomyolipoma rich in epithelioid cells was rendered with subsequent surgical excision and histopathology.

The radical nephrectomy specimen measured 7x5x4 cm. Cut surface showed a reddish yellow growth measuring 4x2 cm in the middle and lower pole, well demarcated from the surrounding renal parenchyma. Sections from the growth showed an admixture of mature adipose tissue, thick walled blood vessels lacking elastic lamina confirmed on Van Gieson's elastin stain. Forming a cuff around the blood vessels were large islands of spindle to polygonal epithelioid cells with low N:C ratio, round nucleus with pale to eosinophilic cytoplasm with a feathery appearance and negligible mitosis (Fig. 3). S-100 positivity in spindle cells and adipocytes and HMB-45 immunoreactivity in the spindle (5%) and in the epithelioid cells (20%), confirmed the diagnosis of angiomyolipoma with areas of epithelioid cell proliferation.

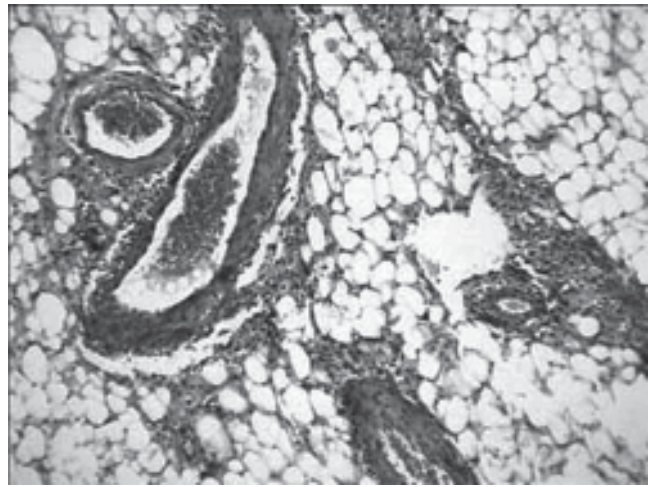


Fig. 3 : HPE of Case 1, classical areas of AML showing admixture of thick walled blood vessels with perivascular epithelioid cells, spindle cells and adipocytes (MGG, x 400).

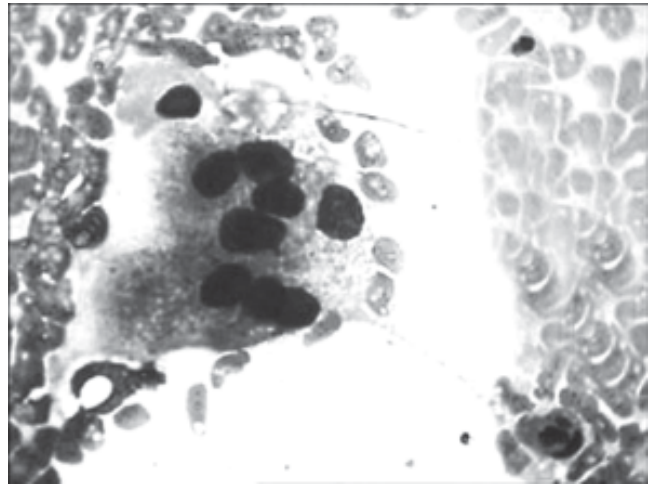


Fig. 4 : FNAC of Case 2, showing a cluster of epithelioid cells with granular cytoplasm with round nuclei and mild anisonucleosis (MGG, x 1000).

Case 2

A 24 year old female presented to the surgical OPD with pain left lumbar region since 4 months. CT revealed an exophytic mass 60x49x25 mm arising from upper pole of left kidney posteriorly and reaching anteriorly up to spleen and another similar mass 15x15x15 mm arising from middle pole anteriorly. Both showed variable fat density admixed with streaky soft tissue component on contrast enhanced CT with splaying of calyces. Possibility of renal cell carcinoma could not be ruled out and patient was referred for CT guided FNAC. Physical examination and review of brain CT, ocular as well as dermatological examination ruled out any stigmata associated with tuberous sclerosis.

There was a predominant population of epithelioid cells (Fig. 4) which in addition to above showed mild hyperchromasia, focal moderate anisonucleosis and nuclear pseudoinclusions of varying sizes in these cells (Fig. 5). Mitosis however was negligible. Absence of spindle cell component, adipocytes and endothelial cells posed a diagnostic dilemma. Possibility of EAML and intermediate cell conventional renal cell carcinoma could not be ruled out and patient was advised surgical excision and histopathology examination. Immunocytochemistry could not be done on FNAC smears.

