Diagnostically Challenging Epithelioid Vascular Tumors

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KEYWORDS

• Epithelioid hemangioma • Intravascular epithelioid hemangioma
• Cutaneous epithelioid angiomatous nodule • Epithelioid hemangioendothelioma
• Epithelioid sarcoma-like hemangioendothelioma • Pseudomyogenic hemangioendothelioma
• Epithelioid angiosarcoma

ABSTRACT

The diagnosis of vascular tumors is a challenging area in soft tissue pathology. Epithelioid vascular tumors pose a particular challenge. Due to the epithelioid morphology of the tumor cells, they can be misdiagnosed as a variety of other entities, including metastatic carcinoma or epithelioid sarcoma. Furthermore, it can be difficult to distinguish between different epithelioid vascular tumors. This review focuses on vascular tumors characterized by epithelioid endothelial cells, including epithelioid hemangioma, cutaneous epithelioid angiomatous nodule, epithelioid hemangioendothelioma, epithelioid sarcomalike hemangioendothelioma/pseudomyogenic hemangioendothelioma, and epithelioid angiosarcoma.

OVERVIEW

Epithelioid vascular tumors can be particularly diagnostically challenging. The epithelioid cytomorphology is, by nature, somewhat generic and elicits a broad differential diagnosis that often includes carcinoma and melanoma. Furthermore, in many epithelioid vascular tumors, the vascular nature of the neoplasm is difficult to recognize. A range of histologic overlap also exists between different epithelioid vascular tumors, and immunohistochemical markers generally do not help in classifying the different entities. This review focuses on the unique clinicopathologic and molecular features of the most common benign (epithelioid hemangioma and cutaneous epithelioid angiomatous nodule), intermediate (epithelioid hemangioendothelioma and epithelioid sarcoma-like hemangioendothelioma/pseudomyogenic hemangioendothelioma) and malignant (epithelioid angiosarcoma) epithelioid vascular neoplasms.

EPITHELIOID HEMANGIOMA

Epithelioid hemangioma was initially described in 1969 by Wells and Whimster as epithelioid angiomatous hyperplasia with eosinophilia.[1] Epithelioid hemangiomas most commonly present on the head and neck, often in a periauricular location, in middle-aged adults with a female predominance.[2,3] However, a wide range of cutaneous locations may be involved.[4–9] They clinically and grossly appear as small erythematous nodules or plaques, commonly with ulceration or excoriation, and commonly as multiple coalescing lesions. As such, epithelioid hemangiomas are often clinically mistaken for a cyst, capillary hemangioma, or pyogenic granuloma.

Epithelioid hemangioma rarely arises as a purely intravascular tumor. Intravascular epithelioid hemangioma was originally described by Rosai and Ackerman[10] under the name intravascular atypical vascular proliferation. Epithelioid hemangioma also occurs in bone, where it mostly affects long tubular bones and can be multifocal in up to 25% of cases, causing concern for malignancy.[9,11–15]

Histologically, conventional epithelioid hemangiomas are circumscribed, dermal, or subcutaneous, lobular proliferations of well-formed capillaries

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Surgical Pathology 8 (2015) 331–351
http://dx.doi.org/10.1016/j.path.2015.05.001
1875-9181/15/$ – see front matter

surrounding a larger central vessel. The proliferation is associated with an inflammatory infiltrate of lymphocytes, sometimes with germinal center formation, with admixed eosinophils, histiocytes, and plasma cells (**Fig. 1**A). Rare giant cells also have been described.[16] In some cases, the brisk nature of the infiltrate can obscure the underlying vascular proliferation at low magnification. The involved capillaries have retained lumina and are lined by epithelioid endothelial cells, which variably hobnail into luminal spaces (see **Fig. 1**B). Mitotic activity may be seen, but atypical mitotic figures are absent.

