

## Angiomyolipoma of the Kidney: The Experience at the University Hospital of the West Indies

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### ABSTRACT

**Objective:** Angiomyolipoma (AML) of the kidney is an uncommon tumour that, until recently, was often misdiagnosed preoperatively as renal cell carcinoma (RCC). Newer radiological techniques have allowed more accurate preoperative diagnosis which can facilitate preoperative counselling and planning for conservative therapy. This study reviews the experience with these uncommon tumours at the University Hospital of the West Indies.

**Methods:** All cases of AML diagnosed during the period 1980 to 2007 were retrospectively identified from the files of the Department of Pathology. From these records, selected data were retrieved and analysed. These included patient demographics, clinical history, clinical diagnosis and pathologic characteristics of the specimen submitted. The total number of primary renal tumours diagnosed in adults during the same period was also determined for comparison.

**Results:** Eleven cases of AML were identified among 149 primary renal tumours in adults. Ten of these cases occurred in women. Amongst these, a single case of tuberous sclerosis was confirmed in a patient with bilateral lesions. Excluding this patient, who was 24 years old, ages ranged from 24 to 86 years with a mean of 44 years (median 40.5 years) and an equal number of lesions was present on each side. Abdominal or flank pain were the most common clinical symptoms, present in six cases but in three cases, the tumours were discovered incidentally. The correct clinical diagnosis was made pre-operatively in a single case. By contrast, a diagnosis of RCC or other malignant tumour was proffered in eight cases. Pathologically, the maximum dimension of the seven excised tumours, in whom such information was recorded, ranged from 3.5 cm to 12 cm with a median of 7 cm. Spontaneous haemorrhage in the tumour was noted in three cases, all greater than 4.5 cm in maximum dimension.

**Conclusions:** These data confirm that AML is uncommon at the University Hospital of the West Indies. There was an overwhelming female preponderance and patients presented, most commonly, in the 3<sup>rd</sup> to 4<sup>th</sup> decades. Tuberous sclerosis was identified in a solitary case. In this series, symptomatic lesions were > 4.5 cm in maximum dimension and haemorrhage complicated three cases. Most cases were incorrectly diagnosed preoperatively.

## El Angiomiolipoma del Riñón: la Experiencia del Hospital Universitario de West Indies

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### RESUMEN

**Objetivo:** El angiomiolipoma (AML) del riñón es un tumor poco común que hasta hace poco era a menudo mal diagnosticado preoperatoriamente como carcinoma celular renal (RCC). Técnicas radiológicas más nuevas han permitido realizar un diagnóstico preoperatorio más exacto, que puede facilitar aconsejamiento preoperatorio y planificar una terapia conservadora. El presente estudio examina la experiencia con estos tumores poco comunes en el Hospital Universitario de West Indies.

**Métodos:** Todos los casos de AML diagnosticados durante el periodo de 1980 a 2007 fueron identificados retrospectivamente a partir de los archivos del Departamento de Patologías. De estos archivos, se seleccionaron datos que fueron recuperados y analizados. Estos abarcaron: la demografía de los pacientes, las historias clínicas, el diagnóstico clínico y las características patológicas del

*espécimen presentado. El número total de tumores renales primarios diagnosticados en adultos durante el mismo período, se determinó también por comparación.*

**Resultados:** *Se identificaron once casos de AML entre 149 tumores renales primarios en adultos. Diez de estos casos ocurrieron en mujeres. Entre éstas, se confirmó sólo un caso de esclerosis tuberosa, en un paciente con lesiones bilaterales. Excluyendo a este paciente, que tenía 24 años de edad, las edades fluctuaron de 24 a 86 años para una media de 44 años (mediana 40.5) y un número igual de lesiones estuvieron presentes en cada lado. El dolor abdominal o el lateral, constituyeron los síntomas clínicos más comunes, presentes en seis casos, pero en tres casos, los tumores fueron descubiertos incidentalmente. El diagnóstico clínico correcto se realizó preoperatoriamente en un solo caso. En contraste con ello, un diagnóstico de RCC u otro tumor maligno se presentó en ocho casos. Patológicamente, la máxima dimensión de los siete tumores extirpados, en los cuales se registró tal información fue registrada, fluctuó de 3.5 a 12 cm con una mediana de 7 cm. La hemorragia espontánea en el tumor fue observada en tres casos, todos mayores de 4.5 cm. de tamaño máximo.*

