CASE REPORT

Epithelioid Hemangioendothelioma of the Nasal Cavity

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Epithelioid hemangioendothelioma (EH) is an unusual vascular neoplasm characterized by proliferation of endothelial cells with epithelioid morphology. It has an indolent course, with the potential for recurrence, but rarely metastasizes. The common locations include soft tissue, skin, viscera and bone. We present an unusual case of EH in the nasal cavity and describe the clinical characteristics, histopathologic findings, differential diagnosis and management. The 25-year-old male patient initially presented with an 8-month history of intermittent epistaxis. Nasal endoscopy revealed a vascular tumor involving the nasal cavity. The tumor was excised and the final histopathologic diagnosis was consistent with EH. EH in the head and neck is extremely rare. Wide excision is the treatment of choice, and regular follow-up is suggested due to the potential for recurrence. Definitive diagnosis depends on histopathologic and immunohistochemical features. [*J Chin Med Assoc* 2005;68(1):45–48]

Key Words: epithelioid hemangioendothelioma, nasal cavity, vascular neoplasms

Introduction

Epithelioid hemangioendothelioma (EH) is an uncommon vascular tumor of soft tissue, which was first reported by Weiss and Enzinger in 1982: the tumor possessed histologic and clinical features intermediate between those of benign hemangioma and conventional angiosarcoma.[1] Reports since then have verified that the tumor can occur not only in soft tissue but also in other sites, including the liver, lung, bone, lymph nodes, brain and heart.[1–5]

Histologically, the neoplasm comprises endothelial cells with eosinophilic or vacuolated cytoplasm. The cells appear in small nests or strands and only rarely form vascular channels. The neoplastic stroma is usually hyalinized and myxoid, resembling hyaline cartilage.

In our review of the English literature, only 29 cases of EH of the head and neck region are reported.[1–5] We present the first case of EH arising from the nasal cavity, and review the relevant literature.

Case Report

A 25-year-old man presented with an 8-month history of intermittent epistaxis. He had visited local clinics several times for treatment, but treatments were ineffective. No nasal congestion, tenderness, or trauma were noted. He denied smoking or alcohol consumption, and his medical history was unremarkable. A rigid nasopharyngoscope revealed a reddish tumor, measuring 1 × 1 cm, located anterior to the uncinate process in the right nasal cavity. A computed tomography scan demonstrated increased soft-tissue density anterior to the right middle turbinate (Figure 1). Under general anesthesia, the patient underwent endoscopic sinonasal surgery to totally remove the bleeding tumor. He made a good recovery without complications.

Microscopic examination of the surgical specimen showed proliferation of epithelioid cells with intracytoplasmic lumina in a "nest-like" arrangement (Figure 2). Erythrocytes were also present in intra-

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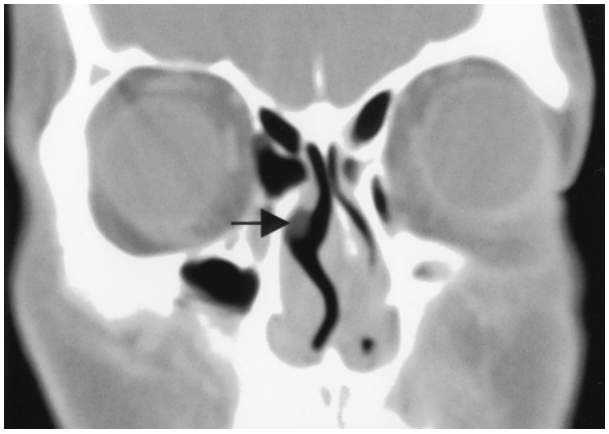

Figure 1. Increased soft-tissue density anterior to the right middle turbinate (arrow).

