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CASE REPORT

Presentation of 2 New Cases of Cutaneous Angiomyolipomas and Literature Review

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Abstract. We present 2 new cases of cutaneous angiomyolipomas with very similar characteristics, located in the postauricular region of 2 women aged 58 and 52 years. The lesions measured 1.5 cm and 1 cm across and had been present for 5 and 2 years, respectively. Both presented a previously unreported clinical sign: change in size according to the ambient temperature. They had well defined borders and a predominance of smooth muscle and vessels, particularly arteries. In contrast to renal angiomyolipomas, which are often associated with tuberous sclerosis, these angiomyolipomas were negative for melanocytic immunohistochemical markers (human melanoma black-45 antigen and melanoma antigen recognized by T cells 1). The clinical characteristics of the 32 cases published until present are reviewed. The relationship of these tumors with angioleiomyomas and renal angiomyolipomas is discussed.

Key words: cutaneous angiomyolipoma, angiolipoleiomyoma, mucocutaneous angiomyolipoma.

ANGIOMIOLIPOMAS CUTÁNEOS: APORTACIÓN DE DOS CASOS Y REVISIÓN DE LA LITERATURA

Resumen. Presentamos dos nuevos casos de angiomiolipomas cutáneos de características muy similares. Se localizaban en región retroauricular de dos mujeres de 58 y 52 años. Tenían un tamaño de 1,5 y 1 cm de diámetro y una evolución de 5 y 2 años, respectivamente. Ambos presentaban un signo clínico no previamente descrito: cambio de tamaño según la temperatura ambiente. Estaban bien delimitados, el elemento predominante era el músculo liso y los vasos, sobre todo arteriales. A diferencia de lo que sucede con los angiomiolipomas renales frecuentemente asociados a esclerosis tuberosa, fueron negativos para los marcadores inmunohistoquímicos melanocitarios (HMB-45 y MART-1). Se revisan las características clínicas de los 32 casos publicados hasta la actualidad. Se discute la relación de estos tumores con los angioleiomiomas y los angiomiolipomas renales.

Palabras clave: angiomiolipoma cutáneo, angiolipoleiomioma, angiomiolipoma mucocutáneo.

Introduction

Angiomyolipomas are tumors composed of mature fat tissue, bundles of smooth muscle fibers, and blood vessels in varying proportions.

Renal angiomyolipomas are much more common, however, and can be solitary or multiple, become large enough to cause complications, and are associated with tuberous sclerosis (TS) in 20% to 40% of cases. Dermatologists are familiar with the renal variant of these tumors because patients with TS must be carefully monitored for this kind of tumor.

Cutaneous angiomyolipomas are much rarer and have been called angiolipoleiomyomas by some authors.[1,2] The lesions are small, solitary, and not associated with TS. Although conventional microscopy may not be able to distinguish these lesions from renal angiomyolipomas, immunophenotyping shows that they are different tumors with a distinct histogenesis.

Angiomyolipomas have been described in many other sites, particularly the liver. They are identical to renal angiomyolipomas and may be associated with them and appear in the context of TS. Those located in the mucosas (oral, nasal, vaginal, etc) are also of note and resemble cutaneous angiomyolipomas.

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We present 2 new cases of cutaneous angiomyolipomas and review the characteristics of 32 cases published to date.[1-19]

Case Descriptions

Two women (58 and 52 years of age, for case 1 and 2, respectively) had nodular, compressible, slow-growing, asymptomatic tumors located in the left retroauricular area, of similar characteristics (Figures 1 and 2). The respective course was 5 and 2 years and the diameter was 1.5 and 1 cm.

Both patients reported a change in lesion size with ambient temperature, as the tumor was considerably more visible in warm environments and virtually undetectable in extreme cold.

Neither patient had signs of TS.

In the first patient, the clinical diagnosis was an angioma of unspecified type and in the second, angiomyolipoma, given the similarity with the previous case.

