Case Report

Fat poor angiomyolipoma with lymphadenopathy: Diagnostic dilemma

Pankaj Kumar Garg, Bhupendra Kumar Jain, Anjay Kumar, Shuchi Bhatt[1], Vibhav Vibhav[2]

Departments of Surgery, [1]Radiodiagnosis, [2]Pathology, University College of Medical Sciences and Guru Teg Bahadur Hospital, University of Delhi, Delhi, India

Abstract

A 24-year-old lady presented with left flank pain of 3 months duration. She had stigmata of tuberous sclerosis complex in the form of angiofibromas on face, ash-leaf macules on back and right upper limb and shagreen patches over back. Computed tomography scan of the abdomen showed 6.5 cm × 5.0 cm × 4.4 cm lobulated intensely enhancing exophytic mass lesion in mid pole of left kidney with significant para-aortic lymphadenopathy with no evidence of fat in the mass. She underwent radical left nephrectomy with a provisional diagnosis of renal cell carcinoma. Histopathological examination showed multicenteric angiomyolipoma involving kidney and para-aortic lymph nodes. This case report underscores the need for further research to differentiate fat-poor angiomyolipoma and lymphadenopathy from renal cell carcinoma.

Key Words: Angiomyolipoma, fat-poor, diagnosis

Address for correspondence:
Dr. Pankaj Kumar Garg, Department of Surgery, University College of Medical Sciences and Guru Teg Bahadur Hospital, Dilshad Garden, Delhi - 110 095, India. E-mail: dr.pankajgarg@gmail.com

Received: 22.01.2011, **Accepted:** 09.04.2011

INTRODUCTION

Renal angiomyolipoma (AML) is an uncommon benign tumor, which comprises of fat, abnormal blood vessels, and smooth muscle elements in varying proportions. Though it constitutes a small number (1–2%) of renal tumors in general population, 50–75% patients of tuberous sclerosis complex (TSC) develop renal AML.[1] AML is classically diagnosed by identifying the intratumoral fat component as evident by negative attenuation on unenhanced Computed tomography (CT) scans.[2] However, fat-poor AMLs defy diagnosis and raise the suspicion of renal cell carcinoma. This suspicion is further emboldened by the presence of enlarged regional lymph nodes and may result in radical nephrectomy. Diagnosis of AML after histopathological examination of the nephrectomy specimen and the lymph nodes coerces one to analyze retrospectively what could had been done to avoid this unnecessary surgery. Presently, there is lack of any conclusive diagnostic technique to solve this mystery. This report presents a case of fat-poor AML with para-aortic lymphadenopathy and entails an insight in various methods, which may be further refined to identify fat-poor AML so that a radical procedure can be avoided confidently.

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/0974-7796.95573

CASE REPORT

A 24-year-old lady was receiving antiepileptic medication for the last 10 years. She had left flank pain for the last 3 months. An ultrasound of the abdomen revealed a left renal mass and she was referred to us for its evaluation. She had no bowel or urinary complaints. On general examination, there were angiofibromas on face, ash-leaf macules on back, and right upper limb and shagreen patches over back. Her abdomen was unremarkable. CT scan of the abdomen showed lobulated intensely enhancing exophytic mass lesion in mid pole of left kidney measuring 6.5 cm × 5 cm × 4.4 cm with para-aortic

lymphadenopathy and no evidence of fat in the mass [Figure 1]. MRI of the abdomen revealed the same findings with no demonstration of fat in the mass [Figure 2]. MRI of brain showed multiple hyper-intense foci (tubers) in cortical/sub cortical location in bilateral cerebral parenchyma with streaky linear/radial hyper-intensities in cerebral white matters and subependymal nodules along lateral ventricles. A provisional diagnosis of TSC with left renal cell carcinoma (RCC) was made because of the absence of fat in the tumor and the presence of enlarged para-aortic lymph nodes. A left radical nephrectomy was performed in view of large size (>4 cm) and mid pole location of tumor, and substantial lymphadenopathy. Enlarged para-aortic lymph nodes (2 cm in size) were noted during the operation. The post operative period was uneventful. Histopathological examination of nephrectomy specimen showed multicenteric AML involving kidney and para-aortic lymph nodes [Figures 3 and 4].

