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Hormone Receptor Expression in Renal Angiomyolipoma: Clinicopathologic Correlation

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Abstract

Objectives—Although renal angiomyolipoma (AML) occurs more commonly in females than males, the origin of this difference in incidence by sex is unknown. Therefore, we investigated the expression of the androgen receptor (AR), estrogen receptor subtypes alpha (ER α) and beta (ER β), progesterone receptor, and the enzyme aromatase in renal AML.

Methods—We evaluated specimens from 110 patients who had undergone resection of a renal AML, including 90 women and 20 men. Immunohistochemistry was performed using monoclonal antibodies on paraffin-embedded tissue sections. Expression was correlated with patient demographics and tumor pathologic features.

Results—ER β was expressed in 100% (106 of 106) of the AML specimens evaluated. Of the 104 specimens that could be assessed for the AR, 82 (79%) demonstrated staining. Of 110 lesions, 31 (28%), 42 (38%), and 11 (10%) expressed ER α , progesterone receptor, and aromatase, respectively. The level of ER β expression was not associated with patient age ($P = 0.92$), sex ($P = 0.82$), a diagnosis of tuberous sclerosis ($P = 0.56$), or histologic subtype of AML ($P = 0.94$). A trend was found toward increased AR expression in men ($P = 0.069$) and younger patients ($P = 0.052$), and ER α was expressed in the AML specimens from 5 (71%) of 7 patients with tuberous sclerosis compared with 26 (25%) of 103 without tuberous sclerosis ($P = 0.018$). Both AR and ER α expression were more common in the triphasic subtype of AML than in the lipomatous tumors ($P = 0.046$ for both).

Conclusions—The results of our study have shown that ER β expression is ubiquitous in renal AML, and the AR is found in most tumors. ER α and progesterone receptor were expressed in approximately one third of cases. These data suggest a potential role for hormones in the pathogenesis and management of renal AML.

Angiomyolipoma (AML) is a benign tumor of the kidney consisting of fat, blood vessels, and smooth muscle. These lesions have a propensity to grow locally,¹ resulting in complications such as flank pain, hematuria, and retroperitoneal hemorrhage. Although AMLs are classically associated with the tuberous sclerosis (TS) complex (TSC), approximately 70% to 80% of renal AMLs occur sporadically,² predominantly in women between the fourth and seventh decade of age. One autopsy series estimated the incidence of AML to be 1 in 330 women compared with 1 in 5000 men.³

The etiology of these tumors remains poorly understood, because, although linkage analysis has identified two genes associated with the TSC, TSC1⁴ and TSC2,^{5,6} the function of these gene products in the development of AML has not been well defined. In addition, loss of

heterozygosity of the TSC2 gene has been reported in only 10% of sporadic renal AML cases,⁷ suggesting a significant role for other, as yet unidentified, genes. It has been proposed that the perivascular epithelioid cell might be a common progenitor cell for AMLs and a family of related lesions.⁸

In addition, the increased incidence of AMLs in women, as well as reports of AML growth in patients undergoing exogenous hormonal therapy⁹ and during pregnancy,^{10,11} suggest a possible role for sex steroids in the pathogenesis of these tumors. To investigate this concept, several studies to date have evaluated the expression of the estrogen receptor (ER), specifically the ER-alpha (ER α) subtype, and the progesterone receptor (PR) in renal AML.^{12–17} However, these studies have involved a limited number of patients and have generated conflicting results. Moreover, a second subtype of the ER, ER-beta (ER β), has been identified¹⁸ and has been found to have a distinct tissue distribution and response to estrogen agonists and antagonists relative to ER α .¹⁹ The objectives of the present study, therefore, were to examine the expression of ER α , ER β , PR, androgen receptor (AR), and the enzyme aromatase in a large series of patients with surgically resected renal AML and to correlate their expression with various clinicopathologic features of AML.

