HMB45 Negative Intramuscular Angiomyolipoma: A Case Report and Literature Review

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Intramuscular angiomyolipoma (AML) is a rare, benign hamartomatous lesion, that typically occurs in the kidney. Extrarenal AMLs are extremely rare and have been commonly described in the liver, spleen, and reproductive system. We report a case of AML of the upper arm and a review of the literature on this condition.

The patient was a 34-year-old man who presented with a palpable mass that was in his left upper arm for 4 years. Histopathologic evaluation demonstrated a hamartomatous lesion consisting of a mixture of thin and thick blood vessels, mature adipose tissue, and smooth muscle bundles in the triceps brachii muscle. Immunohistochemically, tumor cells showed negative immunoreactivity for HMB45. These findings were consistent with an extrarenal AML. This was the second reported case of intramuscular AML arising in the extremities. Pathologists should be aware of such an entity whenever they see extrarenal vascular hamartomas not associated with tuberous sclerosis and HMB45 positivity.

Keywords: Angiomyolipoma, Intramuscular tumor, Extrarenal tumor, Immunohistochemistry, HMB45 negative

INTRODUCTION

Angiomyolipoma (AML) is a rare benign tumor with an unclear histogenesis that mainly occurs in the kidney in middle-aged women. Renal AML is strongly associated with tuberous sclerosis (TS), and testing for anti-melanoma antigen (HMB45) positivity is useful for diagnosis[1,2]. However, extrarenal AML occurs in very rare cases, typically in the liver, spleen, and reproductive system[3-6]. There are a total of five cases of AML reported in the English literature. Two of these cases were cutaneous, one occurred in deep soft tissues, one occurred in the intraarticular and soft tissues, and one was intramuscular[7-11]. Extrarenal AML is not accompanied by TS, unlike renal-type AML[8,12]. In renal AML as well as extrarenal AML occurring in the liver, retroperitoneum, and perinephric space, most smooth muscle cells are HMB45-positive[13,14], but they are negative in the cutaneous type[15].

One case of intramuscular AML that occurred in the extremities as in our case has been reported[11], although it did not accompany TS and was HMB45-negative. We investigate here, through a case presentation and literature review, the clinicopathological characteristics of AML arising in the extremities as well as its association with and difference from HMB45-positive AML.

THE CASE

A 34-year-old man visited a hospital with a chief complaint of a mass in his left upper arm. The mass had been found 4 years previously, diagnosed as a hemangioma, and had been monitored by a different university hospital. The mass was nontender and motile. It was located on the medial side of the left upper arm and involved the triceps brachii muscle according to magnetic resonance imaging (MRI). It was 12.8 × 7.7 × 7.3 cm, showing an enlargement since it was found 4 years previously. As a convoluted tubular structure with an intervening fatty component was observed, a vascular malformation such as an arteriovenous malformation or a venous malformation was diagnosed, and mass excision was scheduled (Figure 1). There were no abnormal findings from the patient's previous medical history or preoperative laboratory check.

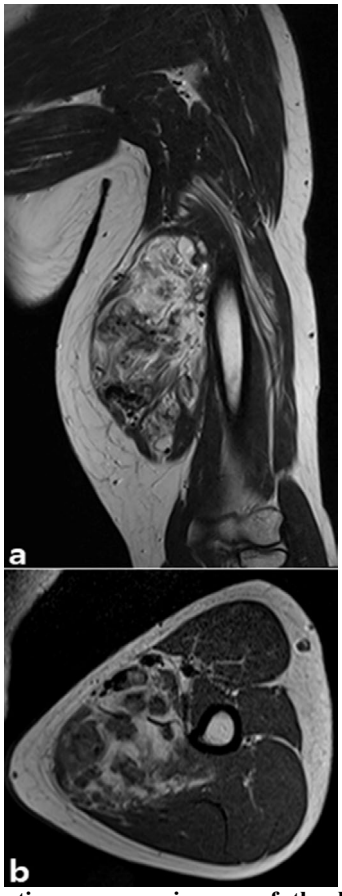

Figure 1. Magnetic resonance images of the left upper arm. Sagittal view (a) and coronal view (b) show a 12.8x7.7 cm mass involving the triceps brachii muscle of the medial side of the upper arm. Convoluted tubular structures suggesting blood vessels with intervening fatty component are identified.