DISCUSSION

TSC, an autosomal dominant disorder results from inactivating mutations in either *TSC1*, located on chromosome 9q34, or *TSC2*, located on chromosome 16p13.3. The incidence of TSC at birth is estimated to be approximately 1 in 6000.[3]

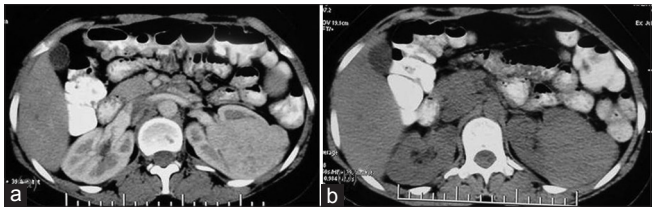

Figure 1: (a) Axial section of contrast enhanced computed tomography (CT) reveals a large homogenously enhancing mass lesion with well defined borders and extension into the renal hilum and the perinephric space (b) Non-contrast axial CT image also does not reveal any fat density with the lesion

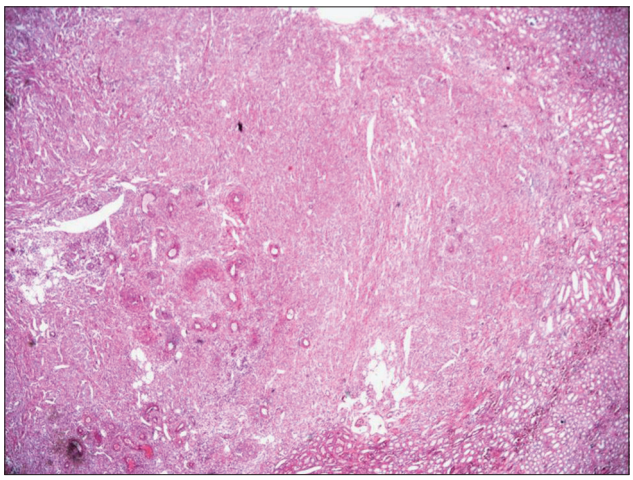

Figure 3: Tumor present on left side showing smooth muscles, vessels and adipose tissue while kidney parenchyma is present on right side (H and E, ×40)

Although many organs are susceptible, most patients exhibit dermatological, renal and neurological manifestations. Renal manifestations include AML (50–75%), benign cyst (17–35%), and renal cell carcinoma (1–2%).[1] AMLs associated with TSC present at an earlier age than sporadic AMLs and tend to be larger, bilateral and do not have any predilection for sex. Classic AMLs are seen sporadically, most often in middle aged women and are usually unilateral.

With the widespread use of ultrasound, more AMLs are being diagnosed incidentally. On ultrasonography, a typical AML appears as a circumscribed, highly reflective mass, which is more echogenic relative to the renal parenchyma. The presence of posterior acoustic shadowing further distinguishes AML from renal cell carcinoma.[4] These features, however, do not confirm the diagnosis. CT scan has been the most reliable modality for confirming the diagnosis of AML. Demonstration of even a small amount of fat within the renal tumor (−20 to −80 Hounsfield units) clinches the diagnosis of AML and virtually excludes renal cell carcinoma. However, one should be sure that the fat is intratumoral, and not the peri-renal fat

