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Clinical Presentation, Management, and Outcome of Patients with Incidental Renal Angiomyolipoma in Qatar

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ABSTRACT

Objectives: Our study aimed to analyze the clinical presentation, management, and outcome of renal angiomyolipoma patients incidentally detected upon computed tomography (CT) examination. ***Methods:*** Between 2004 and 2008, all patients who underwent abdominal CT examination for any reason at the radiology department at Hamad General Hospital, Qatar were retrospectively reviewed. The diagnosis of renal angiomyolipoma was based on abdominal CT evaluation. Angiomyolipoma patients were followed-up by CT evaluation as per standard care for three years to observe any change in size and outcome. ***Results:*** A total of 13,115 patients were screened, of which 56 (40 females and 16 males) had renal angiomyolipoma. The mean age of patients was 52±13 years with 46% Qatar nationals. The majority (95%) of cases had unilateral tumors (52% right-sided and 43% left-sided). Twenty-six cases showed increase in tumor size and the median increase was 0.5cm (0.1–3.6). Surgical intervention was required in four (7%) cases with tumor size ≥4cm. The overall mortality on follow-up was 7%. The cause of death included metastasis, renal failure, hepatic failure and mesenteric thromboembolism. ***Conclusion:*** Renal angiomyolipoma is an uncommon benign tumor with an overall prevalence of 0.4% in Qatar. It has characteristic clinical features and its recognition is often challenging for proper clinical diagnosis and treatment in asymptomatic patients. Asymptomatic patients need regular radiological surveillance. In contrast, surgical interventions are mainly required in symptomatic patients with increased tumor size (≥4cm). Timely diagnosis and treatment is necessary to avoid complications such retroperitoneal hemorrhage and renal impairment.

The frequency of incidental detection of rare neoplasms is increasing with use of imaging tools such as ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI).[1,2] Renal angiomyolipoma is a rare renal cortical neoplasm accounting for 0.3 to 3% of all renal masses[3] and is less frequent among the general population (<0.2%).[4] It is a benign mesenchymal tumor comprised of spindle and epithelioid smooth muscle cells, dysmorphic blood vessels, and fatty tissues; which occurs both sporadically and in combination with tuberous sclerosis complex.[5,6] Usually, patients with small angiomyolipoma remain asymptomatic and might be detected incidentally during abdominal USG or CT examination performed for other clinical indications.[7] In contrast to USG, CT images are more accurate to distinguish angiomyolipoma from renal cell carcinoma and could identify well defined margins and variable proportions of fat and soft tissue suggestive of angiomyolipoma.[7] Interestingly, most of the angiomyolipomas are clinically insignificant benign tumors that could be safely observed without surgical intervention. However, in some cases, surgical intervention is needed which is often indicated by intractable pain, large tumor size (>4cm), malignancy, and risk of bleeding.[8] The preferred treatment approach for angiomyolipoma is nephron-sparing surgery or selective renal artery angioembolization, which are useful to preserve residual renal function in comparison to radical nephrectomy.[9] The current scientific literature

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on the presentation and management of renal angiomyolipoma is largely from western studies. Data on renal angiomyolipoma among the Arab Middle Eastern population is scarce and is reported as small case series or case reports.[10,11]

We retrospectively reviewed the clinical presentation, management, and outcome of angiomyolipoma incidentally detected on CT evaluation in Qatar.

METHODS

A retrospective chart review of all patients that underwent abdominal CT scanning at the Radiology department at Hamad General Hospital (HGH), Qatar, between March 2004 and March 2008 was performed. During the study period, HGH was the only tertiary hospital with CT scan facility in Qatar. Patients were mainly referred for abdominal CT scan to the radiology department by outpatient clinics or accident and emergency departments. The present study included all adult patients that were incidentally detected with renal angiomyolipoma following abdominal CT scan. The diagnosis of sporadic renal angiomyolipoma is often made by imaging studies (usually USG, CT, or MRI), however, in some cases biopsy may be performed for suspected cases on imaging.[3] Ultrasound or MRI was unnecessary for the initial diagnosis in our study as it was based on cases that picked up in CT scanning. Radiological follow-up (CT evaluation) was available for three years to observe any change in mass size and outcomes. All follow-up investigations were performed as part of routine clinical care.

The data was retrospectively reviewed for complete charting records of the patients along with CT scan findings. Patient's data included demographics (age, sex, and nationality), reason for CT examination, number of CT scans performed, site of renal angiomyolipoma, tumor size, duration of radiological and clinical follow-up, change in tumor size on follow-up, co-morbidities, treatment, and outcomes. The increase in size of the lesions was estimated with the first and last imaging study. Ethical approval (IRB# 12112/12) was obtained from the Medical Research Center and waiver consent was approved at Hamad Medical Corporation, Doha, Qatar.