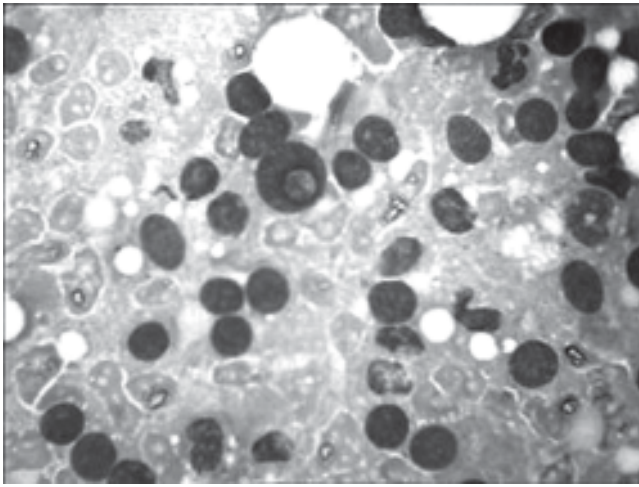


Fig. 5 : FNAC of Case 2, showing naked nuclei stripped of cytoplasm with focal moderate anisonucleosis with nuclear pseudoinclusions (MGG, x 1000).

A partial nephrectomy specimen with friable tissue measuring 8x6x5 cm labeled upper pole of kidney and another small part measuring 3X2.5 cm labeled middle pole of kidney. Gray, friable, haemorrhagic non-encapsulated growth well demarcated from surrounding kidney parenchyma could be identified in both tissues.

Sections from growth showed sheets of polygonal epithelioid cells with similar nuclear morphology as above, separated by hyaline cords (Fig.6). The most striking feature noted was the moderate nuclear pleomorphism, mitosis and multinucleate giant cells. However atypical mitosis was not seen. Extensive areas of necrosis were seen in the tumour. HMB-45 immunostaining was seen in epithelioid cells with positivity of up to 40%. S-100 positivity was also noted. A careful search of the tumour showed tiny foci of classic AML. Diagnosis of epithelioid cell variant of angiomyolipoma was rendered.

Both cases have been on follow up for 1-2 years without any recurrence or metastasis.

Discussion

Angiomyolipoma is a member of a family of lesions characterised by the presence of perivascular epithelioid cell (PEC), which can differentiate in the directions of spindle cells with features of smooth muscle, fat cells and epithelioid cells with clear or eosinophilic cytoplasm.¹ Presence of multiple angiomyolipomas is considered to be presumptive evidence for the diagnosis of tuberous sclerosis and should be included in the report.¹ Most obvious manifestations of tuberous sclerosis being mental retardation, seizures and facial angiofibromas (vogt's triad).¹ None of these features were seen in both cases though both were younger than 50 years, as against observations in literature.¹

CT can render a confirmatory diagnosis of AML in presence of typical fat densities; however presence of predominant smooth muscle and paucity of fat can be a cause of confusion with RCC as was in Case

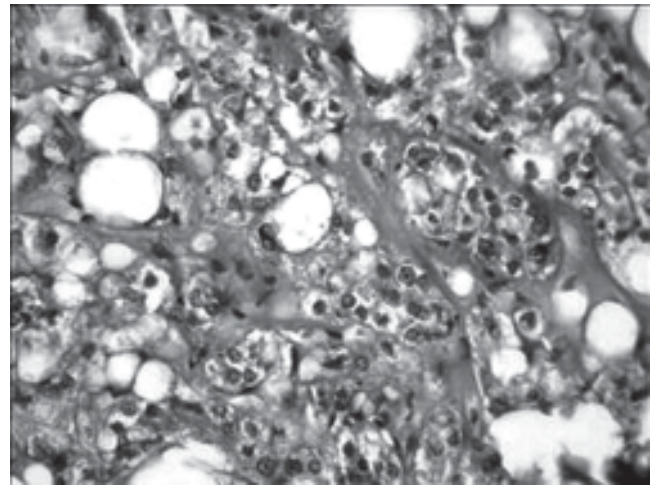


Fig. 6 : HPE of Case 2, showing polygonal epithelioid cells with clear cytoplasm separated by hyaline cords interspersed in scant adipose tissue (MGG, x 400).