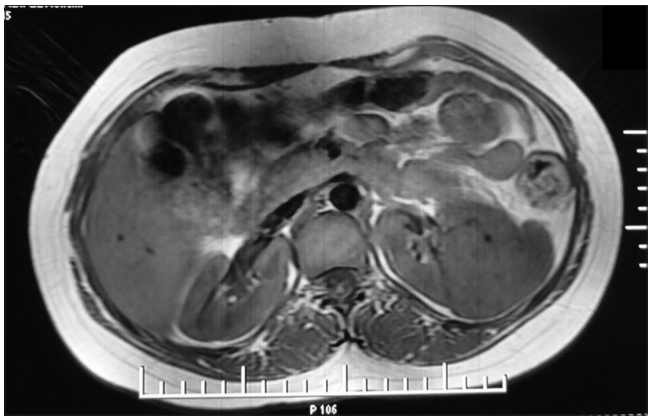

Figure 2: T1 weighted MR image reveals a homogenously isointense left renal mass. A small signal void due to a vessel is seen within the lesion

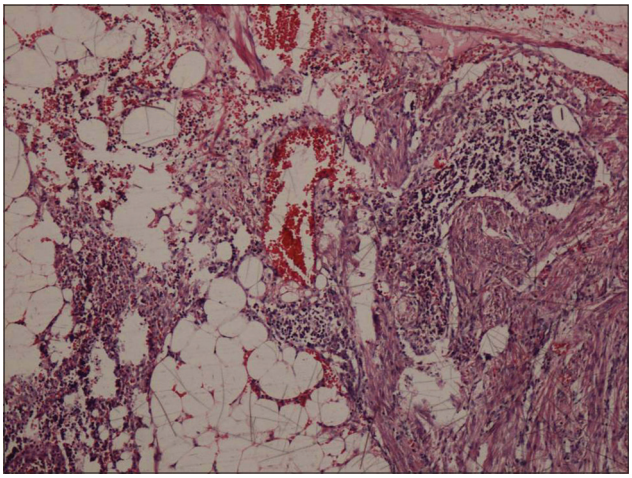

Figure 4: Lymph node with infiltration by angiomyolipoma (H and E, ×100)

that has been engulfed by an expanding renal cell carcinoma.[4] A diagnosis of renal cell carcinoma is favored if there is evidence of calcification coexisting with fat.[5] About 14% of AMLs have fat content low enough to be picked on radiographic imaging. One series of 129 AMLs have reported that 31.7% of AMLs had equivocal radiographic features.[3] Prando A presented a series of 127 AML tumors and proposed a classification based on the radiological evidence of fat.[6] He described four radiological patterns of fat distributions in AML ranging from predominantly fatty (pattern I) to without fat AML (Pattern IV). Pattern IV was seen in 6% tumors in this series which led to surgical removal of these tumors due to inability to distinguish them from renal cell carcinoma preoperatively. Our patient falls in pattern IV AML as no fat could be demonstrated radiologically in the tumor.

The natural history of renal AML has been largely unclear. These lesions tend to increase in size during adolescence and pregnancy suggesting the possibility of hormonal modulation in tumor growth.[6] Reported complications of AML include spontaneous hemorrhage, end stage renal disease and malignant transformation.[7,8] Malignant transformation has been reported in epithelioid variety of AML where perivascular epithelioid cell has been identified as the fourth component.

More than 40 cases of lymph nodal angiomyolipoma associated with renal AML have been reported in the literature.[9] Benign appearance of the tumor in the lymph nodes on histopathological examination and lack of evidence of distant spread or recurrence of the tumor on follow-up of these patients have suggested this phenomenon to be a part of multicenteric nature of the tumor rather than metastasis.[10]

Managing AML is a challenging task considering difficulties in diagnosis and uncertainties in natural course of the disease. A rational approach has evolved based on tumor size, clinical course and symptomatology. Recommended options include observation, selective arterial embolization, or nephron preserving surgery. The risks of hemorrhage, tumor growth, and malignant transformation increase with tumor size.[1] Asymptomatic AML of size less than <4 cm should be observed with ultrasonography every 1–3 years. Asymptomatic large (>4 cm) AMLs require sonographic evaluation every 6 monthly and increase in size will indicate need for intervention. Symptomatic small (<4 cm) AML may be observed for resolution of symptoms or intervention may be undertaken if symptoms fail to get relieved. Symptomatic and large (>4 cm) AML warrants treatment with either selective arterial embolization or nephron saving surgery. Recently, role of CT-guided radiofrequency ablation is also being explored as a minimally invasive modality for treatment of symptomatic AML especially in solitary kidney where maximal preservation of renal parenchyma is highly desired.[11]

