Primary epithelioid hemangioendothelioma of the kidney and penis

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Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor of low malignant potential most commonly found in the lung, liver, and soft tissues. Here we describe the very rare presentations of primary EHE in the kidney and on the penis. One patient is a 59-year-old man with a renal lesion found incidentally on surveillance radiography, and the other is a 26-year-old man with an asymptomatic subdermal glanular lesion. Both were treated surgically via open partial nephrectomy and partial penectomy, respectively. Surgery is standard treatment, and close clinical follow up is necessary due to the unpredictable nature of EHE.

Key Words: epithelioid hemangioendothelioma, primary epithelioid hemangioendothelioma, kidney, penis

Introduction

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor of low malignant potential. EHE tends to occur in the soft tissues, but also occurs in the lung, liver, and bone, with numerous reports of the involvement of other anatomic locations.[1-4] The occurrence of these tumors in the kidney and the penis is particularly unusual. Here we describe two such cases: one of a man with an incidentally found renal lesion on surveillance radiography and an asymptomatic subdermal glanular lesion.

Case one

A 59-year-old man with a history of metastatic esophageal carcinoma, managed by esophagectomy for the primary tumor and successful gamma knife radiosurgery for brain metastases, was later found on surveillance CT to have a renal lesion concerning for metastasis. The lesion was a 2 cm enhancing cystic mass with solid elements on the upper pole of the left kidney. Due to its peripheral location and the patient's prior surgical history, the patient was offered an open partial. Final pathology later confirmed that the tumor was an epithelioid hemangioendothelioma. Notably, immunohistochemical stains for pankeratin were negative, essentially ruling out the possibility of metastatic esophageal carcinoma, while CD 31 stains were positive supporting diagnosis, Figure 1, 2 and 3.

Case two

A 26-year-old smoker with a history of diabetes mellitus type I presented with an asymptomatic subdermal lesion on the distal aspect of his penis. The lesion measured 0.5 cm and abutted the urethral meatus on the right glans of a circumcised penis. The remainder of the glans and penile shaft were normal, and no inguinal lymphadenopathy was appreciated. Of note, the patient denied any prior

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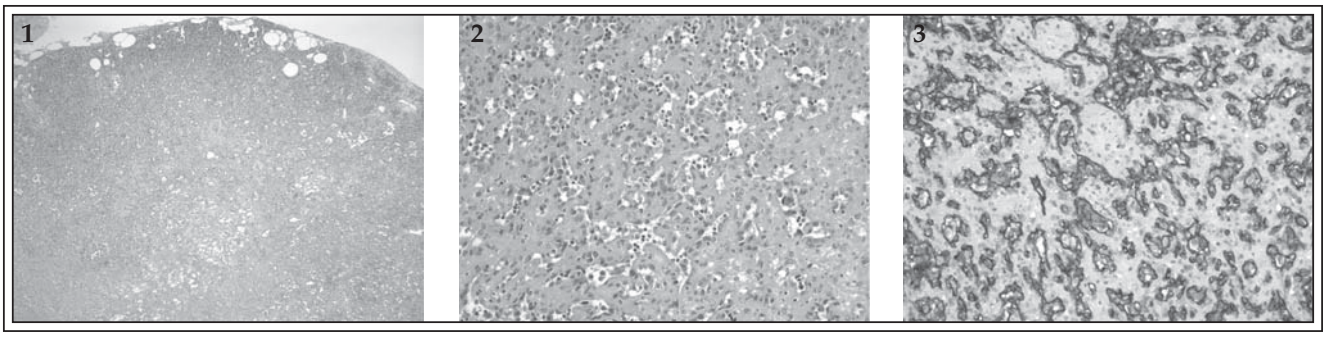

Figure 1. Kidney (4X). The normal kidney parenchyma is predominately replaced by a tumor composed of short strands and cords of rounded to slightly spindled eosinophilic epithelioid endothelial cells. The neoplastic epithelioid endothelial cells are embedded in a distinctive, sulfated acid-rich matrix which is deep pink in color.
Figure 2. Kidney (20X). High power view shows the bland epithelioid endothelial cells with scant mitotic activity.
Figure 3. Kidney (20X). Immunohistochemical stain for CD31, one of the most sensitive and specific endothelial markers in paraffin sections, highlights the vascular network of endothelial cells that compose the tumor.

history of sexually transmitted infections or lesions, and he denied any family history of genitourinary malignancies. Prior to urologic referral, an incisional biopsy was performed; histopathologic workup revealed an epithelioid hemangioendothelioma. Immunohistochemical analysis showed an infiltrating neoplasm composed of large epithelioid cells. The cells stained positive for CD31, von Willebrand factor, and factor XIA. CT scan of the abdomen and pelvis revealed no evidence of metastasis. A partial penectomy was done with frozen sections to minimize cosmetic and functional limitations. The urethra was spatulated and the glans was reconstructed to attain a symmetric appearance. On final pathology, immunohistochemical features of the excised lesion matched those of the patient's prior diagnostic biopsy, Figures 4, 5 and 6.