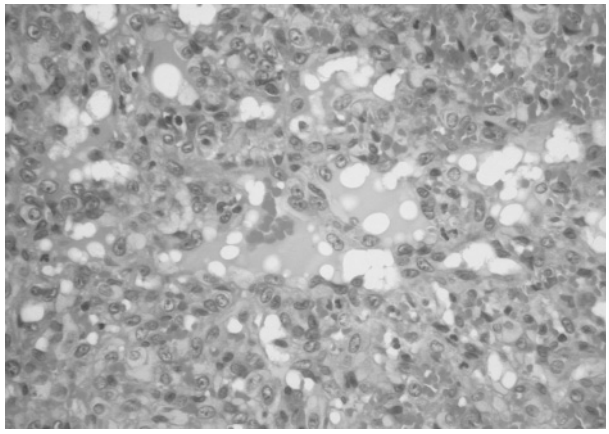

Figure 2. Epithelioid tumor cells are arranged in a "nest-like" pattern (hematoxylin & eosin, × 150).

cytoplasmic vacuoles (Figure 3). Immunostains for CD34 cells (1:60; Dako Corp, Carpinteria, CA, USA), *Ulex europaeus* agglutinin type 1 lectin (UEA-1; 1:50; Dako Corp; Figure 4), and factor VIII-related antigen (1:20; Dako Corp), were positive. The results of cytokeratin (1:100; anti-cytokeratin monoclonal antibody [AE1/AE3], Signet Labs, Dedham, MA, USA) and epithelial-membrane antigen (EMA; 1:30; Dako Corp) testing were negative. There were few mitotic figures and cases of mild atypia noted. From the above histopathologic and immunohistochemical findings, the diagnosis of EH of the nasal cavity was made.

To exclude a multicentric location and distant metastasis, chest X-ray, ultrasound of the neck and whole abdomen, and a whole-body bone scan, were performed, but were not significant. The patient was followed up regularly after surgery, and there was no evidence of recurrence 36 months later.

Discussion

EH is an uncommon vascular tumor of the soft tissues, characterized by proliferation of endothelial cells with an epithelioid morphology.[1] Although diverse anatomic locations of EH, such as in the bone, lung, liver and the extremities, have been reported,[1–5] EH in the head and neck has been seen infrequently. EH can occur at almost any age, but rarely occurs during childhood. It affects both sexes equally. To date, no predisposing factors have been identified, but possible associations with trauma, therapeutic radiation, and hormonal factors have been considered.[4] The tumor cells often develop as a painful mass (1 month to 4 years' duration) in either superficial or deep soft tissue. On gross inspection, the tumor usually has a variegated, white-red color that offers a hint of its vascular nature.[5]

Histologically, the tumor is composed of short strands or solid nests of rounded to slightly spindled endothelial cells. Some canalized vascular channels and clusters of erythrocytes are seen. These tumor cells

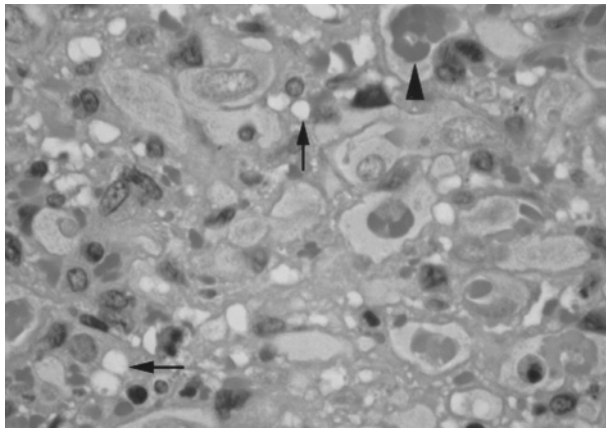

Figure 3. Tumor cells are vacuolated, with intracellular lumen formation (arrows); erythrocytes are also present in intracytoplasmic vacuoles (arrowhead) (hematoxylin & eosin, × 300).

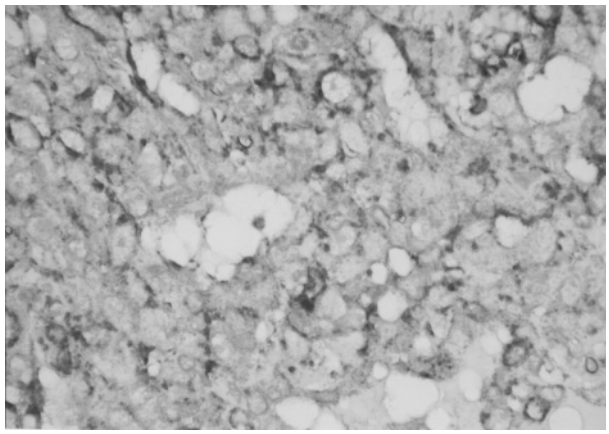

Figure 4. Tumor cells are immunoreactive to *Ulex europaeus* agglutinin type 1 lectin (UEA-1, × 300).

have the characteristics of abundant eosinophilic cytoplasm, with prominent vacuolization and intracellular lumen formation. A few mitotic figures and myxoid changes in the stroma are also identified. An angiocentric growth pattern is sometimes seen.