Data was presented as proportion, median (range), or mean ± standard deviation (SD), as appropriate. Patients were divided into two groups based on gender, nationality (national and non-nationals), and tumor size (<4cm and ≥4cm). Differences in categorical variables were analyzed using the chi-square test or Fisher Exact test if any cell contains variable value less than five. Continuous variables were analyzed using Student t-test. For skewed continuous variables Mann-Whitney U test was performed. A significant difference was considered when the 2-tailed p value was less than 0.050. Data analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 18.

RESULTS

During the study period, 13,115 patients were screened for incidental findings on abdominal CT scan; of which 56 (0.4%) cases were found to have sporadic renal angiomyolipoma. The mean age of patients was 52±13 years, the majority were females (71%) and 46% were Qatar nationals [Table 1]. The primary reasons for abdominal CT scan evaluation included abdominal pain (80%), traumatic injuries (9%), stones (5%), and malignancy (4%). The majority (95%) of cases had unilateral tumors (52% right-sided and 43% left-sided), whereas, bilateral tumors were diagnosed in only 5% of cases. The median duration of CT follow-up was 36 (1–108) months and clinical follow-up was 83 (1–138) months. On initial presentation, the median size of angiomyolipoma was 1cm (0.4–15cm). CT follow-up was only available for 43 cases (26 had changes in size and17 had no changes) and revealed an increase in median size of angiomyolipoma to be 0.5cm (0.1–3.6cm). Of these angiomyolipoma cases, five (9%) had malignancy (three non-renal and two renal), four (7%) showed renal impairment, three (5%) were presented with elevated liver enzymes, and four (7%) cases required surgical interventions.

Table 2 shows the comparison of renal angiomyolipoma cases by gender. The mean age, duration of follow-up, change in tumor size, surgical intervention, and mortality were comparable among both genders.

Table 3 demonstrates angiomyolipoma cases according to nationality. It has been observed that higher proportion of nationals had right-sided tumors in comparison to non-nationals (69% vs. 37%; p=0.030) whereas, non-nationals presented

Table 1: Clinical presentation of renal angiomyolipoma patients (n=56).

Patients	n(%)
Age (mean±SD)	52±13
Age≥60 years	16(29%)
Age <60 years	40(71%)
Gender	
Males	16(29%)
Female	40(71%)
Nationality	
Qatari	26(46%)
Arab non-Qatari	19(34%)
Asian	6(11%)
Others	5(9%)
Number of CT examinations+	1(1-6)
Reason for CT	
Abdominal Pain	45(80%)
Traumatic injury	5(9%)
Stone	3(5%)
Cancer	2(4%)
Others	1(2%)
Site of renal angiomyolipoma	
Bilateral	3(5%)
Unilateral	53(95%)
Right-sided	*29(52%)*
Left-sided	*24(43%)*
CT findings of renal angiomyolipoma	
Initial size (cm)+	1(0.4 –15)
Final size on follow-up (cm)+	1.1(0.5–15)
Change in size (n=26) (cm)*+	0.5(0.1–3.6)
Duration of CT follow-up (months+	36(1–108)
Duration of clinical follow-up (months)+	82.5(1–138)
Tumor Size	
<4cm	48(86%)
≥4cm	8(14%)
Renal impairment/failure	4(7%)
Malignancy	5(9%)
Elevated liver enzyme	3(5%)
Surgery	4(7%)
Bleeding	0(0%)
Mortality (on follow-up)	4(7%)

**No change in 17 cases, 13 had no follow-up*
+ Median, range

Table 2: Patient characteristics by gender.

Patients	Females (n=40)	Males (n=16)	*p*-value
Age (mean±SD)	51±13	54±14	0.430
Follow-up duration (months)*	36(2–108)	24 (1–72)	0.230
Change in size*	0.5(0.1–3.6)	0.6(0.4–2.5)	0.220
Intervention (surgery)	8%	6%	0.870
Mortality*	10%(4)	0%	0.190

**Median, range*

Table 3: Patient characteristics according to nationality.

Patient	Nationals (n=26)	Non-nationals (n=30)	*p*-value
Age (mean±SD)	54±13	50±13	0.260
Gender			
Females	81%	63%	0.150
Males	19%	37%	
Site of renal angiomyolipoma			
Left	31%	53%	0.030
Right	69%	37%	
Surgical intervention	8%	7%	0.880
Mortality	12%	3%	0.230

more with left-sided tumors than nationals (53% vs. 31%; p=0.030). However, age, gender, need for surgical intervention, and mortality rates were comparable among the two groups.

