Primary cutaneous epithelioid hemangioendothelioma with lymph node metastasis

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INTRODUCTION

Epithelioid hemangioendothelioma (EHE) is a vascular tumor of bone and soft tissues with clinical and histologic features that can range between those of hemangioma and angiosarcoma. EHE arises from both vascular endothelial and pre-endothelial cells; therefore, the clinical behavior of EHE tumors can be quite diverse. Before its characterization by Weiss and Enzinger, EHE was initially described as an aggressive form of bronchoalveolar cell carcinoma.[1] Since its discovery, EHE has been found to manifest clinically in a variety of locations, such as the head, neck, breast, lymph nodes, mediastinum, brain, skin, and abdomen.[1-4] This neoplasm is often misdiagnosed, as it accounts for less than 1% of all vascular tumors and between 50% and 76% of patients with internal organ involvement present without symptoms.[2,3] In the same manner, primary cutaneous lesions are difficult to diagnose because of the nonspecific clinical presentation of a red nodule, which may or may not be tender.[5] Dermatologists need to be aware of cutaneous EHE, as delayed diagnosis can lead to significant morbidity and mortality because of the metastatic potential. We report a case of primary cutaneous EHE in a 41-year-old woman originating in the ear with subsequent metastasis to an adjacent lymph node. This patient ultimately required a total auriculectomy, temporal bone resection, and left-sided selective neck dissection followed by adjuvant radiation treatments.

Abbreviation used:

EHE: epithelioid hemangioendothelioma

CASE PRESENTATION

A 41-year-old woman presented to our dermatology clinic complaining of a dry, itchy lesion on her left ear. The patient reported recurrent itching and dryness of the area over the last 3 years with moderate improvement after using a topical steroid. On physical examination, a red, scaly, ill-defined plaque was seen on her left ear (Fig 1). The differential diagnosis included eczema, psoriasis, and irritant dermatitis, and she was treated with clobetasol lotion. At a 1-month follow-up appointment, the plaque on her left ear remained red and scaly and was more painful than at her initial visit. A shave biopsy result was consistent with an atypical epithelioid vascular proliferation. A subsequent deeper biopsy was most consistent with epithelioid hemangioendothelioma; however, angiosarcoma could not be excluded (Fig 2). The histology of both biopsies showed a dermal proliferation of epithelioid cells arranged in cords and small nests within a collagenous stroma. Focal intracytoplasmic lumina were seen. At the periphery of the lesion, there were irregular vascular channels with some hobnail cells. Mitotic activity was present but inconspicuous. Nuclei were relatively bland with focal mildly enlarged nuclei and small nucleoli. Tumor cells were strongly positive for CD31a and focally positive for CD34. These stains also highlighted irregular vascular channels. SMA was focally positive within the tumor as well as in surrounding blood vessels. No tumor cell staining was seen for CD68, SOX10, S100, MART-1, pan cytokeratin, cytokeratin 5/6, or P63.

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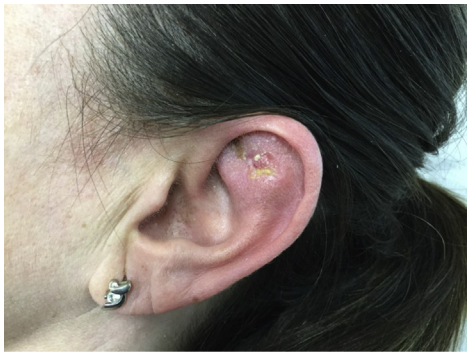

Fig 1. Initial evaluation found a red, scaly, ill-defined plaque on the patient's left ear.

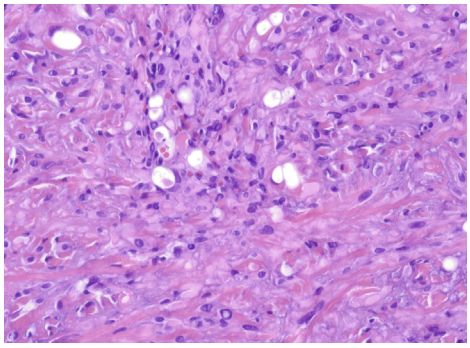

Fig 2. High-power image of shave biopsy shows dermal proliferation of epithelioid cells arranged in cords and nests with intracytoplasmic lumina.