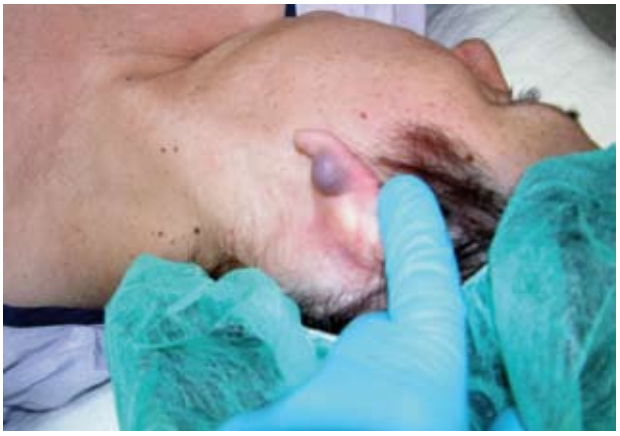

Figure 1. Patient 1. Violaceous nodule with a diameter of 1.5 cm in a 58-year-old woman.

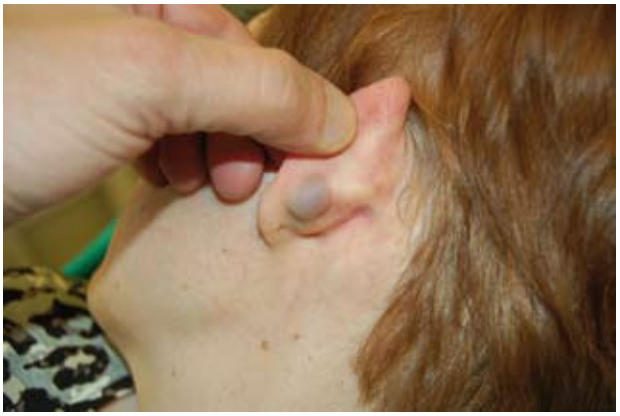

Figure 2. Patient 2. 1-cm tumor in a 52-year-old woman.

Both patients underwent simple resection with local anesthesia; the tumor did not recur during follow-up (26 months and 5 months, respectively).

Histology showed well-circumscribed tumors in a fibrous pseudocapsule and located at the dermal-epidermal junction (Figure 3). The tumors were composed largely of smooth muscle tissue arranged in layers of interconnected bundles and contained aggregates of variable size, consisting of mature adipose tissue (more scant in the second case) and abundant blood vessels of medium size and thick tunica muscularis (Figure 4). Muscle fibers surrounding the blood vessels or extending tangentially from the muscle wall, with no interruption, were often observed.

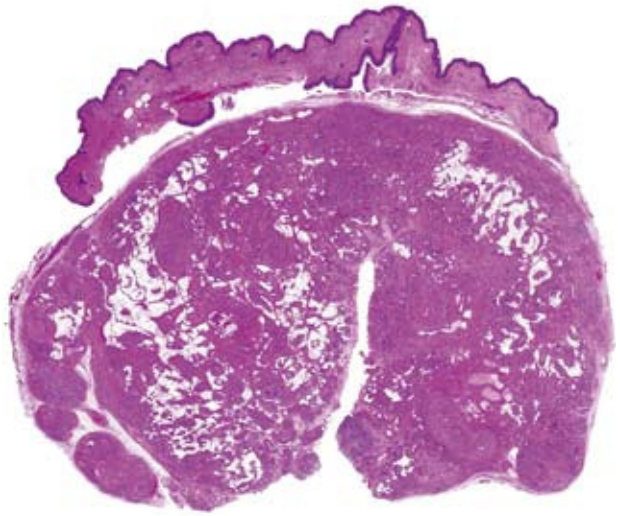

Figure 3. Patient 1. Well-demarcated tumor at the dermal-epidermal junction, composed of smooth muscle, fat, and abundant blood vessels (hematoxylin-eosin, ×20).

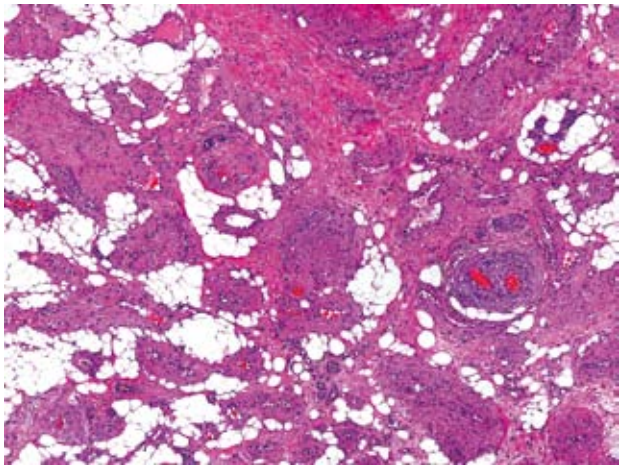

Figure 4. Patient 1. Detailed view of the 3 components of the tumor: fat, smooth muscle, and blood vessels (hematoxylin-eosin, ×200).

