RENAL ANGIOMYOLIPOMAS IN THE UNIVERSITY OF MALAYA MEDICAL CENTRE: ITS SPECTRUM OF PRESENTATION AND MANAGEMENT

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ABSTRACT:

Renal angiomyolipoma, once considered a rare benign renal tumour, is relatively common these days. They account for 0.3-3.0% of all renal masses. Histologically, it is composed of adipose tissue, smooth muscles and blood vessels. Here, we wish to highlight five cases of renal angiomyolipomas which were presented to the University Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia, over a two-year period between June 2005 and June 2007. This study wish to illustrate its varied clinical presentation and the management undertaken for each underlying condition. These cases were presented in the form of spontaneous perirenal haemorrhage, a large asymptomatic renal mass, a small asymptomatic renal mass, a symptomatic renal angiomyolipoma and a case of renal angiomyolipoma mimicking a renal tumour. Each of these cases varied in its clinical presentation; thus, management has become very challenging to clinicians ranging from conservative management to active intervention, be it operatively or non-operatively. *(JUMMEC 2009; 12 (1):39-43)*

KEYWORDS: *angiomyolipoma, spontaneous perirenal haemorrhage, benign renal tumour, renal mass*

Introduction

Renal angiomyolipoma (AML), which was considered a rare benign renal tumour, is relatively common these days. It was once known as renal hamartoma (1). Classically, AMLs are composed of adipose tissue, smooth muscle and blood vessels where it was first described histologically in the early 19th century. These tumours generally account for 0.3 to 3.0% for all renal masses (2, 3). They can occur sporadically or as part of a tuberous sclerosis complex (TSC) where 60-80% of tuberous sclerosis have AMLs (4). AMLs can show a myriad and broad range of clinical presentation. It can differ in its presentation among each other. Association with malignancy is not uncommon and can often be mistaken for renal cell carcinoma. However, with improved methods of immunohistochemical staining, these two entities can be easily differentiated. Though benign, AMLs can be malignant in its variant form otherwise known as epithelioid angiomyolipomas, which have been reported in literatures recently as a variant form of AML (5). Here, we review five cases of renal AMLs that were presented to the Department of Surgery, University Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia, and we illustrate the varied clinical presentation of AML and its management.

Materials and Methods

During the two-year period between June 2005 and June 2007, we reviewed five cases of renal AMLs that were presented to the urology division. The various clinical presentations of renal angiomyolipomas and the outcomes are presented.

Results

The five cases of AMLs with varied clinical presentations are illustrated and highlighted are:

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Case 1 – A case of Spontaneous Perirenal Haemorrhage

Ms LCE, a 24-year-old female with no medical illness, was presented with a two-week history of constant left-sided abdominal pain. She was found to be anaemic. There was also the feature of facial adenoma sebaceum. It was not associated with gastrointestinal symptoms. Her colonoscopy and OGDS was normal. A CT scan abdomen performed revealed multiple renal AML of both kidneys associated with a large left perinephric hematoma and a small liver lipoma. Spontaneous perirenal haemorrhage was identified. She was, otherwise, stable. Embolization was planned and performed for the left sided AML. No complication was encountered post embolization. There was no further follow up as patient defaulted follow up.

Case 2 – A case of asymptomatic, but large renal mass

Mdm NCM, who was 52 years old with a history of diabetes mellitus, hypertension and being a Hepatitis B carrier, was presented to us following an abdominal ultrasound which showed an incidental benign left renal lesion. She was otherwise asymptomatic. A CT scan abdomen performed revealed a huge left renal AML measuring 11.5 x 7.3 x 5.5 cm (Hounsfield unit -70 to -50). She underwent embolization of the AML and encountered no complication. She defaulted further follow up thereafter, but was reviewed back in the clinic one year later where she remained asymptomatic. A repeat CT scan a year later post-embolization showed the AML size was 7.4 x 6.2 x 5.0 cm.