Dilemma in management starts when imaging fails to identify fat in AML. Presence of lymphadenopathy, as in our case, further confounds this issue as and raises the strong suspicion of renal cell carcinoma. This diagnostic dilemma ultimately forces the surgeon to undertake radical nephrectomy. Histopathological examination of nephrectomy specimen finally provides the diagnosis of multicenteric renal AML with lymph node involvement that leaves the surgeon perplexed because of inability to diagnose AML preoperatively. Various modalities are being investigated to solve this uncertainty of preoperative diagnosis of AML.

Fine needle aspiration cytology (FNAC) has been advocated to diagnose AML preoperatively. Various authors have concluded that preoperative diagnosis of AML can be made by image guided FNAC supplemented with immunochemical analysis of the smear with HMB-45.[12,13]

But FNAC has its own pitfalls. First, its accuracy to diagnose AML with certainty has been questioned.[14] Moreover, FNAC cannot be considered to represent all the areas of the tumor. This becomes important in view of earlier case reports of renal cell carcinoma co-existing with AML.[15,16] Others reasons that have been cited to avoid FNAC are the risk of hemorrhage and the propensity of tumor seeding along the tract.[1]

Intraoperative frozen section has also been investigated to diagnose AML so as to obviate the need for nephrectomy. In a study of 23 cases undiagnosed renal masses, intraoperative frozen section erroneously diagnosed two cases of AML as lymphoma and metastatic melanoma/sarcamatoid renal cell carcinoma.[17] Algaba *et al.*[18] cited a number of reasons for high false negativity of intraoperative frozen section including absence of feasible neoplasia (necrosis or fibrosis), cystic nature of tumor, inadequate sampling or representation of tumor, and the problems encountered when trying to preserve the typical cytoarchitecture of most of the carcinomas as frozen section. High false positivity of intraoperative frozen section may be attributed to the overvaluation of crushed tubules mimicking tumor, as well as the intrinsic limitations of the freezing method, that do not enable to precisely identify the size of the nucleus.

Both CT scan and MRI have been extensively studied to differentiate fat-poor AML from renal cell carcinoma. Kim JK *et al.*,[19] in their study 81 patients (19 fat poor AML and 62 RCC), concluded that biphasic helical CT may be useful in differentiating fat-poor AML from RCC, with homogeneous tumor enhancement and prolonged enhancement pattern being the most valuable CT findings. Pixel histogram analysis of unenhanced CT scan images fails to reliably distinguish fat-poor AML from renal cell carcinoma.[20] Double-echo gradient-echo (GRE) chemical shift magnetic resonance (MR)

imaging has also given encouraging results in differentiating fat-poor AML from renal cell carcinoma with a sensitivity and specificity of (a) 96% and 93%, respectively, with a signal intensity index of 25% and (b) 88% and 97%, respectively, with a tumor-to-spleen ratio of −32%.[21]

We conclude there is need for search of new and effective criteria to differentiate fat-poor AML from RCC in the presence of lymphadenopathy.