**Conclusiones:** *Estos datos confirman que la AML es poco común en el Hospital Universitario de West Indies. Hubo una abrumadora preponderancia de casos femeninos, y los pacientes se presentaron con mayor frecuencia en las décadas 3<sup>era</sup> y 4<sup>ta</sup>. La esclerosis tuberosa se identificó sólo en un caso. En esta serie, las lesiones sintomáticas tuvieron > 4.5 cm. de dimensión máxima, y la hemorragia complicó tres casos. La mayoría de los casos fueron diagnosticados incorrectamente en la etapa preoperatorio.*

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## INTRODUCTION

Renal angiomyolipoma (AML) is an uncommon benign neoplasm of the kidney. The tumour is composed of an admixture of blood vessels, smooth muscle and fat, hence, the derivation of its name. Renal angiomyolipomas occur sporadically but there is an increased frequency in patients with tuberous sclerosis in whom the incidence of bilateral lesions is also increased. The occurrence of a recent case of AML, seen in the Pathology department, prompted this retrospective study.

## SUBJECTS AND METHODS

The surgical pathology records in the Department of Pathology at the University Hospital of the West Indies (UHWI) were examined for all cases of AML diagnosed between 1980 and 2007. From these records, the following parameters were extracted and analysed: patient's age, gender, clinical history, clinical diagnosis proffered and the pathologic features of the lesion. The medical records of these patients were also sought to obtain additional clinical information that might not have been submitted with the specimen. In particular, we sought to determine if there was a clinical history of tuberous sclerosis or other indications of that condition such as mental retardation, or if multiple lesions were present. All adult primary renal tumours diagnosed during the same time-period were also recorded and the mean and median ages of those with renal cell carcinoma calculated.

## RESULTS

Eleven cases were identified, 10 of which occurred in women. One case (9%) occurred in a 24-year-old female patient who was diagnosed with tuberous sclerosis. Excluding this case, the age of the others at presentation, ranged from 24 to

86 years with a mean of 44 and a median of 40.5 years (Fig. 1). In 3 (36%) patients, the lesion was an incidental finding

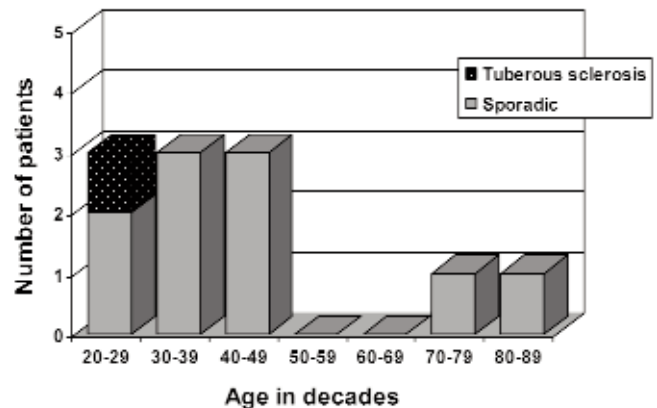


Fig. 1: Age of patients with angiomyolipoma

on imaging for other reasons. The remaining eight patients presented with a variety of symptoms including flank or abdominal pain in six patients, a clinically palpated mass in five patients and haematuria in two patients (Fig. 2). Excluding the patient diagnosed with tuberous sclerosis, who had bilateral lesions, there were five right- and five left-sided lesions.

The correct diagnosis of angiomyolipoma was proffered in only one case, the most recent. This was not in the patient in whom the diagnosis of tuberous sclerosis was clinically made. In contrast, diagnosis of a malignant lesion was proffered in eight cases, seven with renal cell carcinoma (RCC) and another of unspecified "sarcoma". The clinical diagnoses of the remaining two cases were of fibroma and arteriovenous (AV) malformation.

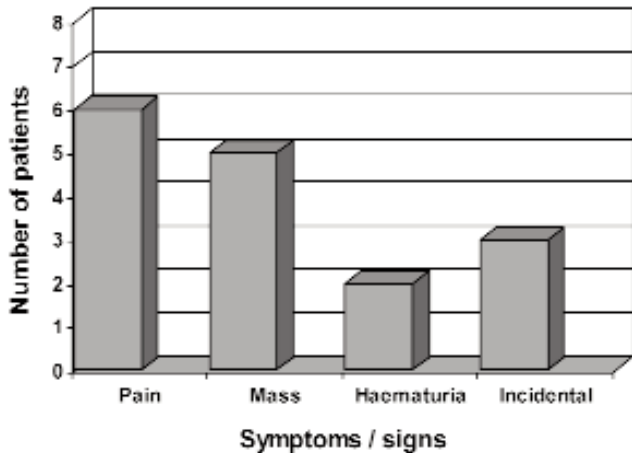


Fig. 2: Clinical features in patients with angiomyolipoma (Numbers not mutually exclusive).