Material and Methods

Patient Selection

After approval from our institutional review board, we reviewed the Mayo Clinic Nephrectomy Registry to identify all patients treated with radical or partial nephrectomy for renal AML from 1970 to 2004. All specimens were pathologically confirmed as AML and subtyped according to their histologic variant.²⁰

Immunohistochemistry

A representative formalin-fixed, paraffin-embedded tissue block from each tumor was selected for immunohistochemical analysis. Tissue sections (5 μ m) were cut from the blocks, deparaffinized in xylene, rehydrated in a graded series of ethanol, and rinsed with distilled water. Antigen retrieval for ER α , ER β , AR, and PR was performed by heat with ethylenediaminetetraacetic acid (pH 8) or Target Retrieval Solution (DAKO, Carpinteria, Calif) in a 98° water bath. No antigen retrieval was required before immunostaining for aromatase. A 5-minute incubation in Endogenous Peroxidase Block (DAKO) was used to quench the endogenous peroxidase activity.

To evaluate for AR, ER β , and aromatase expression, the slides were incubated for 60 minutes at room temperature with a mouse monoclonal anti-human AR antibody (Novocastra Laboratory, Newcastle, UK) diluted 1:20 in DaVinci Green antibody diluent (Biocare Medical, Concord, Calif), a mouse monoclonal anti-human ER β antibody (DAKO) diluted 1:100, or a mouse monoclonal anti-human Cytochrome P450 aromatase antibody (Serotec, Raleigh, NC) diluted 1:25. The slides were next incubated in mouse probe and then polymer from the Mach 3 Mouse Probe HRP Polymer Kit (Biocare Medical). The sections were visualized by incubating in betazoid 3,3'-diaminobenzidine (Biocare Medical).

For ER α and PR staining, the slides were incubated for 30 minutes at room temperature with either a mouse monoclonal anti-human ER α antibody (DAKO) diluted 1:50 in Antibody Diluent (DAKO) or a mouse monoclonal anti-human PR antibody (DAKO) diluted 1:100. Immunohistochemical detection was done using the EnVision+ Dual Link System-HRP (DAKO), followed by incubation with 3,3'-diaminobenzidine substrate-chromogen. All sections were counterstained with hematoxylin, dehydrated in ethanol, cleared in xylene, and mounted with a coverslip.

Negative control tumor sections were treated identically to all other sections, except that the primary antibody was not included in the staining. Breast tissue from archival specimens was used as a positive control for ER α , ER β , and PR expression, prostatic tissue served as the positive control for the AR, and human placenta was used as a control for aromatase.

Staining Evaluation

A single pathologist scored the immunohistochemical expression in a semiquantitative fashion. For the analysis of ER α , ER β , AR, and PR, any distinct, brown nuclear staining was considered a positive result; cytoplasmic staining was recorded for aromatase. The level of expression was assessed by evaluating the percentage of nuclei evaluated that stained positive. A sample evaluation was performed with the pathologist unaware of the clinical data.

Statistical Analysis

The associations of protein staining with the clinicopathologic features were evaluated using the Wilcoxon rank sum, Kruskal-Wallis, chi-square, and Fisher exact tests. Statistical analyses were done using the Statistical Analysis Systems software package (SAS Institute, Cary, NC). All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

We evaluated the AML specimens from 110 patients treated with radical or partial nephrectomy (Table 1). The median patient age at surgery was 55.5 years (range 25 to 84), and the median size of the AML resected was 5.0 cm (range 0.3 to 44.0). Seven patients (6.4%) were known to have TS. In 4 patients, sufficient tumor from the tissue blocks was not available to be evaluated for ER β , and AR expression could not be assessed in 6 patients.

We found that the ER β was expressed by 100% (106 of 106) of the AML specimens evaluated (Fig. 1). Expression was noted in more than 50% of nuclei in 74 (69.8%) of 106 of these cases, 27 (25.5%) of 106 tumors demonstrated staining in 10% to 50% of the nuclei, and only 5 lesions (4.7%) had less than 10% of nuclei positive. AR expression was detected in 82 (79%) of 104 AMLs, ER α was noted in 31 (28.2%) of 110 tumors, and 42 (38.2%) of 110 AMLs demonstrated PR staining. Only 11 (10%) of 110 AMLs expressed aromatase.

Of the 82 AR-expressing AMLs, the extent of expression was heterogeneous, with 36 (43.9%) having less than 10% of nuclei staining positive, 21 (25.6%) having 10% to 50% of nuclei positive, and 25 (30.5%) having more than 50% expression. Expression of both ER α and PR was primarily focal, because 21 (67.7%) of 31 AMLs that expressed ER α had less than 10% of the nuclei staining positive, 9 (29%) had staining in 10% to 50% of nuclei, and 1 (3.2%) possessed immunoreactivity in more than 50% of the nuclei evaluated. Similarly, 29 (69%) of 42 PR-positive tumors demonstrated expression in less than 10% of nuclei, 9 (21.4%) had staining in 10% to 50% of nuclei, and 4 (9.5%) had staining in more than 50% of nuclei.