Our patient was then referred to the otolaryngology department. Positron emission tomography/computed tomography imaging and fine-needle aspiration were arranged. Positron emission tomography/computed tomography discovered (18)F-fluorodeoxyglucose uptake involving the left ear conch scapha, left ear tragus, soft tissue in the posterolateral wall of the left external meatus, and the left level 2B cervical lymph node. Magnetic resonance imaging of the neck found a left subauricular ill-defined mass with enhancement and extension to the left upper external ear and an abnormally enlarged centrally necrotic left-level 2b lymph node. Fine-needle aspiration level 2 lymph node biopsy confirmed the diagnosis of EHE, and the patient subsequently underwent a total auriculectomy, left temporal bone resection, and left selective neck dissection (Fig 3). The surgical defect was repaired with a left temporalis muscle flap reconstruction of the temporal bone defect and a split-thickness skin graft from the left thigh. Final pathology confirmed the diagnosis of EHE and found no evidence of angiosarcoma. Metastatic disease was found in 1 of 12 lymph nodes and at the deep margin of the ear extirpation in the region of the superior aspect of the external

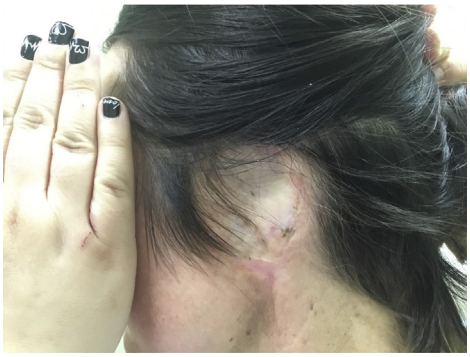

Fig 3. The patient required a total auriculectomy.

auditory canal. The patient was referred for evaluation by the radiation oncology and medical oncology departments. From late July until the beginning of September, she was treated with 6600 cGy adjuvant radiation to the left neck resection bed. Overall, she has tolerated the surgery and the radiation well. She is acclimating to life without hearing in her left ear. She will continue to be followed up by the dermatology and otolaryngology departments with frequent examinations and surveillance imaging studies to monitor for recurrence.

DISCUSSION

EHE is a rare vascular neoplasm of endothelial origin. Like all subtypes of hemangioendothelioma, EHE is classified on the spectrum of vascular neoplasms as intermediate to hemangioma and angiosarcoma in metastatic potential. Other hemangioendotheliomas include intralymphatic angioendothelioma (Dabska tumor), retiform hemangioendothelioma, kaposiform hemangioendothelioma, pseudomyogenic hemangioendothelioma, and composite hemangioendothelioma. These diagnostic entities are distinguishable by characteristic histologic findings on pathologic examination. Anatomically, EHE is typically located in soft tissues or within deep internal structures such as liver, lung, and bone. Metastases from internal organs to the skin have been reported, but primary cutaneous involvement is rare. EHE of the skin seems to have no sex predilection and is most commonly seen in adults, although pediatric and even congenital cases have been reported.[3,6] The pathogenesis of EHE is not fully understood, although certain genetic mechanisms are thought to play a key role. For example, an investigation of the biopsy specimens of 2 patients with EHE found identical translocations between chromosomes 1 and 3.[7] Clinically, cutaneous EHE may exhibit myriad morphologies, and these inconsistencies of presentation present a diagnostic dilemma for clinicians. For example, appearance of EHE may range from a nonspecific, well-circumscribed mass to an ill-defined,

Author	Clinical Morphology
Weiss and Enzinger	Non-specific, well-circumscribed
Mentzel	Ill-defined, infiltrative
Quante	Erythematous, painful dermal nodule
Forschner	Large, moist ulcer with surrounding erythema
Kato	Purplish-red papules and nodules
Ro	Painful nodule