2.²

Typical cytological features described in conventional AML are admixture of large number of adipocytes, endothelial cells and smooth muscle cells (spindle as well as epithelioid), foam cells and giant histiocytes in an inflammatory background.^{1, 2}

However both these cases showed a predominance of solid sheets, clusters and loosely dissociated epithelioid cells with vacuolated to dense cyanophilic cytoplasm which have been characteristically described in epithelioid AML.³ Nuclei of these cells were round with smooth contour with evenly distributed chromatin as observed by other workers.³ Features of moderate anisonucleosis and presence of naked nuclei particularly in Case 2 added to the diagnostic confusion with EAML and RCC.³ Presence of intranuclear pseudoinclusions as observed in Case 2 have been described by various authors in monotypic EAML and conventional RCC. Paucity of spindle cells, endothelial cells and fat is described in cytological aspirates of EAML as was also seen in Case 2.³ However other characteristic features of AML were noted in Case 1 as described above.

On gross examination these tumours are well circumscribed, non infiltrative and may appear yellow to gray white depending on the smooth muscle component.^{4,5} Hemorrhage, necrosis and friability have been described in EAML as was seen in Case 2.^{4,6}

On histopathology examination a classic AML shows an admixture of adipocytes, thick walled blood vessels resembling arteries and lacking an elastic lamina and smooth muscle cells which can be present either as short or long spindle cells with pale

cytoplasm or as polygonal epithelioid cells or admixture of both¹ as was seen in Case 1. These cells usually form a cuff centered around blood vessels with a radial orientation to the vessels as seen in the first case.

A striking feature however noted in both our cases was the presence of sheets of polygonal epithelioid cells separated by hyaline cords which had abundant clear to eosinophilic cytoplasm and eccentric nuclei. Hyperchromatic nuclei, prominent nucleoli and moderate anisonucleosis as seen in Case 2 are described by other workers particularly in EAML.^{4,6} Mitosis and multinucleation in Case 2 were additional alarming features.^{5,6} Areas of necrosis and hemorrhage were also seen. A careful search for other elements of a classic AML revealed only few fat cells interspersed between the tumour cells in Case 2 as also observed by other workers.⁴

Epithelioid cell variant of AML as described by Mai⁴ and Eble⁵ are lesions composed almost entirely of epithelioid cells, scant adipocytes, paucity/absence of spindle cells and scattered thick walled blood vessels. Monotypic EAML or REON (renal epithelioid oxyphilic neoplasms) were characterised by pure proliferation of epithelioid cells with absence of adipocytes, smooth muscle spindle cells and thick walled blood vessels as described by Martignoni et al.⁶ Based on these criteria we categorised our second case as epithelioid variant of angiomyolipoma.

These tumours can also be mistaken for RCC as in our second case. Similar dilemma was faced by other workers as revealed by a review of literature.^{4,6} RCC are CK (+), EMA (+), Vimentin (+) and HMB-45 (-) whereas AML is CK (-), EMA(-), Vimentin (+), and HMB-45 (+).² In addition spindle cells are actin (+) and fat cells S-100 positive as also observed by us.

HMB-45 immunostaining (evidence of melanocytic

differentiation)^{4,6} is the mainstay of diagnosis particularly where epithelioid cells are the only element causing confusion with renal cell carcinoma. The staining is mainly in epithelioid cells with lesser positivity in spindle cells as seen in our cases and those demonstrated by other workers.⁴ Eble⁵ demonstrated 10-70% positivity in these cells. We demonstrated 5-20% positivity in Case 1 and 40% in Case 2; the staining pattern being mainly cytoplasmic with perinuclear accentuation.

We thus emphasize the need for eliminating malignant RCC and EAML with malignant potential in cases where the smears are rich in epithelioid cells. HMB-45 staining in such cases would be a useful adjunct.

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References

1. Eble JN. Angiomyolipoma of kidney. *Semin Diagn Pathol* 1998; 15:21-40.
2. Bonzanini M, Pea M, Martignoni G, et al. Preoperative diagnosis of renal angiomyolipoma. Fine needle aspiration cytology and immunocytochemical characterization. *Pathology* 1994; 26:170-5.
3. Mojica D, Wilfrido, Jovanoska S, Bernacki G. Epithelioid angiomyolipoma. Appearance on fine needle aspiration-report of a case. *Diagn Cytopathol* 2000; 23:192-5.
4. Mai KT, Perkins DG, Collins JP. Epithelioid cell variant of renal angiomyolipomas. Case report. *Histopathology* 1996; 28:277-80.
5. Eble JN, Amin MB, Young RH. Epithelioid angiomyolipoma of the kidney. A report of five cases with a prominent and diagnostically confusing epithelioid smooth muscle component. *Am J Surg Pathol* 1997; 21: 1123-30.
6. Martignoni G, Pea M, Bonetti F, et al. Carcinoma like monotypic epithelioid angiomyolipoma in patients without evidence of tuberous sclerosis. *Am J Surg Pathol* 1998; 22:663-72.