AR, ER α , ER β , and PR expression was localized to cell nuclei, and aromatase was detected in the cytoplasm. Furthermore, ER α immunoreactivity was found primarily in the perivascular cells and myomatous components of the AMLs, with no staining seen in lipid cells. AR, ER β , and PR expression was similarly noted in the perivascular and muscle cells from the tumors but were also detected in the lipid component. Aromatase was focally present in the smooth muscle cells within the walls of tumor blood vessels.

Interestingly, when receptor expression was correlated with patient demographics, we found that AR expression in renal AMLs tended to occur more frequently in male patients, with 18 (95%) of 19 of the AMLs from men staining positive for the AR compared with 64 (75%) of the 85 AMLs from women ($P = 0.069$). However, we found no correlation between the

expression of the other hormone receptors and sex. The AMLs from 5 (25%) of 20 men from our series stained positive for ER α compared with 26 (29%) of 90 AMLs from women ($P = 0.73$). Likewise, 6 (30%) of 20 AMLs from men were PR-positive versus 36 (40%) of 90 AMLs from women ($P = 0.41$). The level of ER β expression similarly did not differ by sex ($P = 0.82$). Moreover, no association between AR ($P = 0.52$), ER α ($P = 0.87$), ER β ($P = 0.86$), or PR ($P = 0.98$) expression with AML size was noted.

In contrast, the expression of ER α , PR, and AR correlated inversely with patient age. Specifically, the median age for the 31 patients with ER α -positive AMLs was 47 years (range 25 to 77) compared with 58 years (range 30 to 84) in the 79 patients with ER-negative AMLs ($P < 0.001$). Similarly, the median age for the patients with AMLs that expressed the PR was 45 years (range 25 to 77) versus 59 years (range 31 to 84) for patients with PR-negative AMLs ($P < 0.001$), and the median age of the 82 patients with AR-positive AMLs was 53 years (range 25 to 79) compared with 58 years (range 37 to 84) in the 22 patients without AR expression ($P = 0.052$). Again, the level of ER β expression remained independent of patient age ($P = 0.92$).

We also examined the association of the expression with the histologic subtype of AML; specifically, we compared the expression in the two most prevalent histologic subtypes from our series, triphasic and lipomatous. We noted that 62 (82%) of 76 triphasic AMLs demonstrated AR staining compared with 9 (56%) of 16 lipomatous tumors ($P = 0.046$). Likewise, 25 (32%) of 77 lesions with a triphasic histologic type expressed ER α compared with 2 (10%) of 20 lipomatous AMLs ($P = 0.046$). No significant correlation between PR immunoreactivity and subtype was found, because 30 (39%) of 77 triphasic AMLs expressed the PR versus 6 (30%) of 20 lipomatous AMLs ($P = 0.46$). The level of ER β expression was similarly independent of AML subtype ($P = 0.94$).

In addition, we found that both ER α and the PR were significantly more likely to be expressed in AMLs that occurred in the setting of TS than in non-TS-associated AMLs. Thus, 5 (71%) of 7 patients with TS possessed AMLs that expressed ER α compared with 26 (25%) of 103 patients without TS ($P = 0.018$). Similarly, the PR was expressed in AMLs from 7 (100%) of 7 patients with TS versus in 35 (34%) of 103 AMLs from patients without TS ($P < 0.001$). AR expression was also detected in the AMLs from all 7 patients with TS compared with 75 (77%) of 104 tumors from patients without TS ($P = 0.34$).

Aromatase expression was not significantly associated with patient age ($P = 0.22$), sex ($P = 1.00$), TS status ($P = 0.53$), tumor size ($P = 0.43$), or AML histologic subtype ($P = 0.11$).

Comment

We present what is to our knowledge the first description of ER β , AR, and aromatase expression, as well as the largest analysis of ER α and PR expression, in renal AML to date. In addition, we evaluated the association of expression with patient demographics and tumor pathologic subtype. We found that 100% of renal AMLs, lesions that have been shown to have a female predominance in incidence,³ expressed ER β , and nearly 80% expressed the AR. In contrast, aromatase, the enzyme responsible for converting testosterone to estrogen, was detected in only 10% of tumors.