Table. Clinical Characteristics of Cutaneous Angiomyolipomas

No.	*Author*	*Year*	*Age*	*Sex*	*Site*	*Size, cm*	*Course*	*Clinical Diagnosis*
1	Fitzpatrick et al[1]	1990	77	M	*	UNK	UNK	Lipoma, cyst
2			63	M	Toe	UNK	6 months	GCTTS, mucoid cyst
3			50	M	*	UNK	UNK	Unspecified tumor
4			59	F	*	UNK	UNK	Nodule
5			52	M	*	UNK	1 year	Lipoma
6			33	M	*	UNK	3 years	Epidermal cyst
7			48	M	*	UNK	2 months	Lipoma
8			39	M	*	UNK	UNK	Subcutaneous nodule
9	Argenyi et al[3]	1991	67	M	Ear	1	40	Epidermal cyst
10	Mehregan et al[4]	1992	49	M	Ear	UNK	UNK	Epidermal cyst
11	Rodríguez-Fernández et al[5]	1993	58	M	Elbow	3×4	15 years	UNK
12	Tamura et al[6]	1994	49	M	Subgaleal, frontal bone	UNK	3 years	Lipoma
13	Ortiz-Rey et al[7]	1996	63	M	Preauricular	1.5	UNK	Angioma
14	Val-Bernal et al[8]	1996	49	M	Ear	2 5 years	Vascular tumor	Tumor vascular
15	Castro-Forns et al[9]	1998	47	M	Nose	1×0.7×0.6	6 months	UNK
16			65	F	Lumbar	5	UNK	UNK
17	Büyükbabani et al[10]	1998	38	M	Ear	2.5	10 years	UNK
18		1998	36	M	Nose	1.5	3 years	UNK
19	Obata et al[11]	2001	54	F	Nose	UNK	5 years	Hemangioma or lipoma
20	Lin et al[12]	2003	65	F	Preauricular	2	10 years	UNK
21	De la Torre et al[13]	2004	35	F	Palm	1.5	10 years	UNK
22	Tsuruta et al[14]	2004	75	M	Nose	UNK	10 years	Lipoma
23	Del Sordo et al[15]	2005	58	M	Ear	2	3 years	Vascular tumor
24	Beer[16]	2005	43	M	Ear	0.4	6 months	UNK
25		2005	56	M	Chin	0.6	Several years	UNK
26		2005	44	F	Ear	0.5	3 months	Cyst
27	Hatori et al[17]	2005	38	F	Popliteal	4×4×3	5 years	Sarcoma
28	Makino et al[2]	2006	16	F	Buttock	2.5×1.5	UNK	Vascular tumor
29	Debloom et al[18]	2006	50	F	Muscle	3	5 years	Cyst, lipoma, angiolipoma
30	Squillaci et al[19]	2008	62	M	Calf	2.2	12 years	Lipoma
31	Sánchez-Estella et al	2009	58	F	Ear	1.5	5 years	Angioma
32		2009	52	F	Ear	1	2 years	Angiomyolipoma

*The site is described, but not separately according to case: 2 ears, 1 nose, 2 elbows, 2 fingers. Abbreviations: F, female; GCTTS, giant cell tumors of the tendon sheath; M, male; UNK, unknown.

The immunohistochemical study was identical in both tumors. All areas were positive for vimentin, whereas myosin, actin, and desmin stained the muscle component and the vessel wall. CD31 and CD34 staining was positive in endothelial cells and D2-40 staining revealed small lymphatic lumens. Staining for human melanoma black (HMB) 45 and melanoma antigen recognized by T-cells (MART) 1 was negative; S-100 was negative, except in some fat cells.