Case 3 – A case of loin discomfort

Mr. AI, a 31-year old with no known medical illness, was presented to us with right loin discomfort. He suffered the discomfort for three months. There were no other associated symptoms. A CT scan of the abdomen revealed a right renal AML measuring about 2.8 x 2.0 cm. He was treated conservatively and was followed up with serial ultrasounds. A six-monthly ultrasound was done showing an increase in the size of AML to 3.6 x 2.8 cm. Another six months later, the size has become 4.5 x 3.2 cm. As he was asymptomatic and not keen for any intervention, he was followed up closely with another repeat ultrasound in another six months.

Case 4 – A case of asymptomatic and small renal mass

Mdm CST, a 86-year-old woman with a history of left renal stones, was presented to us with left-sided emphysematous pyelonephritis. A CT scan abdomen showed an incidental finding of a right AML measuring about 2.0 x 2.0 cm (Hounsfield unit -60) associated with her underlying primary pathology. She was treated for her primary complaint and her right AML was treated conservatively.

Case 5 – A case mimicking conventional renal tumour

Mr. CFS, a 17-year-old male with no past medical illness, was presented with a left-sided abdominal mass. He first noticed some discomfort for three weeks. He was otherwise asymptomatic. Examination revealed a left-sided ballotable mass measuring about 15.0 x 10.0 cm. An ultrasound revealed a suspected complex left flank mass with possible renal in origin. A CT scan was later performed which showed a large multiseptated cystic lesion (Hounsield unit -27) with rim enhancement seen arising from the mid and lower pole of the left kidney measuring 11.2 x 11.8 x 14.2 cm with no major vessel involvement. Initial impression was of a multilocular cytic nephroma. The patient underwent a nephrectomy following that. Post-operative recovery was uneventful and he was discharged on Day 5 of post-operation. On follow-up, the histopathology examination (HPE) revealed the underlying lesion to be an angiomyolipoma with positive staining for vimentin, actin desmin and CD 68. He was subsequently discharged with no further follow up.

Discussion

AMLs are increasingly common these days due to incidental findings on imaging. It is usually asymptomatic and detected incidentally on routine imaging although it can also be present with a classic triad of flank pain, a palpable mass and hematuria. Three of the patients were presented to us symptomically. Nelson et al showed that 59% of patients with AML are present symptomatically. It is also known that AMLs are more common in females (1, 2).

Classically, AML appear in two distinct groups of population where it may occur sporadically or as part

of tuberous sclerosis complex. It has been reported that 70% to 80% of AMLs occur sporadically, whereas only 60% to 80% of patients with tuberous sclerosis have AMLs (4). AMLs in these two groups of population have very different clinical presentation and behaviour altogether which may affect the management and follow-up of the disease process. See table below from Gomez MR for diagnostic criteria for TSC (6): -

Diagnostic criteria for tuberous sclerosis complex (TSC)
The presence of one of the following is diagnostic for TSC: • Multiple renal angiomyolipomas • Tuber in cerebral cortex (on CT or MRI) • Glial nodules in the subependyma (more commonly calcified than cortical tubers) • Retinal hamartoma • Facial angiofibromas (sebaceous adenoma) • Ungual fibromas • Fibrous plaque on the scalp or forehead
The presence of any 1 of the following is suspicious and of any 2 is presumptive: • Multiple renal tumors or cysts • Pulmonary lymphagiomyomatosis • Cardiac rhabdomyosarcoma • Family history of TSC • CNS: infantile spasms, seizures, calcification or hypomyelination • Skin: hypomelanotic macules or a shagreen patch

We have in our study showed four patients who fall into the sporadic group of AMLs and one patient with TSC presenting with multiple renal AML and perirenal haemorrhage.

The sporadic type of AMLs commonly occur as a solitary renal tumour and is less likely to grow compared with those with tuberous sclerosis. It also commonly occurs in the older age groups. It may be symptomatic but less likely to bleed in comparison as compared to tuberous sclerosis associated AMLs (2). There were also reported cases of renal AMLs with extra-renal involvement such as the colon, perirenal fat, lymph nodes and even the bronchial artery. Dire consequences were seen when there were such involvements but that did not alter the prognosis of renal AMLs though (19, 20).