Our findings of ER α expression in 28% of tumors and PR expression in 38% are within the range of expression noted in several previous studies. L'Hostis *et al.*¹⁴ evaluated 46 AMLs and noted ER α staining in 18.6% of cases and PR expression in 27.9%. Cho *et al.*¹⁶ reported ER α expression in 42% of 33 AMLs studied and PR positivity in 15% of cases. In addition, as we found in our study, Cho *et al.*¹⁶ detected ER α and PR expression predominantly localized around the blood vessels within the tumors.

We also noted that all AMLs that occurred in patients with TS expressed the AR and that the tumors from patients with TS were significantly more likely to express both ER α and PR than sporadic AMLs. Similarly, Henske *et al.*¹³ noted an increased expression of the PR in TS-associated AMLs, demonstrating PR staining in 48% of TS-associated tumors evaluated versus in 7% of sporadic cases. These data suggest a possible difference in the biology of sporadic versus TS-associated AMLs.¹³ Furthermore, as did Henkse *et al.*,¹³ we found that patients with AMLs that demonstrated hormone receptor immunoreactivity were significantly younger. Unlike that study, however, we found no association between ER or PR expression and patient sex, although we observed that AR expression tended to occur more frequently in the AMLs from men.

Because the present series provides only an observational association of hormone receptor expression in renal AML, the functional significance of expression in these tumors requires additional study. Although older studies using biochemical receptor assays were able to detect testosterone and dihydrotestosterone receptors in nonneoplastic renal tissue,²¹ a more recent investigation using immunohistochemistry on tissue microarrays did not detect AR, ER, or PR staining in the normal renal parenchyma.²² Moreover, the same report found ER and PR expression in only 1.1% of renal cell carcinoma specimens and AR immunoreactivity in 15% of cases.²² Therefore, although hormone receptor expression has been noted in nontumorous stromal proliferation of the kidney,²³ these receptors might uniquely contribute to the development of renal AMLs. One previous investigation used a cell line derived from a renal AML to demonstrate that growth was stimulated by exogenous estradiol.²⁴ Nevertheless, elucidating the possible role of sex steroids and receptors in the pathogenesis of renal AMLs requires continued investigation.

ER expression has been noted in previous studies of human vascular smooth muscle cells.^{25, 26} Moreover, estrogen has been shown to promote angiogenesis in vitro and in vivo,²⁷ potentially by increasing expression of vascular endothelial growth factor.²⁸ In addition, cells lacking TSC1 or TSC2 have been shown to have enhanced production of vascular endothelial growth factor.²⁹ Together, these data suggest that multiple mechanisms, including a possible role for hormones, are likely to stimulate the proliferation of perivascular smooth muscle, which in turn could contribute to the pathogenesis of renal AMLs.

Because sex steroids might play a role in the pathogenesis of renal AMLs, hormone receptors could be potential therapeutic targets. A recent study of TSC^{+/-} mice demonstrated that estrogen treatment significantly accelerated, and tamoxifen reduced, the development of liver hemangiomas, which are pathologically and immunohistochemically similar to renal AMLs.³⁰ Of particular interest could be the differential expression noted between ER β , which was universally expressed by renal AMLs, and ER α , which was detected in fewer than 40% of cases, because although tamoxifen acts as a partial agonist on ER α , it has a pure antagonist effect on ER β .¹⁹ Similarly, given that most of these lesions expressed the AR, a potential role for the androgen axis in the development of these tumors also awaits further investigation.

Overall, the previous demographic and experimental observations, together with the present data, support continued investigation into the physiologic significance of hormones in the pathogenesis of renal AML and the possible role for hormonal therapy in the management of these tumors, particularly for patients with TS, who tend to develop multiple, bilateral lesions. Additionally, consideration should be given to increase the frequency of surveillance for renal imaging in patients with known renal AML who are undergoing exogenous hormonal therapy⁹ or who become pregnant.^{10,11}

Conclusions

We found ER β expression in 100% of the AMLs evaluated. Most AMLs also expressed the AR, and ER α and PR expression were detected in approximately one third of tumors. These results, along with the known female predominance of these lesions and reports of AML growth in patients with increased circulating hormone levels, suggest a possible role for sex steroids in the pathogenesis and management of renal AML.

