CASE REPORT

Renal angiomyolipoma with intravascular extension into the inferior vena cava: a case report and review of the literature

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A 42-year-old woman with tuberous sclerosis (TS) presented with acute right-sided flank pain. Imaging studies demonstrated numerous bilateral renal angiomyolipomas (AML), the largest located within the right upper pole, extending into the venous system to the level of the infra-hepatic inferior vena cava (IVC). Intravascular extension of AML is quite rare, however, may potentially result in fatal complications if not appropriately treated. We present a case report and a description of the surgical management, and provide a review of the literature concerning this rare finding.

Key Words: angiomyolipoma, venous invasion, venous extension, inferior vena cava

Introduction

Renal angiomyolipoma (AML) is a relatively common, benign sporadically occurring renal neoplasm that occurs in association with tuberous sclerosis (TS). The tumor contains variable amounts of mature adipose tissue, smooth muscle, and endothelial lined blood vessels.[1] Intravascular invasion occurs extending to the renal veins, IVC, or right atrium are extremely rare.[2-12] Herein, we report a case of an AML demonstrating intravascular extension into the infra-hepatic inferior vena cava (IVC) in a patient with TS and perform a comprehensive literature review.

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Materials and methods

Case report

A 42-year-old woman presented to our institution complaining of acute, right-sided flank pain. The patient's past medical history was significant for TS, diagnosed at the time of the birth of her first child 16 years prior. The patient disclosed that she never received a full clinical or radiological TS work up. Upon admission, the patient presented with flank pain beginning acutely 6 hours prior. Physical exam demonstrated very mild facial cutaneous angiofibromas, no costo-vertebral angle tenderness and no palpable masses. The patient's hemoglobin was 13.4 g/dl and her serum creatinine was 0.9 mg/dl. Contrast-enhanced abdominal CT demonstrated bilateral, solid renal masses with negative Houndsfield units, consistent with AML. There was no radiographic evidence of hemorrhage, hydronephrosis, nephrolithiasis, or cholecystitis.

To better delineate the extent of IVC involvement, an abdominal MRI was performed again revealing numerous bilateral, enhancing solid renal masses with signal characteristics consistent with renal AML. The largest renal tumor was located within the right upper pole and measured 9.0 cm x 8.7 cm. The mass abutted Gerota's fascia and demonstrated direct extension into the renal vein and extended approximately 3 cm into the IVC, Figure 1.

Complete TS work-up revealed normal cardiac function in the absence of cardiac rhabdomyomas on echocardiography. Brain MRI demonstrated numerous non-enhancing white matter lesions consistent with cerebral tubers.

The patient thereafter underwent elective right radical nephrectomy and IVC thrombectomy using a standard thoracoabdominal approach. After complete renal mobilization and isolation of the hilar vessels, the renal artery was ligated and divided. After vascular control of the infra renal IVC, contralateral renal vein, and IVC cephalad to the palpable tumor mass, the IVC was opened at the level of the renal ostium to allow complete removal of the tumor. A running prolene suture was used to close the defect over a Satinsky clamp. Total operating room time and estimated blood loss was 165 minutes and 100 ml, respectively. There were no perioperative complications and the patient was discharged on postoperative day 4. With a 22 month follow-up, she has remained asymptomatic and continues to be observed for interval progression of the contralateral renal AMLs.

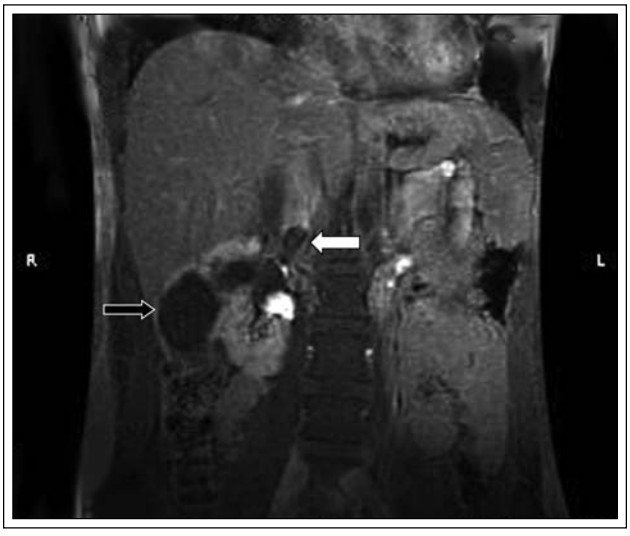

Figure 1. Coronal-reconstruction of abdominal MRI demonstrating a large 9 cm, fat containing lesion of right kidney (black arrow) with invasion into infra-hepatic inferior vena cava (white arrow).