Tuberous sclerosis associated with AMLs tends to be multicentric and bilateral as was seen in our patient in Case 1. It tends to present at an early age with a greater tumour size. It is also most likely to haemorrhage than the sporadic type as was seen in our patient. Spontaneous perirenal haemorrhage remained the most life threatening presentation of all AMLs and most common after renal cell carcinoma. Patients with TSC with multiple renal AMLs can also present with renal insufficiency or failure due to compressive factors or replacement of normal renal parenchyma with AML. Thus, presentation and management of patient with TSC with AML remained very challenging to clinicians (19).

With the advent of good imaging techniques, such as ultrasound and CT scan, diagnoses can be made with almost near certainty. Its peculiar appearance and composition comprising of fat, smooth muscle and blood vessels can easily be detected on the above imaging techniques. A CT scan is most preferable for a more accurate diagnosis of renal AML (7).

An ultrasound will show a distinct appearance of a hyperechoic lesion due to its combination of high fat content, multiple tissue interfaces and extensive vascular tissue. Unfortunately, similar appearance can occur in small renal cell carcinoma and a small percentage of AML does not exhibit this appearance. This can best be illustrated with our patient in Case 5. This renders CT scan to be more accurate in the diagnosis of AML (8).

CT scan is preferable as it is more sensitive and specific than ultrasound where diagnosis of AML is dependent on identifying fat in a renal lesion which is pathognomonic for AML. Fat imaged by CT has a negative density of -20 to -80 Hounsfield units. Early CT scanners were able to correctly diagnosed AML in 75% to 86% of cases and newer helical CT scanners further enhance its sensitivity (9). There is, however, no longer any role of angiography in diagnosing AML as an imaging modality and MRI are used only in special circumstances.

Though considered a benign tumour, there are reported cases of aggressive behaviour of AML suggesting malignancy. This rare entity or variant form is otherwise known as epithelioid AML. None of our patients was presented with this form of

AML. Differentiating this form of AML from the typical ones can present a challenge to clinicians. Immunohistochemical staining has shown to play an important role in differentiating these two forms of AML as well as distinguishing between AML and renal cell carcinoma (10).

As the typical AML and epithelioid AML characteristically stained positive for the melanocyte marker, HMB-45, it has been reported by Kawaguchi *et al* and various reports that these two forms can be differentiated by the detection of p53 gene mutations present in the malignant component of AMLs. This further suggests that p53 mutation may play a role in the malignant transformation of renal AML (11, 12).

The role of HMB-45 enables one to discriminate between renal cell carninoma and AML as both can present similarly on imaging. Further immunohistochemical showing negative epithelial markers such as cytokeratin or CD 34 also further distinguishes AML from renal cell carcinoma. Other markers that are commonly present in AMLs are vimentin, actin and CD 68 (5, 11, 13).

Management of renal AMLs is a challenging task indeed. It may take the form of close observation with conservative management, embolotherapy or nephrectomy (partial or total). Indications for intervention are generally reserved for those with suspicion of malignancy, spontaneous perirenal haemorrhage (see Case 1) or those with significant symptoms. Preserving renal function also remains a concern in whichever intervention undertaken (14, 15).

As for Case 5, a nephrectomy was warranted as the CT scan showed a multilocular cystic nephroma (MCN). MCN, though considered as a renal hamartoma like AML, can differ from AML as it has a potential to be malignant. Following nephrectomy, HPE revealed an AML in our patient, which was considered was a benign lesion. The patient was safely discharged from follow-up.

Benign asymptomatic lesion or small lesion does not require any intervention. Close follow up is required with regular yearly or half yearly imaging to assess disease progression. This is best illustrated in our patients in Case 3 and Case 4 (2).

Treatment for asymptomatic AML remains controversial. In Case 2, the patient was asymptomatic even though it was revealed that she presented a tumour size of 11 cm (> 4 cm). The patient underwent embolization and a repeat scan showed the tumour size remained > 4 cm. However, the tumour size had shrunk. She remained asymptomatic as when she was presented to us initially. Although it is suggested that tumour size > 4 cm are at risk of symptoms and requires intervention as was proposed by Oesterling *et al*, who reported that tumour >4 cm tends to be symptomatic (80 to 90%) with >50% at risk of haemorrhage (16). However, there are recent reports that also suggest that intervention is not necessary for tumours > 4cm which remained asymptomatic (17, 18).

