

# Cutaneous Angiosarcoma of the Lower Leg

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## PRACTICE POINTS

- Cutaneous angiosarcoma is a rare malignant vascular neoplasm typically seen in 3 settings: (1) idiopathic (commonly on the face and neck), (2) following radiation treatment, and (3) classically in the setting of chronic lymphedema following mastectomy (Stewart-Treves syndrome).
- There should be a low threshold for biopsy in patients who present with nonhealing wounds that do not progress in the normal phase of wound healing with suspicion for malignancy.
- Histologic analysis of angiosarcoma shows positive staining for CD34 and vimentin with poorly differentiated endothelial atypia with mitotic figures.

Angiosarcoma is a vascular malignancy that can affect various anatomic sites. Although rare, cutaneous angiosarcoma is the most common clinical manifestation, accounting for approximately 50% to 60% of cases. Cutaneous angiosarcoma typically is known to occur in 3 settings: (1) idiopathic, (2) following radiation treatment, and (3) in the setting of chronic lymphedema following mastectomy (known as Stewart-Treves syndrome). The clinical manifestation of angiosarcoma can mimic other processes. We present a case of cutaneous angiosarcoma on the leg in an elderly woman in the setting of a chronic nonhealing wound and lymphedema. We also discuss the differential diagnosis and treatment options.

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**A**ngiosarcoma is a rare and aggressive vascular malignant neoplasm derived from endothelial cells. In general, sarcomas account for approximately 1% of all malignancies, with approximately 2%

being angiosarcomas.<sup>1</sup> The risk of recurrence at 5 years is estimated to be 84%, and 5-year survival is estimated at 15% to 30%. Poor prognostic factors for angiosarcoma include large tumor size, depth of invasion greater than 3 mm, high mitotic rate, positive surgical margins, and metastasis.<sup>2</sup> Approximately 20% to 40% of patients who are diagnosed with angiosarcoma already have distant metastasis, contributing to the aggressive nature of this neoplasm.<sup>3</sup>

Angiosarcoma can affect various anatomic locations, including the skin, soft tissue, breasts, and liver. Cutaneous angiosarcoma is the most common clinical manifestation, accounting for approximately 50% to 60% of all cases, and typically is known to occur in 3 distinct settings.<sup>2</sup> Primary or idiopathic cutaneous angiosarcoma is most commonly seen in elderly individuals, with a peak incidence in the seventh to eighth decades of life, and presents as a bruise-like lesion predominantly on the head and neck. Angiosarcoma also is seen clinically in patients exposed to radiation treatment, with a median onset of symptoms occurring 5 to 10 years posttreatment, and in patients with chronic lymphedema, usually on the arm following radical mastectomy, which also is known as Stewart-Treves syndrome.<sup>2</sup>

With any sarcoma, treatment typically first involves surgical excision; however, there is no direct approach for treatment of cutaneous angiosarcoma, as an individual plan typically is needed for each patient. Treatment options include surgical excision, radiation, chemotherapy, or a combination of these therapies.<sup>2,4</sup>

We present a rare case of cutaneous angiosarcoma of the left leg in the setting of chronic venous insufficiency with some degree of lymphedema and a nonhealing ulcer. This case is unique in that it does not fit the classic presentation of cutaneous angiosarcoma previously described.

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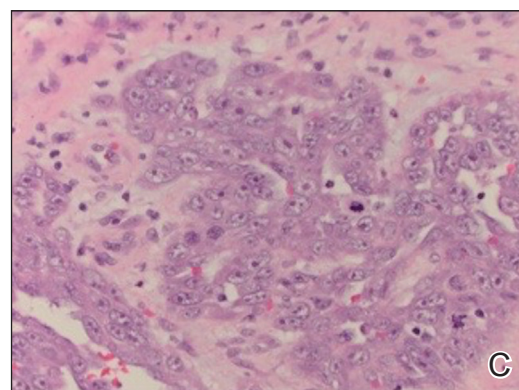
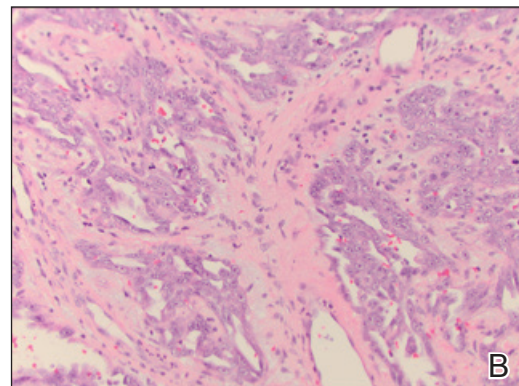
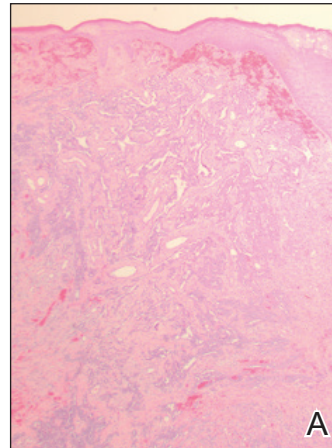
### Case Report