Epithelioid hemangiomas also may have relatively solid areas, a diagnostic pitfall. Solid areas may be more common in tumors at certain sites. For instance, intravascular epithelioid hemangiomas tend to be more solid with less obvious vasoformation (**Fig. 2**A). Intravascular forms also have a less prominent inflammatory infiltrate,

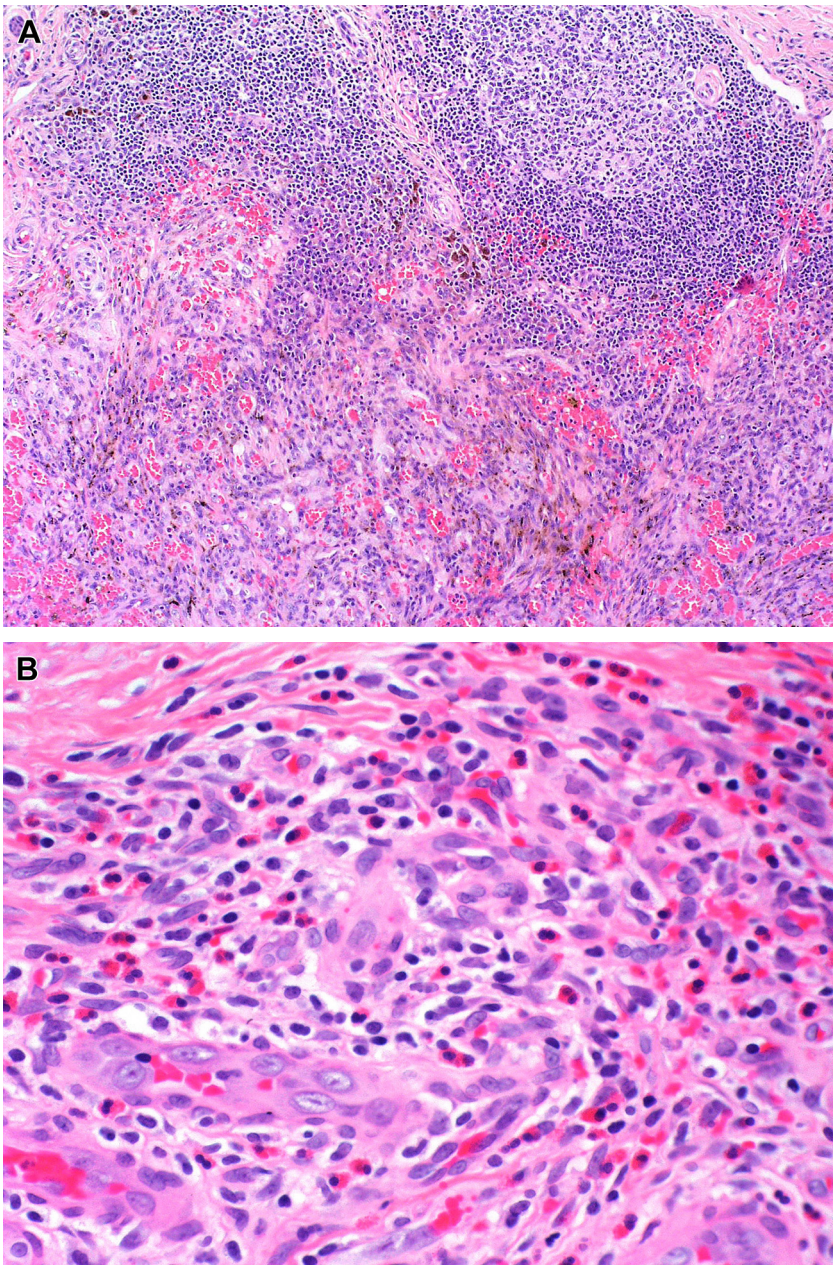

Fig. 1. (*A*) Epithelioid hemangioma. This tumor is composed of a lobular proliferation of capillaries lined by plump epithelioid endothelial cells with abundant eosinophilic cytoplasm. Typically present is an inflammatory infiltrate with lymphoid aggregates, often with germinal center formation and admixed eosinophils. (*B*) Epithelioid hemangioma. This high-power image of epithelioid hemangioma illustrates the plump endothelial cells lining the capillaries and numerous admixed eosinophils (Hematoxylin-eosin, original magnification [*A*] ×100; [*B*] ×400).