Three cases of biopsy showed conventional clear cell carcinoma, unifocal, Fuhrman grade 2 (n=1), ruptured renal tumor in a patient presented with shock (n=1) and liposarcoma (n=1). The main indication for biopsy was large tumor size or rapid increase in tumor size in a short period. To look for the clinical presentation and outcomes based on tumor size, patients were categorized into two groups (<4cm and ≥ 4cm) [Table 4]. A significantly greater proportion of patients (four out of eight) with large tumor size (≥4cm) underwent surgical intervention compared to patients with small tumors (<4cm) (50% vs. 0%; p=0.001).

Table 4: Patient characteristics according to tumor size.

Patients	Tumor size		*p*-value
	<4cm(n=48)	≥ 4cm(n=8)	
Age (mean±SD)	50±13	56±14	0.280
Follow-up duration (months)*	34 (1–108)	44 (5–90)	0.820
Mean tumor size (cm)*	1.3±0.8	7±3	0.001
Size change (cm)*	0.4 (0.1–1.8)	1.85 (0.4–3.6)	0.004
Intervention (surgery)	0%	50%	0.001
Site			
- Left	46%	38%	0.750
- Right	48%	63%	
Mortality	7% (3)	13% (1)	0.550

**Median, range*

Table 5: Four renal angiomyolipoma cases underwent surgery.

Case 1	- Presented with abdominal pain and hypotension and found to have rupture and retroperitoneal bleeding
	- Tumor size 15cm at presentation
Case 2	- Clear cell renal carcinoma
	- Rapid increase in size from 3cm to 5.5cm in one year
	- Malignancy
Case 3	- Rapid increase in size from 4cm to 7.4cm in three years
	- Renal liposarcoma
Case 4	- Elective open partial nephrectomy
	- Size increased from 3.4cm to 5cm

Of the four surgically treated patients [Table 5] nephrectomy was performed for imminent rupture with unusual marked increase in the tumor size (n=1), presentation with shock and ruptured tumor (n=1), liposarcoma (n=1), and clear cell renal carcinoma (n=1). Although, the mean age, site of angiomyolipoma, follow-up duration, and mortality rates were comparable among the groups; the mean tumor size (6.8±3.4 vs. 1.3±0.8; p=0.001) and change in size (1.85 (0.4–3.6) vs. 0.4 (0.1–1.8); p=0.004) were significantly higher in the group with tumor size equal to or greater than 4cm when compared to patients with tumor size less than 4cm. The overall mortality on follow-up was 7% (4 cases). Cause of death was metastasis (n=1), renal failure (n=1), hepatic failure (n=1), and thromboembolic events with sepsis (n=1).

DISCUSSION

This is a unique study from our region to describe the frequency and outcome of patients with renal angiomyolipoma incidentally detected by abdominal CT scan. Renal angiomyolipoma are usually asymptomatic and detected on cross-sectional imaging of the abdomen. It is an uncommon benign renal tumor with an overall frequency of 0.3–3% among the general population.[7] In line with earlier findings, the frequency of renal angiomyolipoma in our population is 0.4% (comparable among national and non-nationals). Previous studies have demonstrated gender disparity among angiomyolipoma patients with predominance of females over males (4:1). Similarly, our study also observed female predominance (71%). A recent study from Germany used abdominal ultrasound to analyze 61,389 patients to determine the frequency and gender association of sporadic angiomyolipomas over 13 years. The authors found an overall prevalence of 0.44%, predominated by females (68%), 57% of cases involved the right kidney, 61% cases were followed over a mean period of 25 months and showed no significant increase in tumor size during the period of follow up.[12]

Predominance in females could be explained by the possible involvement of female hormones in the initiation and progression of tumor genesis.[3,5,13] Moreover, greater risk of tumor rupture and bleeding has been established during pregnancy.[14] A recent study from the US suggested that young women interested in future pregnancy should undergo surgical intervention for angiomyolipoma to avoid the risk of tumor rupture and complications associated with embolization.[15] In our study, 15 (38%) female patients were within the childbearing age (≤45 years). Interestingly, one 35-year-old female patient underwent surgery for tumor rupture. However, information regarding pregnancy status could not be retrieved from the records.

