CLINICAL VIGNETTE

Pseudomyogenic Hemangioendothelioma: Not so Malignant but not a Benign Disorder

Anita Kaul, M.D. and Shahryar Ashouri, M.D.

Case Review

A 60-year-old, otherwise healthy, female had persistent pain in right groin and inner upper thigh interfering with sleep and ambulation. She also noted nodular lesions in the groin area. She was treated with empiric antibiotics and underwent biopsies. The skin lesions gradually increased in size and number over months and extended to involve the vulva. The lesions were purplish and clustered in somewhat linear fashion on the skin and subcutaneous area. There were no enlarged lymph nodes. The pain increased with certain leg positions. There were no other significant findings and no known exposure.

PET/CT scan showed area of hyper metabolism in right femoral neck with corresponding area on CT scan showing a cortical defect. Other lesions were seen as radiolucencies in right femoral head and trochanter. Separate soft tissue lesions with indistinct margins were also seen in the right upper thigh. Some were adjacent to skin with some thickening of the overlying skin. There were hyper metabolic lesions seen in adductor muscle. Other than these clusters of lesions in right proximal thigh, no lesions were described elsewhere or on left thigh. Mild arthritis changes of spine were seen. Lesions ranged in size from less than 1 cm to just over 2 cm and SUV ranged from 2.7 to 9.

MR of the right thigh showed multiple enhancing lesions involving the bone in right femoral head and neck, adductor magnus, and obturator externus muscle as well as subcutaneous tissue and skin of the right inner thigh. At the femur, there were focal regions of cortical destruction involving the greater and lesser trochanter. These lesions enhanced with high signal on T2 images and low signal on T1 images. The lesser trochanter lesion appeared to extend into soft tissue. Similarly, the greater trochanter lesion also appeared to extend locally into soft tissue. There was a slight right hip effusion. Multiple lesions were also noted in muscles. An infiltrating mass was seen in the obtrurator muscle and appeared expansive and vascular in nature. At least 4 infiltrating masses were noted in the adductor muscle. Skin and subcutaneous lesions were seen and extended into volar region.

Biopsies were initially reviewed by dermatopathology, and all infection staining was negative. Due to the initial staining pattern and appearance, fibrohistocytic origin was considered. Biopsy was then reviewed at Dana Farber hospital, and by two regional pathologists.

The biopsy showed dense diffuse pleomorphic spindle cell proliferation with associated mucinous alteration and focally admixed eosinophils and neutrophils. Mitotic activity was present but not dominant. Cells had plump spindle morphology with polymorphism and some polygonal cells and some areas of epitheloid appearing cells. The process extended to upper reticular dermis. Cells had copious brightly eosinophilic cytoplasm and large atypical vesicular nuclei. Focal necrosis was present. Immunostaining was positive for Pankeratin AE1 | AE3 and CD 31 as well as CD99 and diffuse positive ERG with focally positive CD31. Stains were negative for S100, High molecular weight cytokeratin and CD34, SMA and Melan A.There was focal positivity of EMA next to areas of degeneration INI -1 was positive (ie, retained or normal).

The possibility of Sarcoma and Pseduomyogenic Hemangioendothelioma (PMHE) was raised based on morphology and the immunological features, which fitted well with PMHE. Clinically she had multiple lesions that involved multiple tissue planes, skin, and soft tissue as well as underlying bone. These lesions were all clustered in proximal right thigh and nowhere else.

Epitheloid Sarcoma like Hemangioendothelioma (ES-H) is now considered to be same as PMHE.[1] Some of the same cases were also included under different names, including fibroma like variant of epitheloid sarcoma or spindle cell variant of epitheloid sarcoma. These low grade neoplasm often present with cutaneous vascular proliferations to dermatologists.[2] Multiple lesions (multicentric) are grouped together in an anatomical region non-specific clinical appearance. Painful nodules are present in half the cases.[3] The lesions are poorly circumscribed with architectural features of malignant neoplasm including infiltrative borders involving adjacent soft tissue and multiple lesions involving several tissue planes. Differential diagnosis includes sarcoma, Hemangioendothelioma, and Angiosarcoma.[4] ES-H is more often seen in young adults and more often involves distal

lower extremities. Male patients outnumber female patients. These lesions have low to intermediate malignant potential and show frequent local recurrence but infrequent distant metastasis (<7% in one series) with surgical management.[3,4] Dermal lesions can show some epidermal hyperplasia, similar to dermatofibroma. Histologically, most show fascicular patterns and sheets of plump spindle cells with some areas of myxoid stroma and neutrophil infiltration as in our case. Spindle cells often have rounded or oval appearance with brightly eosinophilic cytoplasm vesicular nuclei and prominent nucleoli. Mitosis are infrequent. Some foci of polymorphic cells are seen, and some intravascular invasion into entrapped blood vessels is seen without vasoformations.[3-6]

