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). 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.

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. 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.
We present 2 new cases of cutaneous angiomyolipomas and review the characteristics of 32 cases published to date.\textsuperscript{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.

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 1](image1.png)

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

![Figure 2](image2.png)

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

![Figure 3](image3.png)

**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](image4.png)

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

Table. Clinical Characteristics of Cutaneous Angiomyolipomas

<table>
<thead>
<tr>
<th>No.</th>
<th>Author</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Site</th>
<th>Size, cm</th>
<th>Course</th>
<th>Clinical Diagnosis</th>
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<tbody>
<tr>
<td>1</td>
<td>Fitzpatrick et al</td>
<td>1990</td>
<td>77</td>
<td>M</td>
<td>*</td>
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<tr>
<td>2</td>
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<td>M</td>
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<td>M</td>
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<td>Lipoma</td>
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<td>4</td>
<td></td>
<td>1996</td>
<td>39</td>
<td>M</td>
<td>*</td>
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<td>2 months</td>
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<td>67</td>
<td>M</td>
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<td>40</td>
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<td>M</td>
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<td>UNK</td>
<td>UNK</td>
<td>Epidermal cyst</td>
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<td>7</td>
<td>Rodríguez-Fernández et al</td>
<td>1993</td>
<td>58</td>
<td>M</td>
<td>Elbow</td>
<td>3×4</td>
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<td>M</td>
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<td>Val-Bernal et al</td>
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<td>49</td>
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<td>11</td>
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<td>47</td>
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<td>Nose</td>
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<td>Nose</td>
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<td>F</td>
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<td>UNK</td>
<td>10 years</td>
<td>Lipoma</td>
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<td>2005</td>
<td>58</td>
<td>M</td>
<td>Ear</td>
<td>2</td>
<td>3 years</td>
<td>Vascular tumor</td>
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<tr>
<td>18</td>
<td>Beer et al</td>
<td>2005</td>
<td>43</td>
<td>M</td>
<td>Ear</td>
<td>0.4</td>
<td>6 months</td>
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<tr>
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<td>2005</td>
<td>56</td>
<td>M</td>
<td>Chin</td>
<td>0.6</td>
<td>Several years</td>
<td>UNK</td>
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<tr>
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<td>2005</td>
<td>44</td>
<td>F</td>
<td>Ear</td>
<td>0.5</td>
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<tr>
<td>21</td>
<td>Makino et al</td>
<td>2006</td>
<td>16</td>
<td>F</td>
<td>Buttock</td>
<td>2.5×1.5</td>
<td>UNK</td>
<td>Vascular tumor</td>
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<tr>
<td>22</td>
<td>Debloom et al</td>
<td>2006</td>
<td>50</td>
<td>F</td>
<td>Muscle</td>
<td>3</td>
<td>5 years</td>
<td>Cyst, lipoma, angiolipoma</td>
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<td>23</td>
<td>Squillacci et al</td>
<td>2008</td>
<td>62</td>
<td>M</td>
<td>Calf</td>
<td>2.2</td>
<td>12 years</td>
<td>Lipoma</td>
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<tr>
<td>24</td>
<td>Sánchez-Estella et al</td>
<td>2009</td>
<td>58</td>
<td>F</td>
<td>Ear</td>
<td>1.5</td>
<td>5 years</td>
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<tr>
<td>25</td>
<td>Sánchez-Estella et al</td>
<td>2009</td>
<td>58</td>
<td>F</td>
<td>Ear</td>
<td>1</td>
<td>2 years</td>
<td>Angiomyolipoma</td>
</tr>
</tbody>
</table>

*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.
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, 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.

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 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. 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, given that small foci of fat are seen in up to 2.8% of angioleiomyomas. 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 angiolicioleioymoma. Other specialists have described cases similar to cutaneous cases in mucosa and have proposed the term angiomyolipoma. 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.

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.

References