Discussion

The Table summarizes the clinical characteristics of the 32 cases of cutaneous angiomyolipoma published in the literature. All were solitary and none were associated with TS.

The tumor predominated in men (21 men, 11 women) of middle age (mean, 51.5 years; range, 16-77 years) and was usually located on the head (20/32), and there was a marked preference for acral areas (ears, nose, elbows, fingers, toes).

Most presented as nodules that grew slowly over many years, caused few symptoms, and measured 0.5 to 4 cm. In our patients, we observed a symptom not previously reported: a noticeable change in size with ambient temperature changes that we attributed to a reaction of the abundant muscle vessels seen on histology. Most were clinically interpreted as lipomas, epidermal cysts, or angiomas.

The nodules were reported as readily resectable, and recurrence was observed in only 1 patient,[10] attributed by the authors to incomplete resection.

Histologically, the tumors were found at the dermal-epidermal junction or in subcutaneous tissue, and were well demarcated by a fibrous pseudocapsule. Only 1 patient had a tumor considered by the authors to be poorly defined, due to her young age.[2]

The lesions were composed of a variable proportion of smooth muscle, fat, and blood vessels. The muscle component was usually predominant and formed layers of interlinked bundles of well-differentiated smooth muscle cells that did not show any atypia or mitoses. The pronounced pleomorphism seen in the case described by Rodríguez-Fernández et al[5] was interpreted as degenerative. The muscle component was often seen as a continuation of the blood vessel walls.

The fat component tended to be less abundant and was predominant in only a third of the largest published series.[1] This component consisted of clusters of varying size in the muscle bundles or vessel wall.

The abundant vessels, of medium to large diameter, usually show arterial characteristics, but may occasionally appear to be ectatic and exhibit venous features.

The relationship between cutaneous angiomyolipomas and angioleiomyomas has been debated, and some authors have considered the former to be angioleiomyomas with a fat component,[11,15] given that small foci of fat are seen in up to 2.8% of angioleiomyomas.[1,10,19] However, both the vastly different clinical features and histologic architecture suggest different entities.

Compared to renal angiomyolipomas, cutaneous angiomyolipomas are clearly different tumors with distinct clinical symptoms, histology, and immunophenotyping. When the muscle component of renal type is investigated with the usual techniques, it rarely forms bundles and the cells are less differentiated; pleomorphism and mitoses are common. Foci of epithelioid cells may be observed and can even be the predominant cell type. However, what clearly distinguishes the renal type is that all cell lines stain positive for melanocytic antigen markers (HMB-45 and MART-1) and often express estrogen and progesterone receptors. At present, renal angiomyolipomas are usually included in the group of the perivascular epithelioid cell tumors (often known as PEComas).

The cutaneous angiomyolipomas we reviewed appear to be a separate anatomic and clinical entity. To draw attention to the condition, some dermatologists have proposed the term *angiolipoleiomyomas*.[1,2] Other specialists have described cases similar to cutaneous cases in mucosa and have proposed the term *angiomyolipoma*.[20] Because other sites are possible, nonrenal angiomyolipomas might be a more appropriate term, as it refers to immunophenotyping rather than site. The term *renal angiomyolipoma* would cover tumors found in the kidney, liver, or, rarely, other organs with identical immunophenotypic characteristics.

A cutaneous renal-type angiomyolipoma was recently reported, but we excluded it from our review because we considered it to be a different entity.[21]

The histogenesis of the tumors is uncertain. In contrast, the neoplastic nature of the renal angiomyolipomas is apparently proven, because although all cell lines are of different grades of transformation, they have the same immunophenotype and in some cases clonality has been demonstrated. The defective genes that produce tuberous sclerosis (TSC1 on chromosome 9q34 and TSC2 on chromosome 16p13.3) are known to be involved in tumor suppression. A defect causes loss of expression of hamartin and tuberin, potent inhibitors of the mTOR cascade, and stimulates the proliferation of tumors, such as renal angiomyolipomas. Cutaneous angiomyolipomas, and nonrenal angiomyolipomas in general, are probably hamartomatous in nature.

We conclude that cutaneous angiomyolipomas can be managed by resection alone, and there is no need to rule out the presence of associated tuberous sclerosis.

Conflicts of Interest

The authors declare no conflicts of interest.

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