Neoplastic cells show expression of cytokeratin AE1/AE3, CD 31, ERG. They usually show FLI-1 staining and variable focal and weaker staining for CAM 5.2, smooth muscle actin, epithelial membrane antigen (EMA), and pancytokeratin MNF-116. The cells always keep intact expression of INI-1. Endothelial nature is suggested because of positive ERG, CD 31, and FLI-1 expression. CD34, desmin and S-100 stains are negative.[6-8] FISH showing, t (7, 19) (q22;q13) has been reported in PMHE.[9]

Whenever possible, surgical excision and, if required, post-operative radiation therapy for close margins may be adequate in PMHE. However in our patient, lesions were quite proximal and complete excision would require amputation up to and including hip girdle. Therefore, only partial resection for pain relief and internal fixation of hip was undertaken. During initial treatment, local recurrences in the same region were seen. Some proximal type Epitheloid Sarcomas presenting in similar manner have been reported with more aggressive course, but those are Epithelod myxofibrosarcomas, a clinically more aggressive entity. Along with partial resection, she was treated with Bevacizamab and Temazolamide initially without response and subsequently with Bevacizamab with liposomal paclitaxel and Platinum and radiation of involved field with good partial response clinically. She is being monitored at this time, now 18 months since diagnosis.

REFERENCES

1. **Billings SD, Folpe AL, Weiss SW**. Epithelioid Sarcoma-like hemangioendothelioma (pseudomyogenic hemangioendothelioma). *Am J Surg Pathol*. 2011 Jul;35(7):1088; author reply 1088-9. doi: 10.1097/PAS.0b013e31821caf1c. PubMed PMID: 21677548.
2. **Requena L, Santonja C, Martinez-Amo JL, Saus C, Kutzner H**. Cutaneous epithelioid sarcomalike (pseudomyogenic) hemangioendothelioma: a little-known low-grade cutaneous vascular neoplasm. *JAMA Dermatol*. 2013 Apr;149(4):459-65. doi: 10.1001/jamadermatol.2013.3190. PubMed PMID: 23715533.
3. **Hornick JL, Fletcher CD**. Pseudomyogenic hemangioendothelioma: a distinctive, often multicentric tumor with indolent behavior. *Am J Surg Pathol*. 2011 Feb;35(2):190-201. doi: 10.1097/PAS.0b013e3181ff0901. PubMed PMID: 21263239.
4. **Billings SD, Folpe AL, Weiss SW**. Epithelioid sarcoma-like hemangioendothelioma. *Am J Surg Pathol*. 2003 Jan;27(1):48-57. PubMed PMID: 12502927.
5. **Watabe A, Okuyama R, Hashimoto A, Hosaka M, Hatori M, Kariya Y, Watanabe M, Hashimoto H, Tagami H, Aiba S**. Epithelioid sarcoma-like haemangioendothelioma: a case report. *Acta Derm Venereol*. 2009;89(2):208-9. doi: 10.2340/00015555-0599. PubMed PMID: 19326021.
6. **Miettinen M, Fanburg-Smith JC, Virolainen M, Shmookler BM, Fetsch JF**. Epithelioid sarcoma: an immunohistochemical analysis of 112 classical and variant cases and a discussion of the differential diagnosis. *Hum Pathol*. 1999 Aug;30(8):934-42. PubMed PMID: 10452506.
7. **Cheah AL, Billings SD**. The role of molecular testing in the diagnosis of cutaneous soft tissue tumors. *Semin Cutan Med Surg*. 2012 Dec;31(4):221-33. doi: 10.1016/j.sder.2012.07.008. Review. PubMed PMID: 23174492.
8. **Cheah AL, Goldblum JR, Billings SD**. Molecular diagnostics complementing morphology in superficial mesenchymal tumors. *Semin Diagn Pathol*. 2013 Feb;30(1):95-109. doi: 10.1053/j.semdp.2012.01.005. Review. PubMed PMID:23327733.
9. **Trombetta D, Magnusson L, von Steyern FV, Hornick JL, Fletcher CD, Mertens F**. Translocation t(7;19)(q22;q13) − a recurrent chromosome aberration in pseudomyogenic hemangioendothelioma? *Cancer Genet*. 2011 Apr;204(4):211-5. doi:10.1016/j.cancergen.2011.01.002. PubMed PMID: 21536240.

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