Immunohistochemistry may provide reliable clues about differentiation. The tumor tissue of EH exhibits mesenchymal or endothelial characteristics: staining is moderately to strongly positive for vimentin, indicating a mesenchymal cell nature;[6] and factor VIII-related antigen, CD34, and UEA-1 indicate an endothelial cell nature.[7] The staining is also negative for both cytokeratin and EMA,[8] thus ruling out an epithelial cell origin, while S-100 protein negativity rules out lesions in Schwann cells, cartilage and adipose tissue.[9] On electron microscopy, the tumor cells have characteristics of the endothelium, including a well-developed basal lamina, pinocytotic vesicles, and occasional Weibel-Palade bodies. An abundance of intermediate filaments in the cytoplasm is also noted.[4] In this case, the tumor was firm, dark-brown, well-encapsulated, and measured about 1 × 1 × 0.5 cm. The histopathologic findings were compatible with EH. The tumor cells were immunoreactive for vimentin, CD34, factor VIII-related antigen and UEA-1, while non-reactive for cytokeratin and EMA. From the above findings, the diagnosis of EH was established.

Clinically, nasal EH is hard to differentiate from benign lesions, including pyogenic granuloma, hemangioma, angiomyoma, arteriovenous malformation, and hamartoma. A definitive diagnosis depends on histopathologic and immunochemical features. The microscopic differential diagnosis includes metastatic carcinoma, epithelioid angiosarcoma and epithelioid sarcoma.[4] In comparison with EH, metastatic carcinomas show greater degrees of nuclear atypia, more mitotic figures, and are positive for cytokeratins, whereas EH is negative for cytokeratins and positive for UEA-1. The distinction between a histologically malignant form of EH and an epithelioid angiosarcoma is that the latter shows vascular differentiation with irregular anastomotic vascular channels. In addition, epithelioid sarcoma is composed of rounded eosinophilic cells surrounding cores of necrotic debris and collagen, and often develops in the distal extremities of younger people.

The prognosis of EH in the head and neck region is unpredictable. However, EH displaying features of cellular atypia, mitotic activity (> 1 mitotic figure per 10 high-power fields), necrosis and extensive spindling favors an aggressive course and correlates with poor prognosis.[4] In this case, few mitotic figures and mild cytologic atypia were identified; thus, the histopathologic features were less aggressive.

Enzinger and Weiss indicated that EH has a biologic feature between that of hemangioma and conventional angiosarcoma.[4] In a series of patients with soft-tissue EH, 13% had local recurrences, 31% had developed metastases, and 13% of patients died from the tumor, all within a 4-year period.[10] Half of all metastases are in the regional lymph nodes, and excision of these structures may result in cure, or at least in long-term survival.[10] Therefore, wide local excision is considered the treatment of choice, and is probably curative in most cases.[10] In a few cases, adjuvant treatment with radiotherapy or chemotherapy has been given.[2,3,11] Histologically malignant forms of EH should be treated similarly to other sarcomas, with radical local excision and regional lymph node dissection as indicated.[4] In our case, we performed a detailed survey, including chest X-ray, ultrasound of neck soft tissue and the whole abdomen, and a whole-body bone scan, but no evidence of distant metastasis or multifocal involvement was found. From the above findings and favorable histopathologic picture, we decided not to proceed with further treatment, other than close follow-up. The patient has been free of recurrence for 36 months.

In conclusion, EH is an uncommon vascular tumor of intermediate malignancy, which is occasionally seen in the cervical soft tissue of the head and neck region. Occurrence of EH in the nasal cavity is rare. Definitive diagnosis relies on its histopathologic and immunohistochemical features. Wide excision is the treatment of choice, and the possibility of local recurrence and distant metastasis should be evaluated.

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