Review Article

Update on the Diagnosis and Management of Renal Angiomyolipoma

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Abbreviations and Acronyms

AML = angiomyolipoma
CT = computerized tomography
EBL = estimated blood loss
LAM = lymphangioleiomyomatosis
LPN = laparoscopic partial nephrectomy
MRI = magnetic resonance imaging
mTOR = mammalian target of rapamycin
NSS = nephron sparing surgery
RCC = renal cell carcinoma
SAE = selective arterial embolization
TSC = tuberous sclerosis complex
US = ultrasound

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Purpose: Advances in minimally invasive therapies and novel targeted chemotherapeutics have provided a breadth of options for the management of renal masses. Management of renal angiomyolipoma has not been reviewed in a comprehensive fashion in more than a decade. We provide an updated review of the current diagnosis and management strategies for renal angiomyolipoma.

Materials and Methods: We conducted a PubMed® search of all available literature for renal or kidney angiomyolipoma. Further sources were identified in the reference lists of identified articles. We specifically reviewed case series of partial nephrectomy, selective arterial embolization and ablative therapies as well as trials of mTOR inhibitors for angiomyolipoma from 1999 to 2014.

Results: Renal angiomyolipoma is an uncommon benign renal tumor. Although associated with tuberous sclerosis complex, these tumors occur sporadically. Risk of life threatening hemorrhage is the main clinical concern. Due to the fat content, angiomyolipomas are generally readily identifiable on computerized tomography and magnetic resonance imaging. However, fat poor angiomyolipoma can present a diagnostic challenge. Novel research suggests that various strategies using magnetic resonance imaging, including chemical shift magnetic resonance imaging, have the potential to differentiate fat poor angiomyolipoma from renal cell carcinoma. Active surveillance is the accepted management for small asymptomatic masses. Generally, symptomatic masses and masses greater than 4 cm should be treated. However, other relative indications may apply. Options for treatment have traditionally included radical and partial nephrectomy, selective arterial embolization and ablative therapies, including cryoablation and radio frequency ablation, all of which we review and update. We also review recent advances in the medical treatment of patients with tuberous sclerosis complex associated angiomyolipomas with mTOR inhibitors. Specifically trials of everolimus for patients with tuberous sclerosis complex suggest that this agent may be safe and effective in treating angiomyolipoma tumor burden. A schema for the suggested management of renal angiomyolipoma is provided.

Conclusions: Appropriately selected cases of renal angiomyolipoma can be managed by active surveillance. For those patients requiring treatment nephron sparing approaches, including partial nephrectomy and selective arterial embolization, are preferred options. For those with tuberous sclerosis complex mTOR inhibitors may represent a viable approach to control tumor burden while conserving renal parenchyma.

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Renal angiomyolipoma is an uncommon tumor that, although benign, in most cases can involve difficult management decisions. This entity was first referenced in 1900,[1] and in 1911 Fischer first described the histopathology as including 3 components, ie dysmorphic blood vessels, smooth muscle and mature adipose tissue, from which the tumor derives its name.[2] However, the term angiomyolipoma did not come into wide use until the middle of the 20th century. These tumors can occur sporadically or in association with tuberous sclerosis complex or, more rarely, sporadic lymphangioleiomyomatosis.

Diagnosis and management of renal AML have not been reviewed in a comprehensive fashion in more than a decade.[2] In that time advances in minimally invasive therapies and novel targeted chemotherapeutics have increased the options for management of AML. We provide an up-to-date review of the current diagnosis and management of renal AML, including a management algorithm, which should be of value to the practicing urologist.

METHODS

A PubMed search of all available literature for renal or kidney angiomyolipoma was conducted. Further sources were identified in the reference lists of identified articles. Case series (including at least 10 cases and most followup data) of partial nephrectomy, SAE and ablative therapies as well as trials of mTOR inhibitors for the treatment of AML from 1999 to 2014 were specifically reviewed. A management algorithm was constructed using the available data.

EPIDEMIOLOGY

Renal AMLs occur uncommonly in the general population, with females more commonly affected than males. A screening study for renal neoplasms using ultrasound in 17,941 Japanese adults revealed an overall rate of renal AML of 0.13%, with 0.22% of females affected and 0.1% of males.[3] Historical series demonstrate a female-to-male ratio of 2:1.[1] The proportion of AML cases involving TSC is about 20%.[2] TSC is an autosomal dominant disease with an estimated prevalence of 1 in 12,000, with a birth rate of up to 1 in 6,000.[4] Reported rates of renal AML in association with TSC range from 55% to 90%.[4,5] Renal AML also occurs in 30% to 50% of patients with sporadic LAM, a much rarer condition than TSC that is almost exclusively seen in women.[6] Age at presentation varies, with patients with TSC more likely to present by their 20s or 30s, and patients with sporadic AML in their 40s or 50s.[7,8]

PATHOPHYSIOLOGY

Renal AML can occur as part of TSC sporadically or, less commonly, in association with sporadic LAM. The molecular genetics of TSC have been well characterized, with mutations to *TSC1* at chromosomal location 9q34 and *TSC2* at 16p13.3 identified.[4,5] Although generally considered an autosomal dominant condition, up to two-thirds of patients have sporadic mutations to *TSC1* and *TSC2*.[4] *TSC1* and *TSC2* encode proteins carrying the same names, also known as hamartin and tuberin, respectively. These proteins interact with each other to form heterodimers, whose most important role is inhibition of the mTOR pathway.[4,5]

Loss of TSC1 or TSC2 leads to unchecked activation of mTOR, which leads to unregulated protein synthesis, increased cell growth and proliferation, increased angiogenesis, and changes in cell orientation and migration.[5] These downstream effects of unchecked mTOR activation lead to a variety of clinical manifestations associated with TSC. The most common of these manifestations are seen in the central nervous system, with more than 90% of affected individuals having some combination of epilepsy, neurocognitive impairment and autism due to cortical tubers, subependymal nodules and giant cell astrocytomas.[4,5] The majority of patients with TSC will also have some combination of cutaneous manifestations, which can include hypomelanotic macules, facial angiofibromas, ungual fibromas and shagreen patches.

The prevalence of renal AML in individuals with TSC is high (55% to 90% of cases), and these cases are generally multifocal and bilateral.[4,5] Of women with TSC 40% will manifest some degree of pulmonary LAM, leading to pneumothorax, chylous pleural effusions and cystic lung disease.[4,5] Other major features of TSC can include cardiac rhabdomyomas and retinal hamartomas. To establish a diagnosis of TSC, patients generally must have 2 major features of the syndrome or 1 major and 2 minor features.[4] Genetic testing serves to confirm the diagnosis and the specific mutation involved in those who meet criteria, and can be useful in screening other family members in the case of a sporadic mutation.