References

1. Lemaitre L, Robert Y, Dubrulle F, et al. Renal angiomyolipoma: growth followed up with CT and/or US. *Radiology* 1995;197:598–602. [PubMed: 7480725]
2. Nelson CP, Sanda MG. Contemporary diagnosis and management of renal angiomyolipoma. *J Urol* 2002;168:1315–1325. [PubMed: 12352384]
3. Hajdu SI, Foote FW Jr. Angiomyolipoma of the kidney: report of 27 cases and review of the literature. *J Urol* 1969;102:396–401. [PubMed: 5343474]
4. Van Slegtenhorst M, de Hoogt R, Hermans C, et al. Identification of the tuberous sclerosis gene TSC1 on chromosome 9q34. *Science* 1997;277:805–808. [PubMed: 9242607]
5. Identification and characterization of the tuberous sclerosis gene on chromosome 16. *Cell; The European Chromosome 16 Tuberous Sclerosis Consortium*; 1993. p. 1305–1315.
6. Wienecke R, Konig A, DeClue JE. Identification of tuberin, the tuberous sclerosis-2 gene product. *J Biol Chem* 1995;270:16409–16414. [PubMed: 7608212]
7. Henske EP, Neumann HP, Scheithauer BW, et al. Loss of heterozygosity in the tuberous sclerosis (TSC2) region of chromosome band 16p13 occurs in sporadic as well as TSC-associated renal angiomyolipomas. *Genes Chromosomes Cancer* 1995;13:295–298. [PubMed: 7547639]
8. Martignoni G, Pea M, Reghellin D, et al. Perivascular epithelioid cell tumor (PEComa) in the genitourinary tract. *Adv Anat Pathol* 2007;14:36–41. [PubMed: 17198309]
9. Gould Rothberg BE, Grooms MC, Dharnidharka VR. Rapid growth of a kidney angiomyolipoma after initiation of oral contraceptive therapy. *Obstet Gynecol* 2006;108:734–736. [PubMed: 17018483]
10. Fernandez AM, Minguez R, Serrano P, et al. Rapidly-growing renal angiomyolipoma associated with pregnancy. *Actas Urol Esp* 1994;18:755–757. [PubMed: 7942236]
11. King JA, Stamilio DM. Maternal and fetal tuberous sclerosis complicating pregnancy: a case report and overview of the literature. *Am J Perinatol* 2005;22:103–108. [PubMed: 15731990]
12. Uzzo RG, Libby DM, Vaughan ED Jr, et al. Coexisting lymphangioleiomyomatosis and bilateral angiomyolipomas in a patient with tuberous sclerosis. *J Urol* 1994;151:1612–1615. [PubMed: 8189576]
13. Henske EP, Ao X, Short MP, et al. Frequent progesterone receptor immunoreactivity in tuberous sclerosis-associated renal angiomyolipomas. *Mod Pathol* 1998;11:665–668. [PubMed: 9688188]
14. 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* 1999;23:1011–1020. [PubMed: 10478660]
15. Logginidou H, Ao X, Russo I, et al. Frequent estrogen and progesterone receptor immunoreactivity in renal angiomyolipomas from women with pulmonary lymphangioleiomyomatosis. *Chest* 2000;117:25–30. [PubMed: 10631194]
16. Cho NH, Shim HS, Choi YD, et al. Estrogen receptor is significantly associated with the epithelioid variants of renal angiomyolipoma: a clinicopathological and immunohistochemical study of 67 cases. *Pathol Int* 2004;54:510–515. [PubMed: 15189505]
17. Fine SW, Reuter VE, Epstein JI, et al. Angiomyolipoma with epithelial cysts (AMLEC): a distinct cystic variant of angiomyolipoma. *Am J Surg Pathol* 2006;30:593–599. [PubMed: 16699313]
18. Enmark E, Peltola M, Grandien K, et al. Human estrogen receptor beta-gene structure, chromosomal localization, and expression pattern. *J Clin Endocrinol Metab* 1997;82:4258–4265. [PubMed: 9398750]