Six total nephrectomy specimens and three partial nephrectomy specimens were submitted from nine patients with the remaining two specimens consisting of material obtained via open renal biopsy. Dimensions of the tumour were recorded in seven of the nine resected lesions. The maximum tumour dimensions ranged from 3.5 to 12.0 cm in size, with a mean of 6.8 cm and median of 7.0 cm. Three lesions, whose greatest dimensions ranged from 4.5 cm to 7.5 cm, revealed moderate haemorrhage on pathological examination.

Description of the gross specimen often bore resemblance to the predominant type of tissue seen on histologic examination. All lesions were circumscribed (Fig. 3).

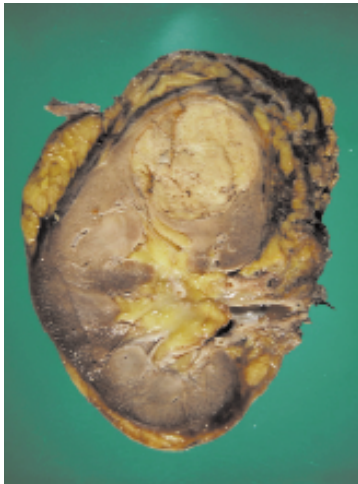


Fig. 3: Gross appearance of typical angiomyolipoma showing a discrete mass in the upper pole of the kidney.

Those described as having a tan-yellow or variegated appearance, generally had an equal admixture of the three histologic components. Two cases described grossly as having a “fatty” appearance contained a predominance of adipose tissue, while another described as “firm and fibrous” in appearance exhibited a predominance of muscle. As with the

gross specimen, the clinical diagnosis was also influenced by the histological components. For example, the lesion submitted with a clinical diagnosis of AV malformation revealed a predominance of vascular structures while that submitted with the clinical diagnosis of fibroma demonstrated a predominance of muscle on histological examination.

During the study period, a total of 149 primary adult renal tumours were identified in the Surgical Pathology records. Angiomyolipoma, therefore, accounted for 7.4% of all adult primary renal tumours on record at the UHWI during that time. Of these, 99 patients were diagnosed with RCC. These ranged in age from 17–87 years with a mean of 56.5 years and a median of 60 years. Nine patients were less than 40 years old but three of these were suspected cases of Von Hippel-Lindau syndrome.

## DISCUSSION

Renal AML is an uncommon tumour whose incidence is often cited as less than 1% of surgically excised renal tumours (1). However, with increasing use of radiological diagnostic technology, including ultrasound, it has been suggested that this incidence is much higher (2). In our experience, this tumour has a prevalence of 7.4% among all primary adult renal tumours.

Renal angiomyolipomas occur sporadically but they are also found in association with tuberous sclerosis. It is estimated that between 50 and 80% of patients with tuberous sclerosis develop AMLs (3, 4). In the present study, we could only confirm one case of tuberous sclerosis amongst the patients with AML which is less than the frequency of tuberous sclerosis-associated AML of 17% described by Steiner *et al* (5). This might, however, be a result of the small sample size or alternately, the result of incomplete clinical data. This patient was recognized clinically as having bilateral lesions, a characteristic feature of tuberous sclerosis-associated AMLs (3, 6). Unfortunately, the diagnosis of renal AML was not proffered in this case despite the well-known fact that AMLs are frequently bilateral in tuberous sclerosis.

An almost universal finding regarding renal AML, whether sporadic or hereditary, is its distinct female preponderance (3–5). This was especially marked in this study with only one male patient. We acknowledge, however, that this overwhelming bias might be a reflection of the small number of cases in the study. The mean age of patients with AML varies depending on whether the lesion is sporadic or associated with tuberous sclerosis. Those associated with tuberous sclerosis tend to present considerably earlier than those that occur sporadically (5). The age of 24-years in the patient with tuberous sclerosis, compared to a median age of 40.5 years for the other cases, is consistent with this observation. The triad of symptoms of haematuria, abdominal pain and a palpable mass in the flank or abdomen classical of renal cell carcinoma (RCC), may also occur in AML. However, the widespread use of computed tomography and ultrasonography for other indications has led to increased detection of

these tumours as an incidental finding by as much as 60% in one study (5). In our experience, tumours were asymptomatic or incidental in only three of the 11 cases. The disparity in symptomatology when compared to the international literature may not solely be an index of the small number of cases but may be a function of the size of the neoplasms which, in this study, had an average diameter of 6.8 cm. It has been shown that when the maximum dimension is above 4 cm, symptoms are reported in 46–80% of patients (5, 7). In a similar study from India, Gogoi *et al* (8) reported that 10 of 12 patients in whom the mean tumour size was 7.4 cm complained of symptoms.