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The mass was partially located in the intramuscular space, and microscopic analysis revealed vascular spaces, smooth muscle bundles, and mature adipose tissues with ill-defined margins with no fibrous capsule. Various kinds of thick- and thin-walled blood vessels with a narrow or dilated lumen were observed. The smooth muscle bundles showed a perivascular or haphazard arrangement, and the adipose tissues consisted of unevenly scattered small groups of variably sized adipocytes. There were no intravascular thrombi, cytologic atypia, or mitotic activity. There was no area of necrosis (Figure 2).

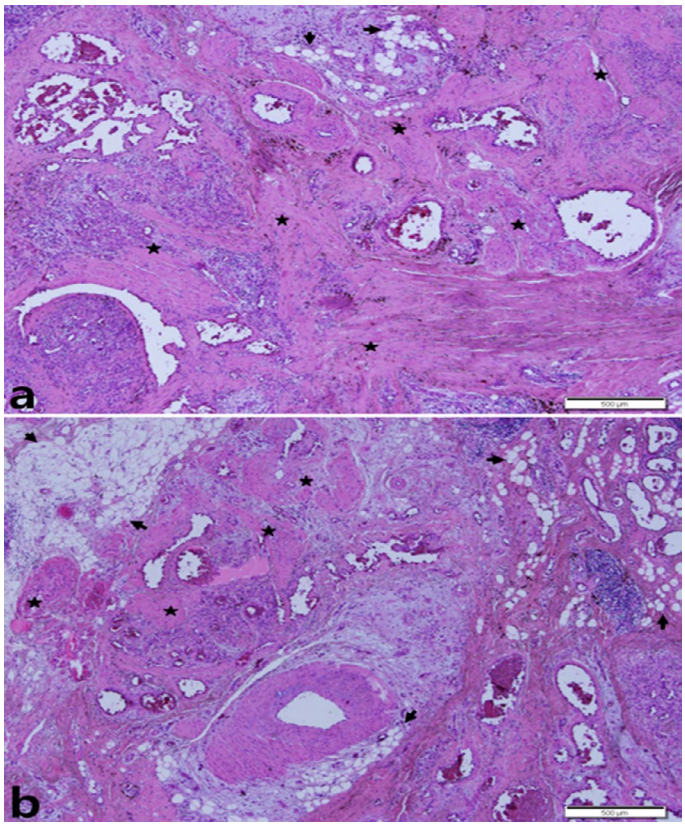

Figure 2. Histopathologic findings of the excised mass. The lesion consisted of variable vascular spaces, perivascular or haphazardly arranged smooth muscle bundles (asterisks) and scattered small groups of mature adipocytes (arrows). Hematoxylin and eosin staining.

The smooth muscle cells were positive for α-smooth muscle actin and desmin and negative for HMB45 (Figure 3).

