

# An unusual presentation of Stewart-Treves syndrome on the lower extremity



Kristen Whitney, DO,<sup>a</sup> Brian Schapiro, MD,<sup>b</sup> and Ann Ammond LaFond, MD<sup>a</sup>  
*Ann Arbor, Michigan*

**Key words:** chronic lymphedema; cutaneous angiosarcoma; lymphangiosarcoma; mastectomy; peripheral edema; Stewart-Treves syndrome.

## INTRODUCTION

Cutaneous angiosarcoma is a rare and aggressive malignant tumor derived from endothelial cells, which can develop *de novo*, in irradiated skin, or in areas of chronic lymphedema. Stewart-Treves syndrome describes the association of cutaneous angiosarcoma arising in the setting of lymphedema. This syndrome was first reported in 1948 by Drs Fred Stewart and Norman Treves, who noted 6 cases of lymphangiosarcoma that developed several years after a Halstead radical mastectomy.<sup>1</sup>

Currently there are few reports in the literature of Stewart-Treves syndrome occurring after primary or secondary causes of chronic lymphedema not attributable to malignancy.<sup>2</sup> Our case is an extremely rare subtype of angiosarcoma arising in a lymphedematous lower limb with no prior malignancy or radiation history.

## CASE REPORT

A 94-year-old African-American woman was admitted for cellulitis of the right lower extremity and a 3-month history of painful and bleeding cutaneous lesions in the same area. The lesions developed rapidly and spread proximally. There was no history of trauma, malignancy, pelvic surgery, long-standing infection, or thrombosis of the lower extremities. The patient's chronic bilateral lower extremity lymphedema appeared at age 34, shortly after the birth of her son, but she denied any significant birth trauma. She also denied a family history of lymphedema. Significant medical history included diabetes mellitus, chronic kidney disease, and chronic venous stasis with ulcerations.

Physical examination found an ulcerated plaque with jagged borders, studded with multiple firm black nodules above the right medial malleolus. Smaller skin-colored to black nodules and a few bullae were dispersed around the lesion and extended up the proximal right lower leg (Fig 1). Diffuse nonpitting edema and hyperpigmented macules and patches were present on the bilateral lower extremities. No popliteal or inguinal lymphadenopathies were noted. Our differential diagnosis included acroangioidermatitis, Kaposi's sarcoma, squamous cell carcinoma, melanoma, and angiosarcoma.

Two punch biopsies were performed at the edge of the tumor, which found an inflamed scale/crust with underlying epidermal hyperplasia and prominent ectasia of the superficial vasculature. In the mid to deep reticular dermis there were poorly formed vessels lined by pleomorphic and hyperchromatic endothelial cells (Figs 2 and 3). Occasional mitotic figures were noted and the vessels dissected between the dermal collagen bundles. The atypical endothelial cells were positive for CD31 and negative with pan cytokeratin stains. Based on the clinical and pathologic findings, a diagnosis of cutaneous angiosarcoma was made, which had arisen within an area of chronic lymphedema of the lower extremity.

Further workup included computed tomography scans of the chest, abdomen, and pelvis, which were unremarkable. The patient declined surgical intervention and chemotherapy because of her age and medical comorbidities. She did receive palliative radiation treatments.

From the Departments of Dermatology<sup>a</sup> and Dermatopathology,<sup>b</sup> St Joseph Mercy Hospital.

Funding sources: None.

Conflicts of interest: None declared.

This case was presented at local meetings in the state of Michigan, which included the Michigan Dermatologic Society meeting in February 2015 and St. Joseph Mercy Resident Research day in April 2015. Both meetings were held at St. Joseph Mercy Hospital-Ann Arbor.

Correspondence to: Kristen Whitney, DO, 607 Washington Road, Lower Level, Pittsburgh, PA 15228. E-mail: [kristende@pcom.edu](mailto:kristende@pcom.edu).  
JAAD Case Reports 2016;2:397-9.

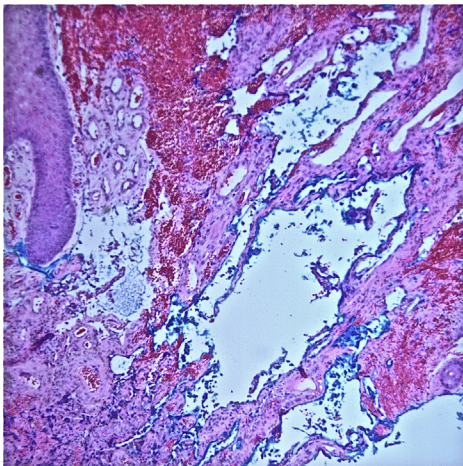
2352-5126

© 2016 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<http://dx.doi.org/10.1016/j.jidcr.2016.08.002>



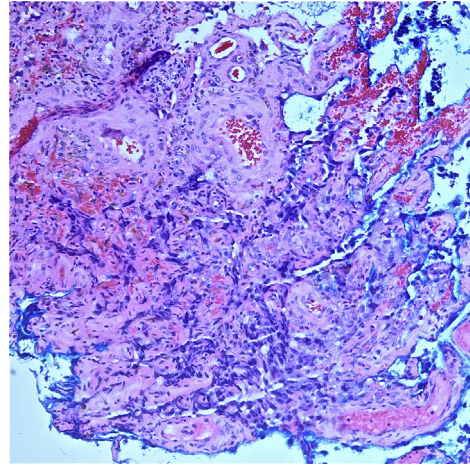
**Fig 1.** Angiosarcoma. Ulcerated plaque on the right medial lower extremity studded with multiple firm black nodules.