Fig. 4. Extensive heterogeneity in the morphology of EHE lesions exacerbates diagnostic difficulty.

infiltrative lesion. Reports of EHE presenting as an erythematous dermal nodule, ulceration, or purplish-red papule or nodule highlight a wide array of morphologies (Fig 4).[1,4-6,8,9] Interestingly, multiple EHEs have been reported in a single patient, although most cases are of solitary lesions.[8] Tumors can be found anywhere on the body, and a spectrum of involvement sites has been reported.[5] The extremities appear to be the most frequently involved, followed by the head and neck, as in our patient. For example, one study of 41 patients with cutaneous EHE reported approximately 58% of lesions located on the extremities, whereas 12% were found on the head and neck.[1] Similarly, another report of 30 patients described approximately 33% of lesions on the extremities and 17% on the head and neck.[4] However, lesions of the palm, trunk, anogenital region, and foot have also been reported.[4-6,8] Because of the wide variety in both lesion morphology and anatomic location, EHE may be difficult to identify initially, with differential diagnosis broadly ranging from irritant dermatitis to skin cancer, depending on initial presentation. As a result, definitive diagnosis often requires multiple clinic visits and several biopsies, as in the case with our patient. Therefore, we recommend obtaining a deep shave or a punch biopsy at initial presentation if an atypical vascular proliferation is suspected to expedite diagnosis, spare patients from unnecessary discomfort, and reduce the risk of metastasis. Histopathology of EHE specimens shows pleomorphic epithelioid cells with intracytoplasmic vacuoles (thought to represent primitive lumen formation) that are arranged in nests, strands, and trabecular patterns within a hyalinized and myxochondroid stroma.[3] Upon immunohistochemical staining, specimens are typically positive for one or more of the following: CD31, CD34, factor VIII–related antigen, α-smooth muscle actin, and cytokeratin.[3-5] Occasionally, Weibel-Palade bodies are present.[1] The histologic differential diagnosis of EHE mainly consists of metastatic carcinoma and epithelioid angiosarcoma. Carcinomas can be readily excluded by presence of CD31 positivity, whereas epithelioid angiosarcoma exhibits high-grade nuclear pleomorphism, significant mitotic activity, high cellularity, lack of collagenous stroma, and presence of necrosis. Angiosarcoma exhibits a more rapidly progressive course compared with EHE. Although microscopic evaluation is necessary to make the diagnosis of EHE, the correlation between histologic features and clinical outcome is unclear.[4]

Cutaneous EHE may result from an internal tumor that metastasizes to the skin or may be a primary lesion with or without associated systemic involvement.[4-6,9] As in the case with our patient, tumor can spread from the skin to other structures through the lymphatics. In general, EHE is considered to be of moderate malignant potential and intermediate potential to hemangiomas and angiosarcomas in both metastatic and mortality rates, although more data specific to cutaneous EHE are needed.[3] In a 1986 review of 46 patients with EHE, approximately 13% had local recurrence after treatment, and 31% had metastases to regional lymph node, liver, and bone.[10] Years later, a review of 24 patients with EHE evaluated at 36 months after diagnosis found 3 to have local recurrence and reported a 21% and 17% metastatic and mortality rate, respectively.[4] Grading schemes based on mitotic activity, nuclear pleomorphism, and tumor size may distinguish tumors of the lung and soft tissues into low-risk and high risk tumors; however, no formal grading scheme predicts outcomes for cutaneous tumors.[2] Using mitotic activity, nuclear pleomorphism, and size, our patient's tumor would have been considered low risk, underlying the need for better prognostic tools for cutaneous EHE. The treatment for isolated cutaneous EHE is largely surgical.[5] In cases of metastatic EHE, more aggressive management with chemotherapy may be warranted.[6] Regardless of treatment strategy, regular follow-up is recommended because of the potential for tumor recurrence or systemic metastasis.[4,10]

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