19. Barkhem T, Carlsson B, Nilsson Y, et al. Differential response of estrogen receptor alpha and estrogen receptor beta to partial estrogen agonists/antagonists. *Mol Pharmacol* 1998;54:105–112. [PubMed: 9658195]
20. Nikaido T, Nakano M, Kato M, et al. Characterization of smooth muscle components in renal angiomyolipomas: histological and immunohistochemical comparison with renal capsular leiomyomas. *Pathol Int* 2004;54:1–9. [PubMed: 14674988]
21. Noronha RF, Rao BR. Increased dihydrotestosterone receptor levels in high-stage renal adenocarcinoma. *Cancer* 1985;56:134–137. [PubMed: 4005782]
22. Langner C, Ratschek M, Rehak P, et al. Steroid hormone receptor expression in renal cell carcinoma: an immunohistochemical analysis of 182 tumors. *J Urol* 2004;171:611–614. [PubMed: 14713771]
23. Tickoo SK, Gopalan A, Tu JJ, et al. Estrogen and progesterone-receptor-positive stroma as a non-tumorous proliferation in kidneys: a possible metaplastic response to obstruction. *Mod Pathol* 2008;21:60–65. [PubMed: 17873894] Epub 2007 Sept 14
24. Yu J, Astrinidis A, Howard S, et al. Estradiol and tamoxifen stimulate LAM-associated angiomyolipoma cell growth and activate both genomic and nongenomic signaling pathways. *Am J Physiol Lung Cell Mol Physiol* 2004;286:L694–L700. [PubMed: 12922981]
25. Karas RH, Patterson BL, Mendelsohn ME. Human vascular smooth muscle cells contain function estrogen receptor. *Circulation* 1994;89:1943–1950. [PubMed: 8181116]
26. Watanabe T, Akishita M, Nakaoka T, et al. Estrogen receptor beta mediates the inhibitory effect of estradiol on vascular smooth muscle proliferation. *Cardiovasc Res* 2003;59:734–744. [PubMed: 14499875]
27. Morales DE, McGowan KA, Grant DS, et al. Estrogen promotes angiogenic activity in human umbilical vein endothelial cells in vitro and in a murine model. *Circulation* 1995;91:755–763. [PubMed: 7530174]
28. Bausero P, Ben-Mahdi M, Mazucattelli J, et al. Vascular endothelial growth factor is modulated in vascular muscle cells by estradiol, tamoxifen, and hypoxia. *Am J Physiol Heart Circ Physiol* 2000;279:H2033–H2042. [PubMed: 11045935]
29. Brugarolas JB, Vazquez F, Reddy A, et al. TSC2 regulates VEGF through mTOR-dependent and – independent pathways. *Cancer Cell* 2003;4:147–158. [PubMed: 12957289]
30. El-Hashemite N, Walker V, Kwiatkowski DJ. Estrogen enhances whereas tamoxifen retards development of TSC mouse liver hemangioma: a tumor related to renal angiomyolipoma and pulmonary lymphangioleiomyomatosis. *Cancer Res* 2005;65:2474–2481. [PubMed: 15781664]

Figure 1. Immunohistochemical staining for ER α , ER β , PR, AR, and aromatase in renal AMLs. Representative images of tissue samples showing (A) ER α -positive, (B) ER β -positive, (C) PR-positive, (D) AR-positive, and (E) aromatase-positive lesions. ER α , ER β , PR, and AR expression confined to nuclei of cells; aromatase detected in cytoplasm. Images A-D represent original magnification $\times 400$; image E represents original magnification $\times 200$.

Table**Patient demographics**

Demographic	n (%)
Sex	
Female	90 (81.8)
Male	20 (18.2)
Symptoms at presentation	
Palpable flank/abdominal mass	3 (2.7)
Discomfort ipsilateral/contralateral side	48 (43.6)
Rash, sweats, weight loss, fatigue, early satiety	15 (13.6)
Gross hematuria	8 (7.3)
Any symptoms at presentation	56 (50.9)
Ipsilateral AMLs (n)	
1	97 (88.2)
2	8 (7.3)
3	2 (1.8)
4	2 (1.8)
5	1 (0.9)
Bilateral AMLs	8 (7.3)
Histologic subtype of AML	
Triphasic	77 (70)
Lipomatous	20 (18.2)
Leiomyomatous	7 (6.4)
Epithelioid	4 (3.6)
Atypical	2 (1.8)

AML = angiomyolipoma.