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Angiosarcoma

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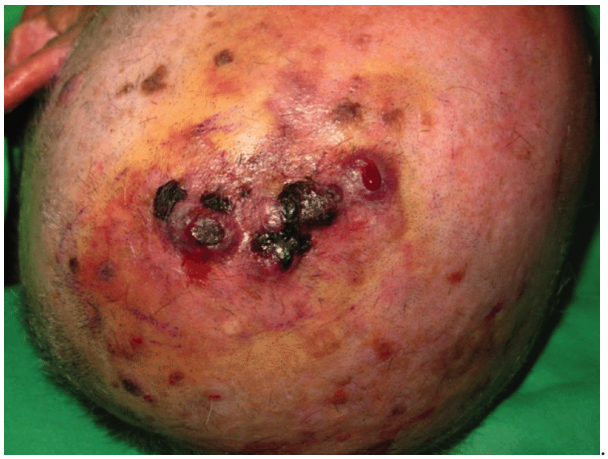
What	Rare, highly malignant tumor of endothelial origin
Who/when	Elderly (over 70 years old) Similar incidence in gender
Why	Associated with radiation, chemical exposure, and chronic lymphedema. While the pathogenesis is often unknown in the majority of developing angiosarcoma cases, other causes such as environmental carcinogens and genetic syndromes, are established playing an important role in this disease.
Where	Head and neck most commonly. Can present any location. Sun-damaged sites. Breast most commonly arises after radiation therapy for breast cancer.

Clinical features

- Single or multiple bluish or red nodules, which often ulcerate or bleed



- Benign-appearing, bruise-like patches on the scalp, forehead, or central face that may advance to violaceous nodules or indurated plaques (seen in photo).
- Swelling and edema may be present.

Credit: By: Cheng, Yung-Sheng & Chen, Tim-Mo & Tsai, Wen-Chiuan & Huang, Tsai-Wang. www.researchgate.net/figure/Cutaneous-angiosarcoma-of-scalp-measuring-645cm-in-size-was-confirmed-by_fig1_313862826

Clinical Ddx:

AVLs, microcystic lymphatic malformation, PILA, RHE, epithelioid hemangioendothelioma (EHE), Kaposiform hemangioendothelioma (KHE), tufted angioma.

Note: It is essential to diagnostically distinguish angiosarcoma versus reactive and benign vascular tumors versus intermediate grade vascular tumors.

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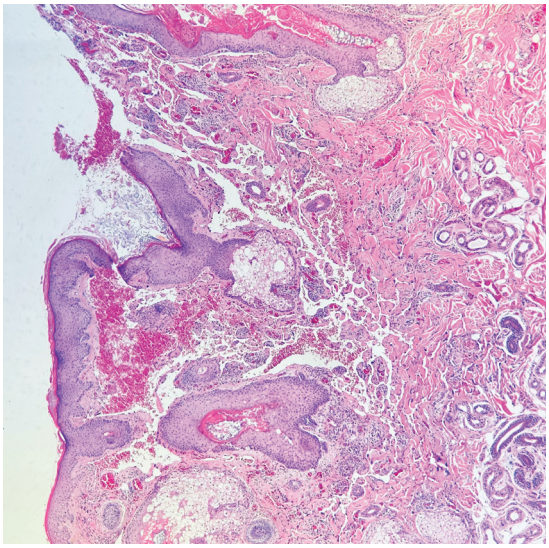
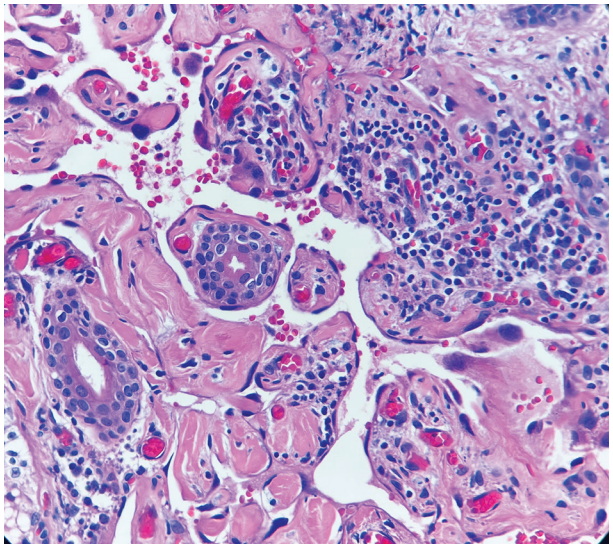
Histologic features





Large, hyperchromatic, pleomorphic tumor cells that dissect between collagen bundles with prominent hemorrhage (Fig. 2, left).

Large, anastomosing vascular networks develop with lining of the vessels by "multi-layered" endothelial cells that crowd on top of one another. Tumor cells can be seen free floating inside the lumen (Fig. 3, right). Note: Poorly differentiated areas may have large epithelioid cells that may not resemble vascular origination.

Immunostaining

CD31+, CD34+, ERG+ (most sensitive and specific), and FLI-1+ (nuclear marker)

Management

Surgical: Most reliable current modality. Very early wide local excision with negative margins.
Radiation: Palliative radiation therapy has been frequently used in treating inoperable and metastatic tumors.

Adjuvant therapies: Conventional cytotoxic chemotherapy has been frequently used in treating inoperable/metastatic tumors. Multiple promising studies in progress include targeted medicines including immunotherapies (i.e., PD-1 inhibitors) as possible treatments in the future.

Prognosis: Poor, known for high rates of lymph node metastasis. The reported rates of advanced/metastatic disease at presentation vary from 16-44%, and the five-year survival is around 30-40%. Most common site for metastasis: lung.

Recurrence: High. Most likely to occur within two years following resection. Up to 30-100% of cases with negative margins on initial resection will recur with possible distant metastasis.

Follow-up: Stringent clinical follow-up every three months for first two years at least, then gradually decrease to every six months for the next three years, and then annually.

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Additional high-yield information

c-MYC amplification (can be detected by FISH or immunostaining) reliably distinguishes between atypical vascular lesions (negative) and radiation-induced angiosarcoma (positive)

Stewart-Treves Syndrome

- Angiosarcoma developing in the setting of chronic lymphedema, usually following breast cancer treatment with axillary lymph node dissection.
- It can also be caused by chronic lymphedema of any origin.

Genetic syndromes that may be associated with primary angiosarcomas

- Bilateral retinoblastoma, NF-1, Ollier Disease, Maffuci Disease, XP, Klippel-Trenaunay Syndrome.

Abbreviations: AVL, atypical vascular lesions. PILA, papillary intralymphatic angioendothelioma. RHE, retiform hemangioendothelioma. EHE, epithelioid hemangioendothelioma. KHE, kaposiform hemangioendothelioma. FISH, fluorescence in situ hybridization. NF-1, neurofibromatosis type I. XP, xeroderma pigmentosum.

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6. Histology slides courtesy of PRW Laboratories; Charlottesville, VA.