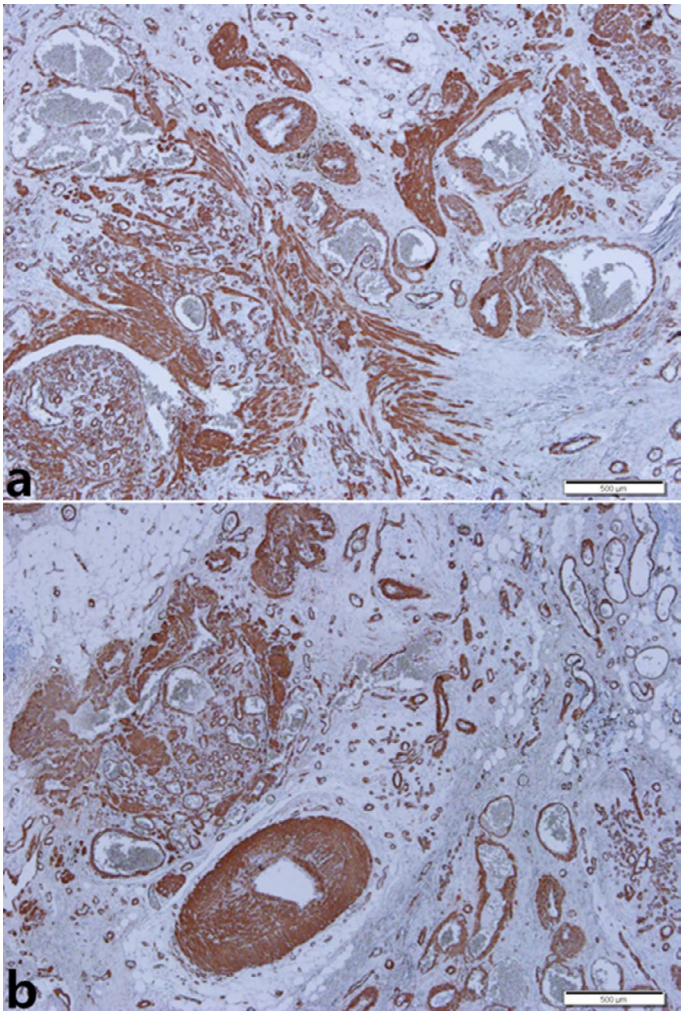

Figure 3. Immunohistochemical findings of the corresponding areas in Figure 2 for α- smooth muscle actin. Smooth muscle bundles (arrows) and thick- or thin-walled blood vessels with a narrow or dilated lumen (asterisks) show strong positive immunoreactivity.

Table 1. Summary of Angiomyolipoma of the Extremities in the Literature

No	Author (Year) [Ref]	Age (years)	Sex	Location	Site	Size (cm)	Tuberous sclerosis	HMB-45	Pain	Duration (years)	Follow-up (months)	Remarks
1	Rodriguez-Fernandez & Caro-Mancilla (1993) [7]	58	M	elbow	cutaneous	4x3	no	NA	no	15	NED (15)	
2	Mahera et al. (1997) [9]	79	F	ankle	deep soft tissue	21x10x5 (initial) 18x14x4 (recur)	no	negative	no	8		recurred after 8 yrs.
3	Kuroda et al. (2000) [11]	41	M	upper thigh	intramuscular	10	no	negative	no	2	NA	
4	Debloom et al. (2006) [8]	50	F	upper thigh	cutaneous	3x2.8x2	no	negative	no	NA	NA	
5	Varshney et al. (2011) [10]	12	F	knee foot	intra-articular soft tissue	15x12 9x4	no	negative	yes	2	NA	multicentric
6	Present case (2020)	34	M	upper arm	intramuscular	12.8x7.7x7.3	no	negative	no	4	NED (14)	

Ref reference in the text, NA not available, NED no evidence of disease

Based on the clinicopathologic findings, we concluded that this tumor represented an intramuscular AML arising in the upper arm. On follow-up 14 months later, at the time of submission of this manuscript, the patient is well with no evidence of disease.

DISCUSSION

Approximately 40% of AMLs show the stigmata of TS[16], but extrarenal AML is not accompanied by TS[8,12]. Although renal AML shows a female preponderance, cutaneous AML shows a male preponderance[8]. However, despite being an extrarenal type, AML that occurs in the liver, retroperitoneum, and perinephric area shows a female preponderance[8,13,14].

In the extremity-invading AMLs, including our case and the ones reported in the English literature, the male-to-female ratio of prevalence was 3:3 showing no sexual difference. The age distribution was wide, ranging from 12 to 79 years (average age 45.7 years), and although most cases were asymptomatic, some had accompanying pain. As most cases involved a long disease history, surgery was performed after an average of 6.2 years of disease progression. The size varied from 3 to 21 cm but was typically large (11 cm on average). Although there was one case with recurrence, the prognosis was generally good, and there was no case with accompanying TS or HMB45 positivity[7-11] (Table 1).

Renal AML and extrarenal AML arising in the liver, retroperitoneum, and perinephric area are HMB45-positive, whereas the cutaneous and intramuscular types were HMB45-negative[13-16].

Furthermore, although AML occurring in the kidney and liver was strongly associated with TS, other extrarenal AMLs did not show an association with TS[13-16].

Taken altogether, AML arising in the kidney, liver, retroperitoneum, and perinephric area is likely to be a different type of tumor from extrarenal AML arising in other areas based on the significant differences in the association with TS, HMB45 immunoreactivity, and sexual preponderance[15,17,18]. This led to a suggestion of using the term ‘angiolipoleiomyoma’ for HMB45-negative cutaneous AML to avoid terminological confusion and distinguish it from HMB45-positive renal type AML[17,18]. Enzinger and Weiss described that the term ‘angiomyolipoma’ should be reserved for a specific lesion arising most commonly in one or both kidneys as a solitary or multicentric mass[19].

Hence, considering that intramuscular AML occurring in the extremities is HMB45-negative without an association with TS, in addition to cutaneous AML, it could also be considered to belong to the group proposed as ‘angiolipoleiomyoma’.

CONCLUSION

The intramuscular AML in the upper arm reported in this study is the sixth AML arising in the extremities and the second intramuscular type of AML reported in the English literature. It is speculated to be a different type of tumor from renal-type AML due to its lack of association with TS and HMB45 negativity.

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