Discussion

Epithelioid hemangioendothelioma was first described by Weiss and Enzinger in 1982,[5] and is part of a family of vascular proliferations linked by the presence of epithelioid endothelial cells. It is thought of as a low grade malignant tumor with the high grade version being epithelioid angiosarcoma. Hemangioendotheliomas are intermediate in malignant potential between the benign hemangioma and the more aggressive sarcoma. The rate of recurrence of EHE is nearly 40%. Mortality rates differ by anatomic location and have been reported as 13% in soft tissues, 35% in the liver, and 65% in the lung. Rates of metastasis similarly differ by location and are approximately 20% with soft tissue primaries, 25% with liver primaries, and 15% with lung primaries.[6,7] Of note, the often confused epithelioid hemangioma

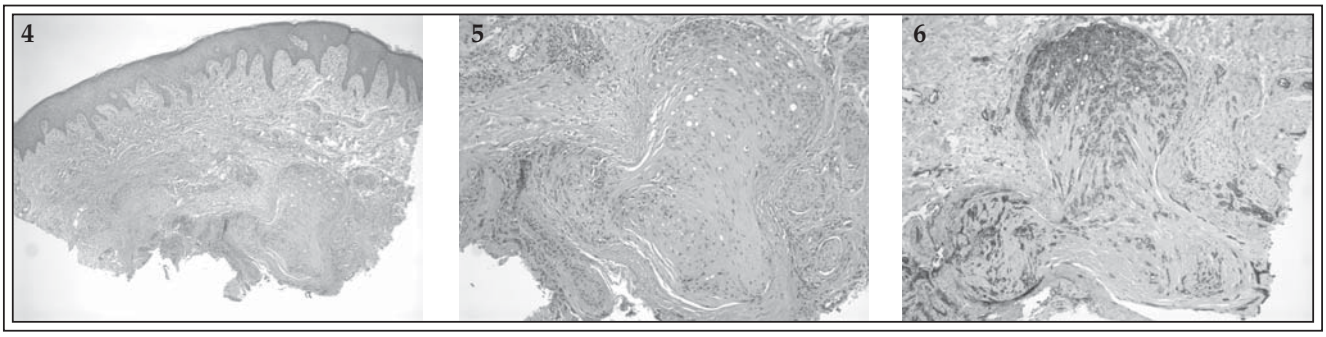

Figure 4. Skin from penis (4X). This sections shows skin with some overlying epidermal hyperplasia and an expansile dermal lesion at the base of the biopsy.
Figure 5. Skin from penis (20X). The dermal lesion is an infiltrative tumor composed of large epithelioid cells with a focal myxoid matrix. Additionally, there are foci of epithelioid cells present within the lumens of vessels.
Figure 6. Skin from penis (20X). Immunohistochemical stain for CD31 highlights the vascular network of epithelioid endothelial cells that compose the tumor.

is more often found cutaneously whereas epithelioid hemangioepitheliomas are rarely cutaneous.[8]

The liver is a well-documented primary site of EHE. Hepatic EHE carries an estimated incidence of 1 in 1,000,000 in the general population. As opposed to other primary hepatic malignancies, hepatic EHE does not seem to be related to chronic liver disease. Instead, contraceptive pills, vinyl chloride, and hepatic trauma are likely pathogenic contributors.[9,10] At the time of diagnosis, clinical presentations of EHE may range from right upper quadrant pain, hepatomegaly, and weight loss, to lack of symptoms. The most commonly used and most successful treatment modality is liver transplantation, with 44.8% of cases treated in this manner.[9] Five and 10 year posttransplantation survival rates are 83% and 74%, respectively.[11] Palliative options include chemotherapy and radiation. Overall treatment for hepatic EHE is decided on a case-by-case basis, taking multiple factors into account.

Despite the intermediate malignant potential of pulmonary EHE, extensive pulmonary involvement and systemic spread have been described. This neoplasm is often incidentally diagnosed on radiography, as many patients will not have symptoms. It is four times more common in females than males, with a median age of onset of 36 years and a 15-30 year life expectancy.[12-14] Therapeutic options have not been standardized, but include surgical resection and chemotherapy. The choice of treatment depends on the degree of intrathoracic spread and systemic involvement. Radiotherapy has not proven effective, due to the relatively slow growth of the tumor cells.[6,15]

Renal EHE is an incredibly rare manifestation of the disease, with only one prior existing report. In this report, a 16-year-old boy presented with syncopal episodes and headaches. CT and MRI studies revealed lytic bone lesions in all areas of the skeleton, including lesions in the lungs, liver, and kidneys.[16] In our case, primary renal EHE was discovered in a patient with metastatic esophageal carcinoma. We decided that the appropriate management is removal and regular follow up. With negative surgical margins, regular follow up includes semi annual visitations and CT scans for the first year, followed by annual visits and studies.

