Spindle Cell Hemangioendothelioma

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GOAL

To understand spindle cell hemangioendothelioma (HE) to better manage patients with the condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Identify the primary sites of origin of spindle cell HE.
2. Describe the radiographic and histologic presentation of spindle cell HE.
3. Discuss treatment options for spindle cell HE.

CME Test on page 136.

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Prior to the 1980s, the term hemangioendothelioma *(HE) loosely applied to a spectrum of vascular tumors ranging from benign tumors, such as capillary hemangiomas, to fully malignant angiosarcomas. In the early 1980s, the term* epithelioid HE *was used to describe a heterogeneous group of vascular tumors with an intermediate clinical course between hemangiomas and conventional angiosarcomas, thereby bringing to notice the borderline nature of these tumors. Since then, HEs have become a distinct entity, being further classified into spindle cell HE, retiform HE, kaposiform HE, and polymorphous HE. We present a case of spindle cell HE that began as an interdigital nodule and progressively became multifocal to involve the entire right upper extremity and chest wall, despite multiple surgical excisions, resulting in severe ongoing disfigurement of the patient.*

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Case Report

A 43-year-old woman presented with several painful nodules on her right arm, shoulder, and right side of the chest wall. When the patient was 5 years old, an isolated, small, nontender, flesh-colored nodule at the tip of the right index finger developed, which was thought to be a keloid. The lesion gradually grew, and

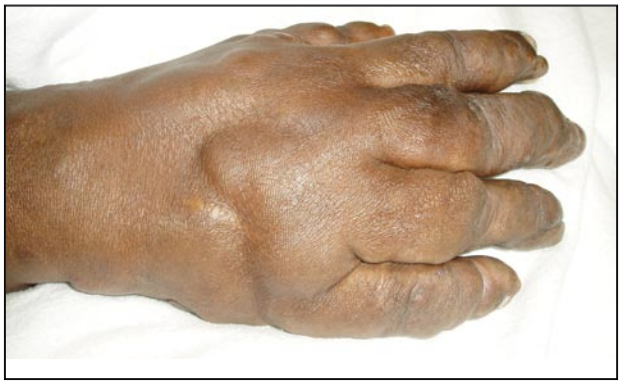

Figure 1. The dorsal aspect of the patient's right hand has multiple soft tissue masses without discoloration or ulceration of the overlying skin.

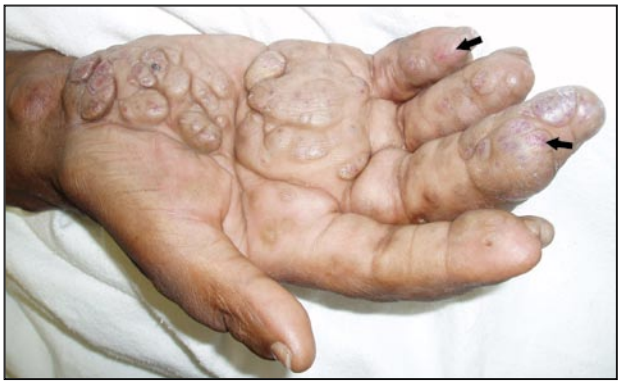

Figure 2. Multiple soft tissue masses on the palmar aspect of the patient's right hand, some of these nodules with reddish-violet discoloration (arrows), suggestive of a vascular lesion. No ulceration of the overlying skin is present.

multiple nodules appeared on her right hand and forearm. Despite multiple surgical excisions, the lesions not only continued to recur in operated sites but also progressed proximally to involve the entire right upper extremity as well as the right chest wall. Results of a physical examination revealed poorly demarcated nodules, less than 1 to 3 cm in diameter, some with a reddish-violet tinge but with no ulceration of the overlying skin (Figures 1 and 2). The nodules were soft, compressible, nonpulsatile, tender to palpation, and movable within the subcutaneous tissue. Port-wine stains and varicosities were noticeably absent. Hand function was mechanically compromised and wrist extension was very weak.