The most important differential diagnosis for AML of the kidney is undoubtedly RCC which is the most common primary renal malignancy. There are, however, clinicopathologic differences. Renal cell carcinoma has a peak incidence between the 6<sup>th</sup> and 8<sup>th</sup> decades and is unusual in patients younger than 45 years of age (9). It is noteworthy that, in four of our cases where RCC was suspected clinically and total nephrectomy was performed, the patients were less than 40 years old. The infrequency of RCC in patients less than 40 years, presenting with a renal mass, must be appreciated. Review of our own data over the time period of this study confirmed that, excluding the probable cases of Von Hippel-Lindau disease, fewer than 6% of patients diagnosed with RCC were 40 years old or less.

Opinions have varied regarding the accuracy of preoperative diagnosis of AML by diagnostic imaging methods with one author even suggesting that the diagnosis can be made in nearly all cases because of the characteristic appearance of these tumours (10). However, because of the diversity in the relative amounts of the cellular components, the radiological features of AML can be varied as was the situation in two of the cases in this report where elements other than fat were predominant. Furthermore, some cases of AML and its differentials may be atypical (11). Image-guided confirmative biopsy can be helpful in dubious cases (12, 13) to improve preoperative diagnosis which is important, as it can facilitate patient counselling and planning for conservative therapy in appropriate cases. However, it is recognized that needle biopsy does have inherent problems including haemorrhage and the risk of seeding if indeed the mass proves to be RCC. It is noteworthy that open biopsy, which is a safer and more reliable method for diagnosis, was performed in two cases. Conservative treatment options, including embolization and partial nephrectomy are particularly recommended in patients with bilateral AML (14).

The most important complication of classic AML is retroperitoneal haemorrhage which can be life-threatening. The risk of haemorrhage is increased in tumours measuring more than 4.0 cm in greatest diameter (7). This propensity for haemorrhage is thought to be related to the rigid, non-compliant nature of the blood vessels in the lesion and a defect in the elastic tissue of the abnormally thick blood vessels predisposing to aneurysm formation within these tu-

mors. All three tumours in this series, that exhibited haemorrhage, were larger than 4.5 cm in greatest diameter. However, notwithstanding size as an important predictor of haemorrhage, other factors clearly influence this risk. For example, it is noteworthy that the two largest tumours in this study, showed no evidence of haemorrhage. Histologically, these lesions were significantly less vascular than the others, being composed predominantly of fat, a finding that potentially mitigated the risk of haemorrhage.

Histologically, renal AML is a triphasic tumour comprised of smooth muscle, vascular tissue in the form of thick-walled blood vessels and mature adipose tissue, present in varying amounts in given neoplasms. Although previously thought of as a hamartoma, recent evidence supporting its clonal origin confirms its neoplastic nature (15). In addition, current evidence suggests that dysregulation of the mammalian target of rapamycin (mTOR) pathway is responsible for the development of sporadic and hereditary AML (16). In fact, the identification of a specific molecular pathway responsible for tumourigenesis has led to the development and use of specific targeted medical therapy in clinical trials (16). The common progenitor is now thought to be the multipotential perivascular epithelioid cell (PEC). This cell gives rise to a number of other tumours collectively known as PEComas, all of which are positive for the melanocytic marker HMB-45. It has been demonstrated that there is an immunophenotypic and ultrastructural unit, resembling the premelansome present in the cells of this tumour (17). It remains to be determined, what is the physiological counterpart of the PEC. This and the histogenesis of the angiomyolipoma continue to be the subject of intense research.

In summary, the data confirm that AML is uncommon at the University Hospital of the West Indies. There was an overwhelming female preponderance and patients presented, most commonly, in the 3<sup>rd</sup> to 4<sup>th</sup> decades. Tuberous sclerosis was infrequently diagnosed. In this series, symptomatic lesions were > 4.5 cm in maximum dimension and haemorrhage complicated three cases. Most cases were incorrectly diagnosed preoperatively highlighting the need for accurate preoperative diagnosis.

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