REFERENCES

1. Winterkorn EB, Daouk GH, Anupindi S, Thiele EA. Tuberous sclerosis complex and renal angiomyolipoma: Case report and review of the literature. Pediatr Nephrol 2006;21:1189-93.
2. Sherman JL, Hartman DS, Friedman AC, Madewell JE, Davis CJ, Goldman SM. Angiomyolipoma: Computed tomographic-pathologic correlation of 17 cases. AJR Am J Roentgenol 1981;137:1221-6.
3. Orlova KA, Crino PB. The tuberous sclerosis complex. Ann N Y Acad Sci 2010;1184:87-105.
4. Lemaitre L, Claudon M, Dubrulle F, Mazeman E. Imaging of angiomyolipoma. Semin Ultrasound CT MR 1997;18:100-14.
5. D'Angelo PC, Gash JR, Horn AW, Klein FA. Fat in renal cell carcinoma that lacks associated calcifications. AJR Am J Roentgenol 2002;178:931-2.
6. Prando A. Radiological classification of renal angiomyolipomas based on 127 tumors. Int Braz J Urol 2003;29:208-15.
7. Ewalt DH, Sheffield E, Sparagana SP, Delgado MR, Roach ES. Renal lesion growth in children with tuberous sclerosis complex. J Urol 1998;160:140-5.
8. Bissler JJ, Kingswood JC. Renal angiomyolipomata. Kidney Int 2004;66:924-34.
9. Türker Köksal I, Tunç M, Kiliçaslan I, Ander H, Ozcan F, Kaplancan T. Lymph nodal involvement by renal angiomyolipoma. Int J Urol 2000;7:386-9.
10. Handa U, Nanda A, Mohan H. Fine-needle aspiration of renal angiomyolipoma: A report of four cases. Cytopathology 2007;18:250-4.
11. Prevoo W, van den Bosch MA, Horenblas S. Radiofrequency ablation for treatment of sporadic angiomyolipoma. Urology 2008;72:188-91.
12. Pancholi V, Munjal K, Jain M, Munjal S, Agrawal R, Nandedkar S. Preoperative diagnosis of renal angiomyolipoma with fine needle aspiration cytology: A report of 3 cases. Acta Cytol 2006;50:466-8.
13. Singh D, Kashyap S, Kaur S. Renal angiomyolipoma, a diagnostic dilemma: A case report. Indian J Pathol Microbiol 2007;50:622-3.
14. Kulkarni B, Desai SB, Dave B, Tongaonkar HB, Kulkarni JN, Chinoy RF. Renal angiomyolipomas–a study of 18 cases. Indian J Pathol Microbiol 2005;48:459-63.
15. Khallouk A, Ahallal Y, Doublali M, Tazi MF, Mellas S, El Fassi MJ, *et al*. Concurrent bilateral renal angiomyolipoma and renal cell carcinoma in a patient with tuberous sclerosis complex. Rev Urol 2009;11:216-8.
16. Krishnan B, Lechago J, Ayala G, Truong L. Intraoperative consultation for renal lesions. Implications and diagnostic pitfalls in 324 cases. Am J Clin Pathol 2003;120:528-35.
17. Kim JK, Park SY, Shon JH, Cho KS. Angiomyolipoma with minimal fat: Differentiation from renal cell carcinoma at biphasic helical CT. Radiology 2004;230:677-84.
18. Algaba F, Arce Y, López-Beltrán A, Montironi R, Mikuz G, Bono AV. Intraoperative frozen section diagnosis in urological oncology. Eur Urol 2005;47:129-36.
19. Catalano OA, Samir AE, Sahani DV, Hahn PF. Pixel distribution analysis: Can it be used to distinguish clear cell carcinomas from angiomyolipomas with minimal fat? Radiology 2008;247:738-46.
20. Simpfendorfer C, Herts BR, Motta-Ramirez GA, Lockwood DS, Zhou M, Leiber M, *et al*. Angiomyolipoma with minimal fat on MDCT: Can counts of negative-attenuation pixels aid diagnosis? AJR Am J Roentgenol 2009;192:438-43.
21. Kim JK, Kim SH, Jang YJ, Ahn H, Kim CS, Park H, *et al*. Renal angiomyolipoma with minimal fat: Differentiation from other neoplasms at double-echo chemical shift FLASH MR imaging. Radiology 2006;239:174-80.

How to cite this article: Garg PK, Jain BK, Kumar A, Bhatt S, Vibhav V. Fat poor angiomyolipoma with lymphadenopathy: Diagnostic dilemma. Urol Ann 2012;4:126-9.

Source of Support: Nil, **Conflict of Interest:** None.