Cutaneous Angiosarcoma of the Knee: A Case Report and Review of the Literature

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Cutaneous angiosarcoma is a rare, malignant, vascular tumor that usually occurs in the scalp and face region of elderly white men. The tumor also can involve areas of prior irradiation; chronic lymphedema, otherwise known as Stewart-Treves syndrome; and preexisting vascular lesions. We report an unusual case of angiosarcoma occurring on the knee of a 70-year-old white woman with a strong family history of malignant melanoma in the absence of any known predisposing features.

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Angiosarcoma is a rare type of vascular endothelial-derived malignancy that represents less than 1% to 2% of all sarcomas.[1] Cutaneous involvement occurs in approximately 60% of reported cases of angiosarcoma,[2] usually in elderly white men.[1] Up to 95% of cutaneous angiosarcomas involve the scalp and face.[3] Angiosarcomas also have a well-documented tendency to occur in areas of prior irradiation, such as the breast after radiation therapy for breast cancer[4]; in the extremities in the setting of chronic lymphedema, called Stewart-Treves syndrome[5]; and in preexisting vascular lesions.[6] There have been fewer than 10 reported cases of angiosarcoma arising in the lower extremities in the absence of predisposing factors. We report a particularly unusual case of cutaneous angiosarcoma occurring in the context of a strong family history of malignant melanoma.

Case Report

A 70-year-old white woman presented with a 6-month history of a painful bleeding growth on her left knee at the site of a mole that had been present for many years. She had no history of skin cancer and the remainder of her medical history was unremarkable. Her family history was significant for malignant melanoma in both her father and daughter. A review of systems disclosed a 40-lb unintentional weight loss over the past year.

Physical examination revealed a cachectic woman with a 4.5×5.0-cm tumor on her left knee composed of firm, coalescent, pink nodules with an eroded crusted nodule at the lower pole. No lower extremity edema was noted, and there was no lymph node involvement. The differential diagnosis at the time was malignant melanoma versus angiosarcoma (Figure 1).

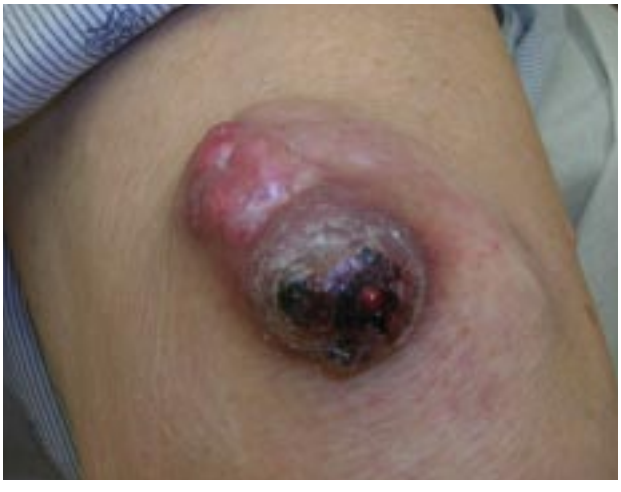

Figure 1. A rapidly growing, hemorrhagic, multilocular tumor on the knee.

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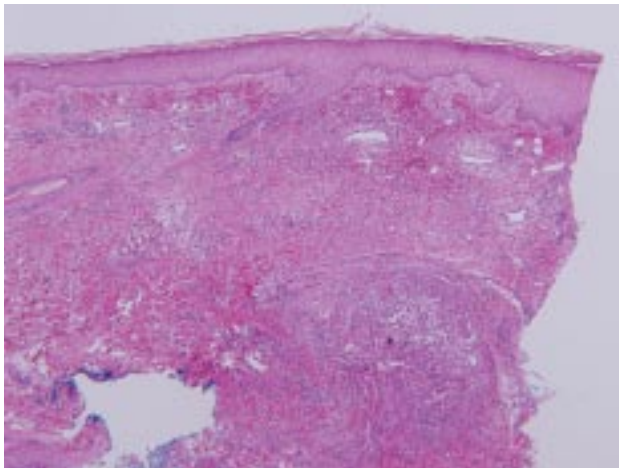

Figure 2. A hemorrhagic dermal proliferation of atypical cells arranged in strands, cords, and nests, demonstrating increased vascularity (H&E, original magnification ×4).