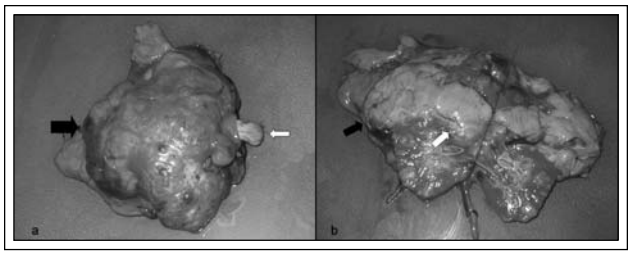

Figure 2. Right nephrectomy specimen: A) Intact specimen demonstrating yellow fatty tumor (black arrow) with direct thrombus extending 3 cm beyond the renal vein ostium (white arrow). B) Specimen coronally-opened (dotted line) demonstrated numerous yellow fatty angiomyolipomas and a large upper pole neoplasm (black arrow) with direct extension into renal sinus (white arrow) and into the inferior vena cava.

Surgical pathology

The resected right kidney specimen weighed 320 g. The specimen contained multiple yellow tumors ranging 2 cm-9 cm in diameter. Tumor thrombus protruded 3 cm from the renal vein but did not demonstrate invasion of the adjacent venous wall, Figure 2. The masses and thrombus were composed primarily of mature adipose tissue with abnormal blood vessels and islands of mature smooth muscle without evidence of cellular atypia, securing the diagnosis of AML.

Literature review

A MEDLINE review of the English language was performed evaluating vascular extension of angiomyolipoma. As summarized in Table 1, this is the 34th documented case of intravascular AML extending to at least the IVC, but only the sixth such case in a patient with tuberous sclerosis. A strong female predisposition of intravascular AML was observed with 85% (28/33) of cases. Mean age of reported cases was 46.9 (range 16-75) with an average tumor size of 9.5 cm (range 4.5-20.5).

Discussion

Renal AML is a benign, mesenchymal tumor composed of mature adipose tissue, smooth muscle, and aberrant blood vessels. On CT and MRI, AML typically appears as a solid fat containing mass. With an incidence of 13/100000 in the general population, AML accounts for 2%-6.4% of all renal tumors, generally occurring sporadically as a single, unilateral mass. Most commonly, this tumor presents incidentally in 45-55 year-old women with a female:male predominance of 4:1.[2,13] Approximately 20% of AMLs occur in patients with the autosomal dominant disorder TS. Chromosomal defects found on

TABLE 1. **Reported cases of renal angiomyolipoma with tumor thrombus extension into the inferior vena cava and/or right atrium**

Author	Age	Sex	Tumor size (cm) §	Thrombus extension	TS	Side	Solitary/ multiple	Symptoms
Morris, 1994[2]	58	F	Large	IVC	-	R	Solitary	Flank pain, fever
Sasaki, 1994[3]	34	F	NA	IVC	+	L	Solitary	Abdominal and flank pain
Bernstein, 1997[4]	45	M	5	IVC	-	R	Solitary	None
Rubio-Briones, 1997[5]	64	M	6.5	IVC	-	R	Solitary	None
Toda,1999[6]	41	F	18	RA	-	R	Solitary	Flank pain
Davydov, 2001[7]	46	F	6	RA	-	R	Solitary	Flank pain
Hatakeyama, 2002[8]	31	F	11	IVC	-	R	Solitary	None
Islam, 2003[9]	16	F	Large	IVC	-	R	Solitary	Flank pain
	45	NA	10	IVC	-	L	Solitary	Flank pain, anemia
	45	F	9	IVC	-	R	Multiple	Flank pain, gross hematuria
	62	F	4.5	RA	-	L	Solitary	Congestive heart failure
	22	F	Small	IVC	+	R	Multiple, bilateral	Abdominal pain, gross hematuria
	22	F	8.5	IVC	-	R	Multiple, bilateral	Flank pain, hematuria
	56	F	13.5	IVC	-	R	Solitary	Lower extremity
	75	F	16	IVC	-	B	Multiple, bilateral	Abdominal pain, hematuria
	58	F	> 10	RA	-	R	Solitary	Abdominal pain
	58	F	NA	IVC	-	R	Solitary	None
	36	F	Large	IVC	+	R	Multiple, bilateral	Abdominal enlargement
	34	F	Huge	IVC	+	R	Multiple, bilateral	Abdominal mass
	53	F	6.5	IVC	-	R	Solitary	None
	31	F	10	IVC	-	NA	Solitary	None
	30	F	NA	IVC	-	R	Solitary	None
	64	M	6.5	IVC	-	R	Solitary	None
	65	F	6	IVC	-	L	Multiple, bilateral	None
	67	M	6	IVC	-	R	Multiple, bilateral	Flank pain, hematuria
	52	F	NA	IVC	-	R	Solitary	Flank pain
	40	F	NA	RA	-	R	Bilateral	Flank pain
	42	M	20.5	IVC	-	R	Solitary	Abdominal mass, flank pain, weight loss
	69	F	10	IVC	-	R	Solitary	None
	40	F	11	IVC	-	R	Solitary	None
Game, 2003[10]	56	F	4.5	IVC	NA	NA	Solitary	Flank pain
Schips, 2003[11]	NA	F	10.5	IVC	-	L	Solitary	Flank pain
Bierer , 2005[12]	36	F	NA	IVC	+	B	Multiple, bilateral	NA
Schade, 2007	42	F	9	IVC	+	R	Multiple, bilateral	Flank pain
Mean value	**46.9**	**28F**	**9.5**	**29-IVC**				
	9	**5M**		**5-RA**				