Clinically, angiomyolipomas are often presented as sporadic tumors, or patients had a known genetic predisposition for developing angiomyolipomas, such as tuberous sclerosis complex.[7,16] Angiomyolipomas associated with tuberous sclerosis are usually multifocal, larger in size, and distributed proportionately among both the genders.[16] The majority of the isolated angiomyolipoma cases occur sporadically (70–80%) involving mainly females. Although, the present study lacks information on the proportion of tuberous sclerosis the majority (86%) of the tumors were small (<4cm) indicating the possibility of sporadic tumors with asymptomatic presentation. Moreover, the vast majority of cases had unilateral tumors (94.6%) which corroborates with an earlier study that found the frequency of single angiomyolipoma to be 87%.[8] On the other hand, previous studies have reported that 80% of the tuberous sclerosis associated angiomyolipoma cases were symptomatic and had bilateral tumors.[8] The symptomatic patients usually present with flank pain, palpable tender mass, and gross hematuria, and less frequently nausea/vomiting, fever, and anemia.[17,18]

The size of angiomyolipoma varies from a few millimeters to more than 20cm.[7] A recent study on renal amgiomyolipoma demonstrated the association of clinical presentation with the increased tumor size. The authors found a correlation of symptoms with tumor size ≥4cm while, patients with tumor <4cm remained asymptomatic.[19] These findings are also supported by an earlier study by Dickinson et al.[20] Yamakado and colleagues[21] also reported a correlation of enlarged tumors (≥4cm) with the increased risk of aneurysmal rupture. Bleeding into the retroperitoneal space or the urinary collection system is the primary complication of angiomyolipoma,[3,18] which is correlated with the size and grade of tumor and possibly with tuberous sclerosis.[3,21,22] It has been demonstrated that the lesion size of less than 4cm is associated with a 13% increased risk of bleeding which escalates to 51% for lesion sizes equal to or greater than 4cm.[3,18] In our study, the median tumor size on follow-up CT was 1.1cm (range; 0.5–15) with an increase in size of 0.5cm (range; 0.1–3.6). Therefore, angiomyolipoma cases in our study were mainly asymptomatic with smaller tumor size and showed lower tumor progression over the three years follow-up.

The management of renal angiomyolipoma mainly depends upon the clinical presentation, tumor size, single or multiple lesions, and potential of malignancy. Previous studies suggested radiological surveillance of asymptomatic angiomyolipoma cases with smaller tumor size (<4cm).[23,24] Also, investigators suggested a tumor size equal to or greater than 4cm, sudden-onset of pain, presence of symptoms, and spontaneous hemorrhage are the primary indicators of surgical intervention.[22,25] In our study, no patients with tumor size less than 4cm required surgery; whereas half of cases with tumors equal to or greater than 4cm required surgical interventions. Consistent with our findings, Steiner et al,[6] reported no surgical intervention for small tumors (<4cm) but 30% of the large tumors (≥4cm) were managed surgically. Surgical intervention in symptomatic patients includes enucleoresection, arterial embolization, or conservative surgery.[26] Moreover, patients with bleeding, large tumors, or suspected renal cell carcinoma should be managed by radical nephrectomy.[27] In our study, surgery was performed in four cases; one patient was operated for clear cell renal carcinoma, one for rupture, and two for nephrectomy (one required left nephrectomy and other had partial nephrectomy). Usually, partial nephrectomy is indicated for cases that either failed to respond or remains unfit to receive embolization therapy. Moreover, prophylactic embolization is the preferred option in selected high-risk cases such as younger females interested in future pregnancy or patients in whom radiological surveillance remains impractical.[3]

Patients that are asymptomatic patients should be managed conservatively with long-term radiological surveillance. In contrast, surgical interventions are mainly required in symptomatic patients with unusual increased tumor size (≥4cm). In some cases there is a rapid increase in renal angiomyolipoma size, which might be associated with development and rupture of micro or macro-aneurysms causing retroperitoneal hemorrhage. For instance, one of our patients with increased tumor size (15cm) had rupture and retroperitoneal bleeding which was managed surgically. Also, the growing angiomyolipoma tends to occupy normal renal tissue which might lead to renal insufficiency or failure.

A limitation of the present study is the retrospective nature which might have skewed our data. Moreover, information regarding clinical symptoms is lacking as we have reviewed the incidentally detected angiomyolipoma cases. The present study also lacks information on the proportion of tuberous sclerosis, pregnancy, post-surgical complications and recurrence. Also, the radiological follow-up based on CT evaluation was available for only 43 (77%) cases.

CONCLUSION

Renal angiomyolipoma is an uncommon benign tumor with an overall prevalence of 0.4% in Qatar. It has characteristic clinical features and its recognition is often challenging for proper clinical diagnosis and treatment in asymptomatic patients. Therefore, for timely diagnosis and treatment, emergency physicians and nephrologists should be familiar with clinical course and presentation of angiomyolipoma. Asymptomatic patients need regular radiological surveillance. In contrast, surgical interventions are mainly required in symptomatic patients with increased tumor size (≥4cm). Timely diagnosis and treatment is necessary to avoid complications such retroperitoneal hemorrhage and renal impairment.

Disclosure

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