**Fig 2.** High-power view of the reticular dermis shows interanastomosing vascular channels dissecting through the dermal collagen.

## DISCUSSION

Cutaneous angiosarcoma is a destructive and often fatal vascular tumor. The tumor can occur de novo or secondary to well-documented risk factors, which include radiation exposure and chronic lymphedema. Stewart-Treves syndrome is defined by the development of angiosarcoma in the presence of chronic lymphedema. Although originally described



**Fig 3.** Numerous hyperchromatic and pleomorphic endothelial cells at the dermal-subcutaneous junction.

in patients after a radical mastectomy, this syndrome can occur in the setting of congenital or hereditary lymphatic malformations (ie, Turner's syndrome, Noonan's syndrome, Milroy's disease, lymphedema praecox, lymphedema tarda), chronic infections, chronic venous stasis, morbid obesity, malignant obstruction, and surgical procedures that disrupt lymphatic flow.<sup>3,4</sup> Our patient had lymphedematous limbs for approximately 60 years until the diagnosis of angiosarcoma. The underlying etiology of her lymphedema remains unknown.

Clinically, de novo lesions of angiosarcoma appear as enlarging and persistent bruise-like lesions often on the head and neck of elderly patients. Angiosarcoma occurring in a background of radiation dermatitis or chronic lymphedema typically presents with multicentric red-purple papules and nodules. Angiosarcoma can be easily missed at initial presentation for more common diagnoses such as cellulitis, trauma or ecchymoses in de novo lesions and Kaposi's sarcoma, stasis dermatitis, or acroangiokeratosis in the papulonodular form.

The pathophysiology of Stewart-Treves syndrome is largely unknown, but theories of immune dysregulation predominate. It is believed that disruption of lymphatic flow secondary to injury from radiation or chronic lymphedema leads to an impairment of the regional immune system, which can promote atypical angiogenesis and neoplasia.<sup>5</sup>

Pathologic findings are critical in making the diagnosis of cutaneous angiosarcoma. Tumors can range from well-differentiated subtypes, making distinction from benign vascular tumors and proliferations difficult, to poorly differentiated tumors in which it can be challenging to set apart from other vascular tumors, sarcomas, melanomas, and carcinomas.

Histologic features consistent with cutaneous angiosarcoma include an infiltrative network of sinusoidal vessels invading the dermal collagen. Large pleomorphic and hyperchromatic cells may form papillary projections lining the endothelial lumen. Significant hemorrhage and blood-filled cavities can occur. A large percentage of angiosarcomas stain positive for CD31 and CD34, of which, CD31 is the more sensitive and specific of the two. Cytokeratin stains may be positive in some epithelioid angiosarcomas.<sup>6,7</sup>

Treatment is based on the general health of the patient, tumor location, histologic subtype, and extent of involvement. Localized and advanced cutaneous disease are frequently treated similarly with neoadjuvant chemotherapy followed by wide local excision or amputation and radiation therapy.<sup>6,8</sup> Additional therapeutic options for locally advanced disease include the use of locoregional modalities such as isolated limb perfusion, limb infusion, and electrochemotherapy.<sup>9</sup> Radiation affords a palliative treatment option in patients not desiring radical therapies as seen in our case.

Despite treatment, the prognosis of cutaneous angiosarcoma regardless of subtype remains poor. Survival rates range from 51% at 5 years to 43% at 10 years. Patients with localized disease have a better overall outcome with 5- and 10-year survival rates of 62% and 54%, respectively. Those with distant

metastasis had a 6.2% chance of survival at both 5 and 10 years.<sup>10</sup>

#### REFERENCES

1. Stewart FW, Treves N. Lymphangiosarcoma in postmastectomy lymphedema; a report of six cases in elephantiasis chirurgica. *Cancer*. 1948;1:64-81.
2. Lee R, Saardi KM, Schwartz RA. Lymphedema-related angiogenic tumors and other malignancies. *Clin Derm*. 2014;32(5):616-620.
3. Sharma A, Schwartz RA. Stewart-Treves syndrome: pathogenesis and management. *J Am Acad Dermatol*. 2012;67(6):1342-1348.
4. Berebichez-Fridman R, Deutsch YE, Joyal TM, et al. Stewart-Treves Syndrome: A Case Report and Review of the Literature. *Case Rep Oncol*. 2016;9(1):205-211.
5. Ruocco V, Brunetti G, Puca RV, et al. The immunocompromised district: a unifying concept for lymphoedematous, herpes-infected and otherwise damaged sites. *J Eur Acad Dermatol Venereol*. 2009;23(12):1364-1373.
6. Morgan MB, Swann M, Somach S, Eng W, Smoller B. Cutaneous angiosarcoma: A case series with prognostic correlation. *J Am Acad Dermatol*. 2004;50(6):867-874.
7. Ohsawa M, Naka N, Tomita Y, et al. Use of immunohistochemical procedures in diagnosing angiosarcoma. Evaluation of 98 cases. *Cancer*. 1995;75(12):2867-2874.
8. Ravi V, Patel S. Vascular sarcomas. *Curr Oncol Rep*. 2013;15:347-355.
9. Campana LG, Valpione S, Tosi A, et al. Angiosarcoma on lymphedema (Stewart-Treves Syndrome): A 12-Year follow-up after isolated limb perfusion, limb infusion and electrochemotherapy. *Case Rep Oncol*. 2016;9(1):205-211.
10. Albores-Saavedra J, Schwartz AM, Henson DE, et al. Cutaneous angiosarcoma. Analysis of 434 cases from the surveillance, epidemiology and end results program, 1973-2007. *Ann Diagn Pathol*. 2011;15(2):93-97.