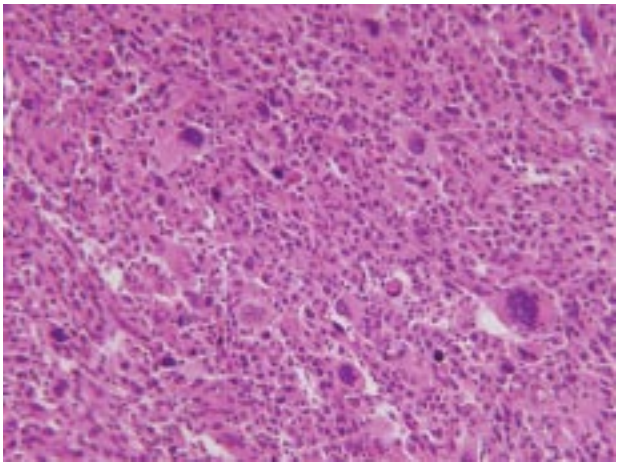

Figure 3. Plump, hyperchromatic, pleomorphic cells with numerous mitotic figures (H&E, original magnification ×40).

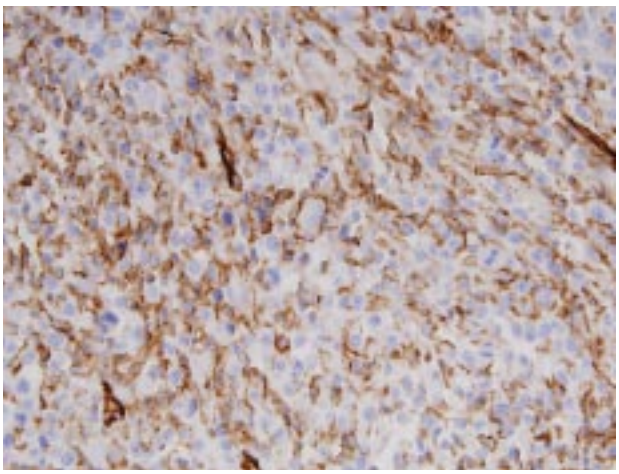

Figure 4. Diffuse positive staining with CD31 immunostain (original magnification ×40).

Histopathologic examination of the initial skin biopsy showed increased vascularity with plump, hyperchromatic, pleomorphic cells in a mucinous stroma arranged in strands, cords, and nests (Figure 2). Atypical mitotic figures were seen throughout (Figure 3). Immunohistochemical staining was positive for CD31 (Figure 4) and vimentin and negative for S100. Examination of the resected tumor showed a large hemorrhagic neoplasm composed of similar pleomorphic cells arranged in sheets demonstrating invasion into underlying skeletal muscle. The CD31 was intensely positive in some areas of the tumor and less so in other areas, vimentin was positive, and again the S100 was negative. Additional stains were performed, including smooth muscle actin, CD99, CD34, and cytokeratin, which were all negative. The pathologic diagnosis was high-grade angiosarcoma.

The patient was scheduled for immediate wide local excision by general surgery. Negative margins were achieved after removing a 9.5×6.0×3.0-cm ellipse that included skeletal muscle. A positron emission tomographic scan at the time of surgery was normal. Her surgery was followed by local radiation therapy. A repeat positron emission tomographic scan at her 5-month follow-up showed no evidence of metastatic disease.

Comment

Angiosarcoma, previously known as hemangiosarcoma, was initially described in 1945 by Caro and Stubenrauch.[7] Up to 95% of all cutaneous angiosarcomas involve the scalp and face and they typically occur in elderly white individuals, with a male to female ratio of 3 to 1 and an average age of 75 years.[3] Early lesions usually are asymptomatic, red to violaceous macules resembling a bruise, with slow progression toward a nodule, with rare symptoms of bleeding, ulceration, and pain. Because of the initial nonspecific appearance, diagnosis often is delayed or initially incorrect with a median of 5.1 months from the onset of symptoms to correct identification.[8]

In 1948, Stewart and Treves[5] reported 6 cases of angiosarcoma in patients treated for breast cancer who had postmastectomy lymphedema. They found that angiosarcomas appeared at an average of 12.5 years after radical mastectomy.[5] Stewart-Treves syndrome is now applied more broadly to angiosarcoma resulting from chronic lymphedema secondary to trauma, infection, radiotherapy, or idiopathic causes.[9-11]