Fifteen years earlier, a radiograph of the patient's right hand demonstrated multiple soft tissue masses with multiple phleboliths (Figure 3); a biopsy specimen of the lesion examined at our hospital was interpreted as cavernous hemangioma. There were no such lesions elsewhere on the body. Results of radiographs of the right hand and forearm from the patient's current visit demonstrated multiple soft tissue masses with marked increase in the number of phleboliths but no bony growths or

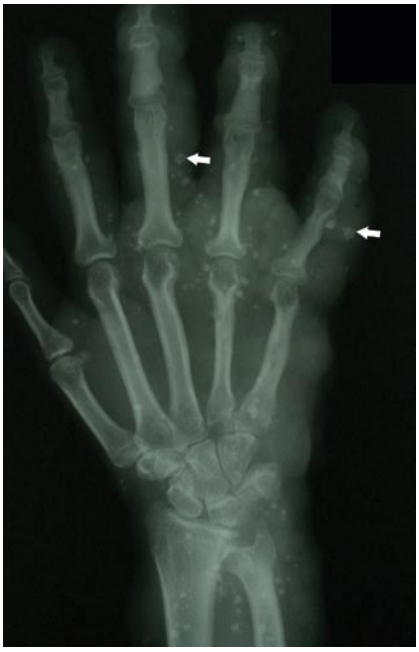

Figure 3. Fifteen years prior to presenting at our office, a radiograph of the right hand showed multiple phleboliths (arrows) within the soft tissue masses. There were no bony outgrowths or fractures.

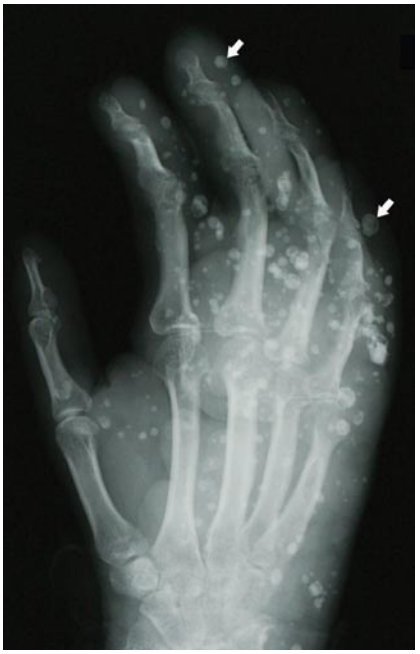

Figure 4. Radiograph results of the right hand from the current presentation demonstrated marked increase in the number of phleboliths (arrows) within the soft tissue masses. There were no bony outgrowths or fractures.

deformities (Figure 4). Results of an ultrasound examination did not show deep venous thrombosis. Results of magnetic resonance imaging of the right hand and forearm again revealed multiple soft tissue masses (Figure 5). Angiogram and tomogram results revealed pooling of blood in cavernous spaces of the soft tissue masses but no arteriovenous malformations (Figure 6). Findings from a surgical dissection revealed right forearm extensor tendon involvement. The surgical dissection was followed by excisional biopsy (with minimal healthy margins) and skin grafting.

Results of histologic examination 15 years prior revealed a poorly circumscribed dermis and subcutis, with thin-walled cavernous spaces containing focal areas of organizing thrombosis and spindle-shaped cells admixed with solid cellular components. At high power magnification, no mitotic activity was seen either in the endothelial or spindle cells. Despite multiple surgeries, embolizations, and radiation, the lesions continued to progress proximally, resulting in marked disfigurement of the involved extremity. The patient currently uses a custom surgical compression stocking for her right arm.

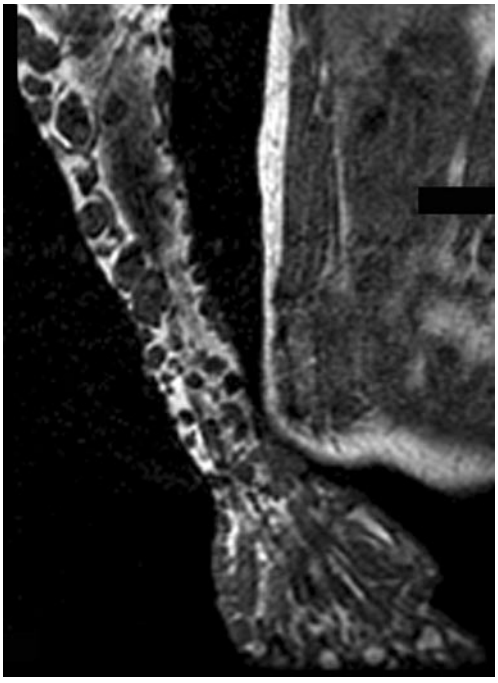

Figure 5. Results of magnetic resonance imaging of the right hand and forearm confirmed soft tissue masses.

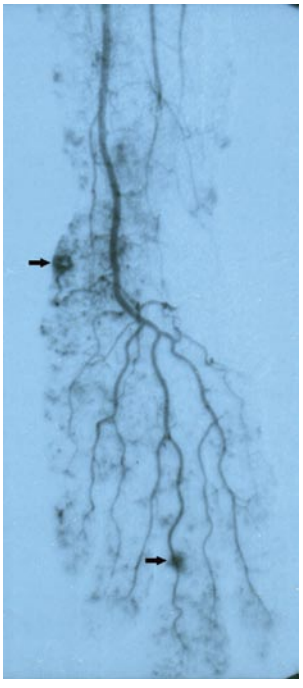

Figure 6. Angiogram results of the right hand showed pooling of blood (arrows) in cavernous spaces of the soft tissue masses.