§Tumor size indicates the diameter of the tumor at its greatest dimension. Key: (F) Female, (M) Male, (RA) right atrium, (IVC) inferior vena cava, (+) positive, (-) negative, (R) right, (L) left, (B) bilateral, (NA) not available

chromosomes 9 and 16 are responsible for the presentation of TS. First described in the 1880s, tuberous sclerosis complex, also known as Bourneville's disease, is a genetic disease that affects multiple organs. It can cause tumors in the skin, kidneys, brain, heart, eyes, lungs, teeth as well as other organ systems. In most individuals, the disease affects only some of these organs. The severity of TS can range from mild skin abnormalities to, in severe cases, mental retardation or renal failure. Many TS manifestations also develop later in life. Most individuals who are mildly affected by TSC lead active and productive lives, but it is important to realize that TS is a life-long companion and individuals should receive continuous follow-up care.

From a urological perspective, AML develops in 40%-80% of patients with TS, most often presenting earlier between the ages of 25-35 as multiple bilateral renal neoplasms.[4,13] As such, all patients with suspected TS should undergo a thorough investigation including dedicated renal imaging. Since these patients are at high risk for synchronous bilateral tumors, every effort for nephron sparing surgery should be made.

AML is slow growing and the lesions often remain asymptomatic. The most common symptoms result from growth and hemorrhage with increasing risk as tumor size increases to > 4 cm.[14] AML may demonstrate rapid growth during pregnancy which may be explained by the tumors' expression of both the estrogen and progesterone receptors.[1,8] Rarely, AML progression has been reported with nodal involvement[15] and isolated cases of sarcomatous degeneration have been documented.[16] As this case demonstrates, intravascular invasion may also occur with direct invasion into the renal vein and extend as far as the IVC or right atrium. When intravascular invasion occurs, prompt surgical removal is mandated as there is a potential for large lethal pulmonary tumor embolism if untreated.[17]

Our literature review demonstrates that this is the 34th documented case of intravascular AML extending to at least the IVC, but only the sixth such case in a patient with tuberous sclerosis, Table 1. Reported intravascular AML occurred more commonly in females (85% (28/33)) with a mean age of 46.9 (range 16-75). Together, sex and perimenopausal age, suggests a hormonal relationship with estrogen and progesterone. Likewise, size is a likely risk factor with an average tumor size of 9.5 cm (range 4.5-20.5) suggesting tumor size > 4 cm increases risk of invasion. Seventy nine percent (26/33) of renal AMLs with intravascular invasion have occurred from the right kidney. Since there is no lateral predisposition for AML, the shorter length of the renal vein to the inferior vena cava may help explain the higher incidence of right-sided tumors with IVC involvement.

Since approximately 20% of AMLs occur in patients with TS,[4] and only six of the 35 (17.1%) confirmed cases of intravascular AML occurred in the setting of TS, it does not appear that TS is an independent risk factor for intravascular invasion. However, in those patients with TS, the mean age was significantly lower than those patients without TS (34 versu 49.3 years, $p = 0.02$), suggesting invasive AMLs present earlier in these patients. This may be related to bilateral, multifocal tumors with greater growth rates when compared to sporadic AMLs. □

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