Therefore, according to Nelson *et al*, treatment of asymptomatic patient should be based on multiple factors in addition to tumour size such as co-morbidity, association with tuberous sclerosis, renal reserves, pregnancy plans and patients social background (2).

Conclusion

AML can be present with varied clinical presentations. Its management can be very challenging; ranging from conservative management to active intervention when it occurs as symptomatic with spontaneous perirenal haemorrhage or suspicion of malignancy.

References

1. Badrinath RK, Dreicer R, Williams R. Renal Parenchymal Neoplasms. In: Tanagho EA, McAninch JW. ed. Smtihs Urology, 16th ed. Lange; 2004: 346-347.

2. Nelson CP, Sanda M. Contemporary diagnosis and management of renal angiomyolipoma. *J Urol* 2002; 168: 1315-1325.

3. Hajdu SI, Foote FW. Angiomyolipoma of the kidney: a report of 27 cases and review of literature. *J Urol* 1969; 102: 396-401.

4. Kothary N, Soulen MC, Clark TWI, *et al*. Renal angiomyolipoma: long term results after arterial embolization. *J Vasc Interv Radiol* 2005; 16: 45-50.

5. Chandrasoma SB, Moatamed N, Chang A, *et al*. Angiomyolipoma of the kidney: expanding disease spectrum demonstrated by 3 cases. Appl Immunohistochem *Molecul Morphol* Sep 2004; 12(3): 277-283.

6. Gomez MR. Phenotypes of the tuberous sclerosis complex with a revision of diagnostic criteria. *Ann NY Acad Sci* 1991; 615: 1.

7. Siegel CL, Middleton W, Teefey SA, *et al*. Angiomyolipoma and renal cell carcinomas: US differentiation. *Radiology* 1996; 198: 789.

8. Silverman SG, Pearson GD, Seltzer SE, *et al*. Small hyperechoic renal masses: comparison of helical and convention CT for diagnosing angiomyolipoma. A*m J Roentgenol* 1996; 167: 877.

9. Bret PM, Breatnolle M, Gaillard D, *et al*. Small asymptomatic angiomyolipomas of the kidney. Radiology 1985; 154: 7.

10. Frago PS, Camison CDAA, Sanz MJG, *et al*. Controversies related to epithelioid variant of renal angiomyolipoma: a review of literature. *Urology* 2006; 67: 846.

11. Kawaguchi K, Oda Y, Nakanishi K, *et al*. Malignant transformation of renal angiomyolipoma: a case report. *Am J Surg Pathol* April 2002; 26: 523-529.

12. Ashfaq R, Weinberg AG, Albores-Saavedra J, *et al*. Renal angiomyolipoma and HMB 45 reactivity. *Cancer* 1993; 71: 3091-3097.

13. L'Hostis H, Deminiere C, Ferriere JM, *et al*. Renal angiomyolipoma: a clinicopathologic, immunohistochemical and follow-up study of 46 cases. *Am J Surg Pathol* Sep 1999; 23(9): 1011.

14. Zhang JQ, Fielding JR., Zou, KH. Etiology of spontaneous perirenal hemorrhage: A meta-analysis. *J Urol* April 2002; 167: 1593-1596.

15. Daskalapoulos G, *et al*. Spontaneous peririenal hemorrhage: a 10 year experience at our institution. Int Urol Nephr 2004; 3: 15-19.

16. Oesterling JE, Fishman EK, Goldman SM, *et al*. The management of renal angiomyolipoma. *J Urol*, 1986; Vol 135: 1121.

17. Minervini A, Giubilei G, Masieri L, *et al*. Simple enucleation for the treatment of renal angiomyolipoma. *BJU Int* 2007; 99: 887-891.

18. Gibbs P, Coughlin G, Davies M, *et al*. Management of angiomyolipoma in a single centre. *BJU Int* 2007; 99: 11.

19 De Luca S, Terrone C, Rosetti SR. Management of renal angiomyolipoma: a report of 53 cases. *BJU Int* 1999; 83(3): 215-218.

20 Maffezzini M, Vlassopolous G, Simonato A, *et al*. Renal angiomyolipoma with extrarenal involvement in vascular, lymph node and perirenal tissue. Report of four cases. *Scand J Urol & Nephr* 1995; 29(3): 327-329.