An 83-year-old woman with a medical history of advanced dementia, congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, type 2 diabetes mellitus, hypertension, and chronic venous insufficiency with stasis dermatitis presented to the emergency department following a mechanical fall. Most of her medical history was obtained from the patient's family. She had a history of multiple falls originally thought to be related to a chronic leg ulcer that had been managed with wound care. Recently, however, the lesion was noted to have increasing erythema surrounding the wound margins. An 8×8-cm erythematous plaque on the anterior lateral left leg with a firm central nodule with hemorrhagic crust that measured approximately 4 cm in diameter was noted by the emergency department physicians (Figure 1). In the emergency department, vitals and other laboratory values were within reference range, and a radiograph of the left tibia/fibula was unremarkable. Cellulitis initially was considered in the emergency department and cephalexin was started; however, since the patient was afebrile and had no leukocytosis, plastic surgery also was consulted. Biopsies were obtained from the superior and inferior parts of the lesion. Histologic analysis revealed a poorly differentiated vascular neoplasm of epithelioid endothelial cells with considerable cell atypia that extended through the entirety of the dermis (Figure 2). The tumor cells stained positive with vimentin and CD34. Pathology noted no immunohistochemistry stains to synaptophysin, S-100, human melanoma black 45, MART-1, CK20, CK7, CK8/18, CK5/6, and p63. The pathologic diagnosis was consistent with cutaneous angiosarcoma. Computed tomography of the chest, abdomen, and pelvis revealed no local or distant metastases.



**FIGURE 1.** Cutaneous angiosarcoma presenting as a large erythematous plaque on the anterior lateral left lower leg with a firm central nodule with overlying hemorrhagic crust.

A wide excision of the cutaneous angiosarcoma was performed. The initial frozen section analysis revealed positive margins. Three additional excisions still showed positive margins, and further excision was held after obtaining family consent due to the extensive nature of the neoplasm and lengthy operating room time. The final defect after excision measured 15×10×2.5 cm (Figure 3A), and subsequent application of a split-thickness graft was performed. Additional treatment



**FIGURE 2.** Histologic analysis revealed a poorly differentiated vascular neoplasm extending through the dermis (A) with epithelioid endothelial cells (B)(H&E, original magnifications ×40 and ×100). Considerable cell atypia and mitotic figures were appreciated on higher power (C) (H&E, original magnification ×400).

options were discussed with the family, including radiation therapy, amputation of the left lower leg, or no treatment. The family opted not to proceed with further treatment. The graft healed without signs of reoccurrence approximately 3 months later (Figure 3B), and the patient received physical therapy, which allowed her to gain strength and some independence.

### Comment

**Clinical Manifestation**—Cutaneous angiosarcoma is a rare malignant vascular neoplasm that when clinically diagnosed is typically seen in 3 settings: (1) idiopathic (commonly on the face and neck), (2) following radiation treatment, and (3) classically following mastectomy with subsequent chronic lymphedema. Our patient did not classically fit these settings of cutaneous angiosarcoma due to the location of the lesion on the lower leg as well as its occurrence in the setting of a chronic nonhealing ulcer and lymphedema.

Chronic lymphedema is a common clinical manifestation that is likely secondary to other medical conditions, such as in our patient. As a result, these patients are at increased risk for developing chronic ulcers due to poor wound healing; however, as seen in our patient, chronic nonhealing ulcers require a broad differential because they may clinically mimic many processes. Patient history and visual presentation were crucial in this case because a biopsy was obtained that ultimately led to the patient's diagnosis.

**Differential Diagnosis**—Initially, a venous ulcer secondary to chronic venous insufficiency was considered in the differential for our patient. She had a history of congestive heart failure, kidney disease, and type 2 diabetes mellitus, all of which contribute to lymphedema and/or poor wound healing. However, venous ulcers usually are

located on the medial ankles and are irregularly shaped with an erythematous border and fibrinous exudate with central depression, making it a less likely diagnosis in our patient. Additionally, an infectious process was considered, but the patient was afebrile and laboratory values demonstrated no leukocytosis.