EHE of the soft tissues is the most common type of EHE. It usually occurs as a solitary lesion, shows no sex predilection, and follows an indolent course.[17] The penis, however, is an unusual location for this disease, with only eight papers describing penile EHE appearing in the literature. As with renal EHE, if no metastases are present, complete excision and close follow up is the usual management.[18] Metastatic EHE of the penis has been reported, but no consistent management or chemotherapeutic strategy has been established due to the paucity of cases. Our patient underwent partial penectomy. While Mohs micrographic surgery was also an option, it was felt that the location and morphology of the lesion was most amenable to simple resection. □

References

1. Dail DH, Liebow AA, Gmelich JT et al. Intravascular, bronchiolar and alveolar tumor of the lung (IVBAT): an analysis of twenty cases of a peculiar sclerosing endothelial tumor. *Cancer* 1983;51(3):452-464.
2. Ishak KG, Sesterhenn IA, Goodman ZD, Rabin L, Strohmeyer FW. Epithelioid hemangioiendothelioma of the liver: a clinicopathologic and follow-up study of 32 cases. *Hum Pathol* 1984;15(9):839-852.
3. Chow LT, Chow WH, Fong DT. Epithelioid hemangioendothelioma of the brain. *Am J Surg Pathol* 1992;16(6):619-625.
4. Resnik KS, Kantor GR, Spielvogel RL, Ryan E. Cutaneous epithelioid hemangioendothelioma without systemic involvement. *Am J Dermatopathol* 1993;15(3):272-276.
5. Weiss SW, Enzinger FM. Epithelioid hemangioendothelioma. A vascular tumor often mistaken for a carcinoma. *Cancer* 1982; 50(5):970-981.
6. Weiss SW, Ishak KG, Dail DH, Sweet DE, Enzinger FM. Epithelioid hemangioendothelioma and related lesions. *Semin Diagn Pathol* 1986;3(4):259-287.
7. Bollinger BK, Laskin WB, Knight CB. Epithelioid hemangioendothelioma with multiple site involvement. Literature review and observations. *Cancer* 1994;73(3):610-615.
8. Fetsch JF, Weiss SW. Observations concerning the pathogenesis of epithelioid hemangioma (angiolymphoid hyperplasia). *Mod Pathol* 1991;4(4):449-455.
9. Mehrabi A, Kashfi A, Fonouni H et al. Primary malignant hepatic epithelioid hemangioendothelioma. A comprehensive review of the literature with emphasis on the surgical therapy. *Cancer* 2006;107(9):2108-2121.
10. Gelin M, Van de Stadt J, Richaert F et al. Epithelioid hemangioendothelioma of the liver following contact with vinyl chloride: Recurrence after orthotopic liver transplantation. *J Hepatol* 1989;8(1):99-106.
11. Lerut JP, Orlando G, Adam R, et al. The place of liver transplantation in the treatment of hepatic epithelioid hemangioendothelioma: report of the European liver transplant registry. *Ann Surg* 2007;246(6):949-957.
12. Kitaichi M, Nagai S, Nishimura K et al. Pulmonary epithelioid haemangioendothelioma in 21 patients, including three with partial spontaneous regression. *Eur Respir J* 1998;12(1):89-96.
13. Einsfelder B, Kuhnen C. Epithelioid hemangioendothelioma of the lung (IVBAT) — clinicopathological and immunohistochemical analysis of 11 cases (in German). *Pathologe* 2006;27(2):106-115.
14. Rock MJ, Kaufman RA, Lobe TE, Hensley SD, Moss ML. Epithelioid hemangioendothelioma of the lung (intravascular bronchioloalveolar tumor) in a young girl. *Pediatr Pulmonol* 1991;11(2):181-186.
15. Dail DH, Liebow AA, Gmelich JT et al. Intravascular, bronchiolar, and alveolar tumor of the lung (IVBAT). An analysis of twenty cases of a peculiar sclerosing endothelial tumor. *Cancer* 1983;51(3):452-464.
16. Adler B, Naheedy J, Yeager N, Nicol K, Klamar J. Multifocal epithelioid hemangioendothelioma in a 16-year-old boy. *Pediatr Radiol* 2005;35(10):1014-1018.
17. Ellis GL, Kratochvil FJ. Epithelioid hemangioendothelioma of the head and neck: a clinicopathologic report of twelve cases. *Oral Surg Oral Med Oral Pathol* 1986;61(1):61-68.
18. Deyrup AT, Tighiouart M, Montag AG, Weiss SW. Epithelioid hemangioendothelioma of soft tissue: a proposal for risk stratification based on 49 cases. *Amer J Surg Path* 2008;32(6):924-927.