Cutaneous Malignant Vascular Neoplasms

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KEYWORDS

• Angiosarcoma • Atypical vascular lesion • Epithelioid hemangioendothelioma
• Cutaneous vascular tumors • Molecular pathology

KEY POINTS

- Angiosarcoma may be sporadic or may arise in the setting of chronic lymphedema (eg, Stewart-Treves syndrome) or secondary to radiation therapy.
- The increased use of adjuvant radiation therapy to treat various cancer types led to the awareness of radiation-induced atypical vascular lesion.
- Differentiating radiation-induced atypical vascular lesion and early evolving angiosarcoma requires precise microscopic evaluation in conjunction with clinicopathologic correlation and ancillary studies.
- Epithelioid hemangioendothelioma is a malignant vascular tumor that generally behaves in a less aggressive fashion than conventional angiosarcoma.
- Newer molecular techniques provide more accurate classification of cutaneous malignant vascular tumors.

CUTANEOUS ANGIOSARCOMA

Overview

Cutaneous angiosarcoma is a rare malignant vascular neoplasm that can develop in practically any body site. It is typically divided into 3 distinct groups: (1) primary sporadic angiosarcoma, (2) postradiation angiosarcoma, and (3) chronic lymphedema-associated angiosarcoma. Many examples of angiosarcoma frequently exhibit both vascular and lymphatic differentiation. Therefore, the historical terms, *hemangiosarcoma* and *lymphangiosarcoma*, are no longer applicable.

Clinical Features

Primary sporadic cutaneous angiosarcoma typically affects elderly adults, most commonly occurring in sun-damaged skin of the head and neck region. The

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demographic suggest an etiologic role for ultraviolet exposure, but this concept is still debatable, as the presence of *TERT* promoter mutation (ultraviolet light-signature mutation) was not detected in a recent study.[1] Clinically, the early stage of superficial disease can be very deceptive and often confused with other cutaneous processes (eg, cellulitis or bruise). As the tumor progresses, it transforms into elevated plaques and nodules with or without ulceration. Approximately half of the patients initially present with multifocal satellite lesions that are close to the original tumor. In these cases, clinically determining the extent of the disease process is often difficult; thus, mapping biopsy strategy in the anatomic area of suspicion is recommended.

By definition, postradiation angiosarcoma develops within a prior radiation field. The incidence of postradiation angiosarcoma has increased as breast-conserving surgery with adjuvant radiation therapy has become standard care for those patients with early breast cancer. Although the usual antecedent malignancies are breast or gynecologic malignancies, it can occur in patients with a wide range of benign and malignant disorders, such as eczema, sinusitis, hemangiomas, hematolymphoid malignancies, head and neck and penile squamous cell carcinomas, and rectal carcinomas.[2] In the setting of breast cancer, the mean interval preceding angiosarcoma is shorter than that of other postradiation sarcomas. The mean latency is approximately 5 years and may present as soon as 1 to 2 years after radiation therapy.[3,4] Notably, when the radiation therapy is administered for benign antecedent disorders, which typically receive less irradiation, the median interval preceding angiosarcoma is 22 years (range, 4–40 years).[5]

Chronic lymphedema-associated angiosarcoma typically affects patients who have undergone radical/modified radical mastectomies and axillary lymph node dissection for breast carcinoma (Stewart -Treves syndrome). Most frequently, the lesion begins to develop on the inner aspect of the arm affected by lymphedema. This clinical subtype is decreasing because of the shift toward breast-conserving lumpectomy surgery and sentinel lymph node biopsy, as mentioned previously. Angiosarcoma may also develop in association with chronic congenital, posttraumatic, idiopathic, infectious (eg, filariasis), and obesity-associated lymphedema.[6,7] The average period from the onset of postmastectomy lymphedema to the appearance of angiosarcoma is approximately 10 years. Those lesions arising in the setting of chronic congenital and filariasis lymphedema often have a later onset (>20 years). The affected areas typically show pitting, indurated, or “peau d’orange” skin with violaceous macular, papular, or polypoid tumors.

Histopathologic Features

Regardless of the clinical subtype, cutaneous angiosarcoma has a broad morphologic spectrum.[3,4] Classically, angiosarcoma consists of architecturally complex, anastomosing vessels that dissect through dermal collagen (**Fig. 1**). The vessels are lined by atypical hyperchromatic endothelial cells with multilayering of endothelial cells. In some cases the atypia is subtle and multilayering may be absent or focal. The neoplastic vessels sometimes take on a sinusoidal growth pattern (see **Fig. 1**). Epithelioid angiosarcoma has vasoformative channels lined by tumor cells with enlarged round nuclei and abundant amphophilic cytoplasm or solid sheets of epithelioid tumor cells (**Fig. 2**).[8] Other cases may show solid fascicles of hyperchromatic spindled cells. In cases of a predominantly sheetlike or fascicular pattern, intratumoral hemorrhage is often a clue to consider the possibility of angiosarcoma.[9] Vasoformative areas are often present at the periphery of the tumor (**Fig. 3**). Cases may also have a mix of vasoformative and solid areas. In the setting of postradiation angiosarcoma of the breast, 2 additional patterns have been described. The tumor can be arranged in clusters of