Cutaneous angiosarcoma also has been described in the background of radiation and other vascular lesions. In 1981, Maddox and Evans[12] reported the first case of angiosarcoma following radiation therapy for breast cancer. With increasing use of radiation in the treatment of breast cancer and other

Cases of Cutaneous Angiosarcoma

Author (Year)	Study	Age/Sex	Location	Size	Treatment	Outcome
Girard et al[13] (1970)	Case series with 2 relevant cases	Unknown	Lower extremities	Unknown	Excision, amputation, details unknown	2 with metastasis: 1 to lymph nodes; 1 to heart and lungs
Wolf and Pasquino[16] (1990)	Case report	40 y/male	Left sole	4 cm	Wide surgical excision followed by amputation	No long-term follow-up
Naka et al[17] (1995)	Review: 7 extremity lesions (1 with chronic lymphedema)	Mean age, 55 y/6 males; 1 female	Extremities, additional details unknown	<5 cm in 1 case, 5–10 cm in 1 case, >10 cm in 2 cases, unknown in 3 cases	Surgery in 1 case; chemotherapy in 1 case; surgery and chemotherapy in 1 case; radiation in 2 cases; chemotherapy and radiation in 1 case; surgery, chemotherapy, and radiation in 1 case	All 7 lesions metastasized
Huber et al[18] (2000)	Case report	88 y/female	Left lower leg	9×7 cm	Excision, palliative XRT, then above-knee amputation	Local recurrences
Diaz-Cascajo et al[19] (1998)	Case report	77 y/female	Medial aspect of left foot	Unknown	Amputation, combination chemotherapy	Metastasis to inguinal lymph nodes and lung

Abbreviation: XRT, radiation therapy.

carcinomas, multiple cases of this phenomenon have been reported. Girard et al[13] first described 3 cases of angiosarcoma occurring in port-wine stains. Cutaneous angiosarcoma also has been reported in 9 cases of benign hemangiomas.[6] Other reported risk factors for the development of cutaneous angiosarcoma include trauma and environmental exposures, such as thorium dioxide, vinyl chloride, and arsenic.[14,15]

There are only rare reports of cutaneous angiosarcoma arising in the lower extremities in the absence of chronic lymphedema, radiation, and vascular malformations (Table). Girard et al[13] reported 4 cases of cutaneous angiosarcoma in the legs, 2 of which had no prior risk factors. Wolf and Pasquino[16] also reported a case of cutaneous angiosarcoma on the left sole in a 40-year-old man. A review of 99 cases in Japan revealed only 7 cases of cutaneous angiosarcoma in the extremities, of which 6 were not associated with chronic lymphedema or prior radiation.[17] Additional details for the individual cases were not provided. Huber et al[18] described a case of cutaneous angiosarcoma on the left lower leg of an 88-year-old woman without any prior surgery or radiation. There also is a single report of verrucous angiosarcoma in a 77-year-old woman on the medial aspect of her left foot in the absence of lymphedema or radiation.[19]

Angiosarcoma is thought to derive from endothelial cells that line blood vessels and lymphatic channels. High-grade lesions can be difficult to

histologically distinguish from poorly differentiated carcinomas, other sarcomas, and malignant melanomas. Immunohistochemical stains such as CD31, factor VIII–related antigen, and ulex europaeus lectin 1 are useful endothelial markers to help identify angiosarcomas.[17]

This locally aggressive malignancy portends an unfavorable prognosis. Median survival ranges from 15 to 28 months with a 5-year local recurrence rate of 84% and an overall 5-year survival of 34%.[3] The risk for lymph node metastases ranges from 10% to 20%.[1] The most important determinants of outcome include tumor diameter (>5 cm), tumor depth of invasion (>3 mm), positive surgical margins, tumor recurrence, and metastases.[3] Currently, no formal staging system exists for angiosarcoma.

Optimal treatment involves wide local excision of the tumor followed by postoperative radiation to the site and regional lymphatics.[2] Palliative chemotherapy with medications, such as doxorubicin hydrochloride, gemcitabine hydrochloride, ifosfamide, paclitaxel, and vinorelbine tartrate, has been performed in patients with unresectable disease. However, the role of adjuvant chemotherapy is still under investigation.[2] The reported cases in the Table had a high rate of distal metastases and need for amputation. Thus far, our patient remains disease free with wide local excision but will continue to be closely monitored.

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