Comment

In 1982, Weiss and Enzinger[1] were the first to use the term *epithelioid hemangioendothelioma* (HE). Spindle cell HE was first described by Weiss and Enzinger[2] in 1986 and was characterized by the presence of thin-walled, cavernous, vascular spaces, some containing phleboliths, alternating with cellular stroma composed of spindled fibroblastic cells. Perkins and Weiss[3] extensively evaluated 78 cases of spindle cell HE to reassess the lesion's biologic behavior. Males and females were found to be equally affected with a median age of onset of 32 years (range, 8–78 years).[3] Patients with spindle cell HE typically present with slow growing, infiltrative, uninodular, or multinodular dermal or subcutaneous masses originating most commonly in the distal extremities, with a tendency to cluster in one region.[3,4] The head, neck, chest, and abdomen also have been reported as primary sites of origin in a minority of cases.[3] These masses often cause little or no discoloration of the overlying skin, which precludes identification as a vascular lesion, though reddish-brown discoloration observed in some patients can be suggestive of spindle cell HE.[3,4] Patients often seek medical attention late, with a delay of 10 years or more in nearly one third of patients.[3]

Radiograph findings of spindle cell HEs can show phleboliths within circumscribed soft tissue masses, suggesting the vascular nature of these tumors. In our case, the notable absence of enchondromas distinguishes it from Maffucci syndrome, which is seen in approximately 5% of patients with spindle cell HE.[3] The absence of port-wine stains, varicosities, and arteriovenous malformations differentiates our case from Klippel-Trenaunay syndrome and Klippel-Trenaunay-Weber syndrome.

Histopathologic findings of these HE masses typically show 2 zones. The first zone is comprised of thin-walled cavernous spaces lined by flattened differentiated endothelial cells. These spaces either may be empty or filled with erythrocytes, thrombi, or phleboliths. The second zone typically consists of differentiated spindle-shaped fibroblastic cells interspersed by collapsed cavernous spaces, some areas with polygonal endothelial cells (epithelioid) and cytoplasmic vacuolation,[3] which in our case, combined with a nonreactive human immunodeficiency virus test, differentiates it from Kaposi sarcoma. These spindle cells almost never contain significant nuclear atypia or mitotic activity. Because metastases have not been reported in association with spindle cell HE, except in one case that was believed to be radiation-induced sarcomatous transformation,[3] the very introduction of this entity as a low-grade angiosarcoma has been questioned. It is now believed that spindle cell HE is most likely a benign reactive process that develops because of aberrations in local blood flow,[3-6] which Perkins and Weiss[3] have restudied and recommended that the entity be renamed *spindle cell HE* for solitary lesions and *spindle cell hemangiomatosis* for multifocal lesions.

Treatment for these tumors should be conservative because of their benign clinical behavior. Several therapeutic approaches, including surgery, systemic steroids, cryotherapy, laser therapy, radiation therapy, cytotoxic drugs, and selective embolization, have been used.[7] Recombinant interleukin 2, a T-cell derived lymphokine with immunologic functions (eg, induction of lymphokine-activated killer cells, augmentation of activities of cytotoxic T cells and natural killer cells), has been tried with success. Radiation therapy should be discouraged because of a report of sarcomatous transformation with subsequent metastasis.[3,7] Clinical surveillance is mandatory with spindle cell HE and Maffucci syndrome because of increased risk of chondrosarcoma and other neoplasms.[3]

Conclusion

Spindle cell HE is a rare vascular tumor of benign behavior that often starts as a soft tissue nodule in distal extremities that multiplies over time, with a tendency to cluster in one region. Patients often seek medical attention for cosmetic reasons and present late. Radiograph findings may demonstrate phleboliths, and an increase in the number of phleboliths may suggest progression, as seen in our case. Associated conditions include Maffucci, Klippel-Trenaunay, and Klippel-Trenaunay-Weber syndromes. Histologically, it is important to differentiate this entity from others that may assume a spindle appearance (eg, Kaposi sarcoma) or an epithelioid appearance (eg, metastatic carcinoma, various sarcomas). Although best treated with surgical resection, these tumors tend to have local and regional recurrence. Radiation therapy, as delivered in our case, should not be used because of the possibility of malignant transformation.

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