Marjolin ulcer was highly suspected because the clinical presentation revealed a nodule with hemorrhagic crust and induration in the setting of a chronic nonhealing ulcer. The pathogenesis of malignancy in chronic ulcers is thought to be due to continuous mitotic activity from regeneration and repair of the wound, especially in the setting of repeated trauma to the area.<sup>5</sup> In our patient, the history of multiple falls with possible multitrauma injury to the chronic ulcer further increased suspicion of malignancy. The most common and frequently seen malignancy that develops in chronic ulcers is squamous cell carcinoma (SCC) followed by basal cell carcinoma. Plastic surgery suspected an SCC for the working diagnosis, which prompted a punch biopsy; however, the histologic analysis was not consistent with SCC or basal cell carcinoma. Marjolin ulcer also may demonstrate a periosteal reaction,<sup>5</sup> which was not the case with our patient after a radiograph of the left tibia/fibula was unremarkable.

Another potential malignancy to consider is melanoma. There are few case reports of biopsy-proven melanoma from an enlarging chronic ulcer.<sup>6,7</sup> Additionally, poorly differentiated angiosarcoma can mimic melanoma<sup>2</sup>; however, immunohistochemistry stain was negative for S-100, human melanoma black 45, and MART-1, making melanoma unlikely.

Kaposi sarcoma (KS) and angiosarcoma are both malignant vascular tumors that similarly present with



**FIGURE 3.** Wide surgical excision of the cutaneous angiosarcoma yielded a final defect measuring  $15 \times 10 \times 2.5$  cm (A). Approximately 3 months following excision and subsequent split-thickness skin graft, the patient was healing well with no evidence of reoccurrence (B).



red to purple patches, plaques, or nodules, making it difficult to distinguish between the two conditions. It is important to note that KS usually is lower grade, and the pathogenesis is linked to human herpesvirus 8, which can be identified on immunohistochemistry staining. There have been cases of KS reported in patients who have no history of human immunodeficiency virus/AIDS, thus the classic subtype of KS may have been considered in this patient.<sup>8</sup> The histologic appearance of KS may vary from dilated irregular endothelial cells lining the vascular space to mild endothelial cell atypia. Histology also shows hemosiderin-laden macrophages, extravasated red blood cells, and an inflammatory infiltrate. An additional malignant vascular neoplasm that needs to be differentiated is epithelioid hemangioendothelioma. Cutaneous presentation of an epithelioid hemangioendothelioma may be similar to what was seen in our patient but histologically will usually show neoplastic cells with pale eosinophilic cytoplasm and vesicular nuclei of plump, oval, polygonal cells in cords or aggregates surrounding vascular channels. These neoplasms also tend to occur around medium- to large-sized veins.<sup>1,9</sup> With our patient, even though human herpesvirus 8 was not tested with immunohistochemistry, gold standard immunohistochemistry confirmation with CD34 and vimentin staining combined with poorly differentiated endothelial atypia with mitotic figures on histologic analysis favored angiosarcoma versus KS or epithelioid hemangioendothelioma.<sup>10,11</sup>

**Management**—Cutaneous angiosarcoma is a rare and aggressive vascular neoplasm accounting for approximately 2% of all combined sarcomas, with an estimated 20% to 40% having distant metastasis at diagnosis.<sup>1,3</sup> For this reason, computed tomography was performed in our patient and revealed no local or distant metastasis. Therefore, chemotherapy was not an appropriate adjunct treatment option.<sup>12</sup> With no evidence of metastasis, initial treatment began with surgical removal but proved to be difficult in our patient. Although the implications of positive surgical margins remain unclear with regard to overall patient survival, surgical resection followed by radiation therapy has been shown to be optimal, as it reduces the risk of local recurrence.<sup>3</sup> There have been reported cases of cutaneous angiosarcoma of the leg that were treated with amputation without signs of recurrence or metastasis.<sup>10,13,14</sup> Given the results from these cases and considering that our patient had no metastasis, amputation seemed to be a good prognostic option;

however, considering other factors regarding the patient's comorbidities and quality of life, her family decided not to pursue any further treatment with amputation or radiation therapy.

## Conclusion

There should be low threshold for biopsy in patients who present with nonhealing wounds that do not progress in the normal phase of wound healing with suspicion for malignancy. As seen with our patient, cutaneous angiosarcoma can clinically mimic many disease processes, and although rare in nature, it should always be considered when a patient presents with a rapidly growing lesion in the setting of chronic lymphedema or venous ulcer.

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