

Case report

Spindle-cell hemangioendothelioma of the oral cavity. A case report

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We describe a vascular tumor classified as SCH by histological criteria that was found in the mandibular-buccal fold of a 12-year-old girl. Microscopically, the lesion consisted of thin-walled cavernous spaces containing thrombi and phleboliths, and cellular areas composed of spindle-shaped, epithelioid and vacuolated cells. Immunohistochemically, the endothelial vascular lining was highly reactive with HAM56 antibody, while variable reactivity was observed for factor VIII-associated antigen. All cell types were positive for vimentin and anti-PCNA stained less than 3% of the tumor cells. This is the first report of SCH in the oral cavity.

Key words: soft tissue tumors; spindle cell hemangioendothelioma; vascular tumors.

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Spindle cell hemangioendothelioma (SCH) was first described by WEISS & ENZINGER in 1986 (1) as a vascular tumor resembling cavernous hemangioma and Kaposi's sarcoma. It presents as solitary or multiple nodules, the latter frequently occupying the same anatomical region (1). The superficial soft tissues of the distal portions of the extremities are the most commonly involved sites (1, 2).

Histologically, SCH is characterized by the presence of cavernous vascular channels and interstitial spindle-shaped cells occasionally forming slit-like spaces (1, 2). There are also variable numbers of epithelioid endothelial cells and cells with cytoplasmic vacuolation (2, 3). The proportion of cavernous spaces and spindle cells may vary from portion to portion in the same lesion, and from case to case as well as among different tumors in the same patient (1, 2, 4). Cavernous spaces with organizing thrombi predominate as the lesion becomes older (5).

The tumor is considered as slowly progressing and locally aggressive, with a tendency to recur and without convincing evidence of metastasis (2). It is

regarded as a neoplasm of intermediate malignancy (6) or a reactive vascular lesion (4, 5).

We describe a vascular tumor classified as SCH by histological criteria that was found in the mandibular-buccal fold of a 12-year-old girl. To our knowledge this is the first report of SCH in the oral cavity.

Case report

A 12-year-old girl presented in 1986 with an asymptomatic, circumscribed, approximately 1 cm in diameter soft tissue nodule located in the left mandibular-buccal fold of the premolar region. The tumor was blue in color and elastic in consistency; it was freely movable and covered by intact mucosa. The medical and dental history of the patient were unremarkable.

An excisional biopsy was performed with the clinical differential diagnosis of "hemangioma or pyogenic granuloma." The patient was lost to follow-up. No recurrent or second primary tumor of the same patient have since been recorded in the files of the Department

of Oral Pathology, Faculty of Dentistry, University of Athens.

Pathologic findings

On gross examination, the surgical specimen was a circumscribed soft tissue mass measuring 0.7×0.7×0.6 cm. The cut surface was red with brown foci.

Five-micron thick formalin-fixed and paraffin-embedded tissue sections were stained with hematoxylin-eosin (H&E) and periodic acid-Schiff (PAS). Immunohistochemical staining was performed using the avidin-biotin complex (ABC) method (7). The primary monoclonal antibodies were directed against vimentin (dilution 1:3, Enzo Diagnostics, New York, NY, USA); factor VIII-associated antigen (factor VIII-AG – 1:3, Enzo); HAM56 (1:3, Enzo); and proliferating cell nuclear antigen (PCNA/ clone PC10 – 1:200, Dako, Copenhagen, Denmark). Sections stained for factor VIII-AG were treated with phosphate-buffered 0.1% trypsin (Sigma T-8235, St. Louis, MO, USA) for 30 min at 37°C before the addition of the antibody.

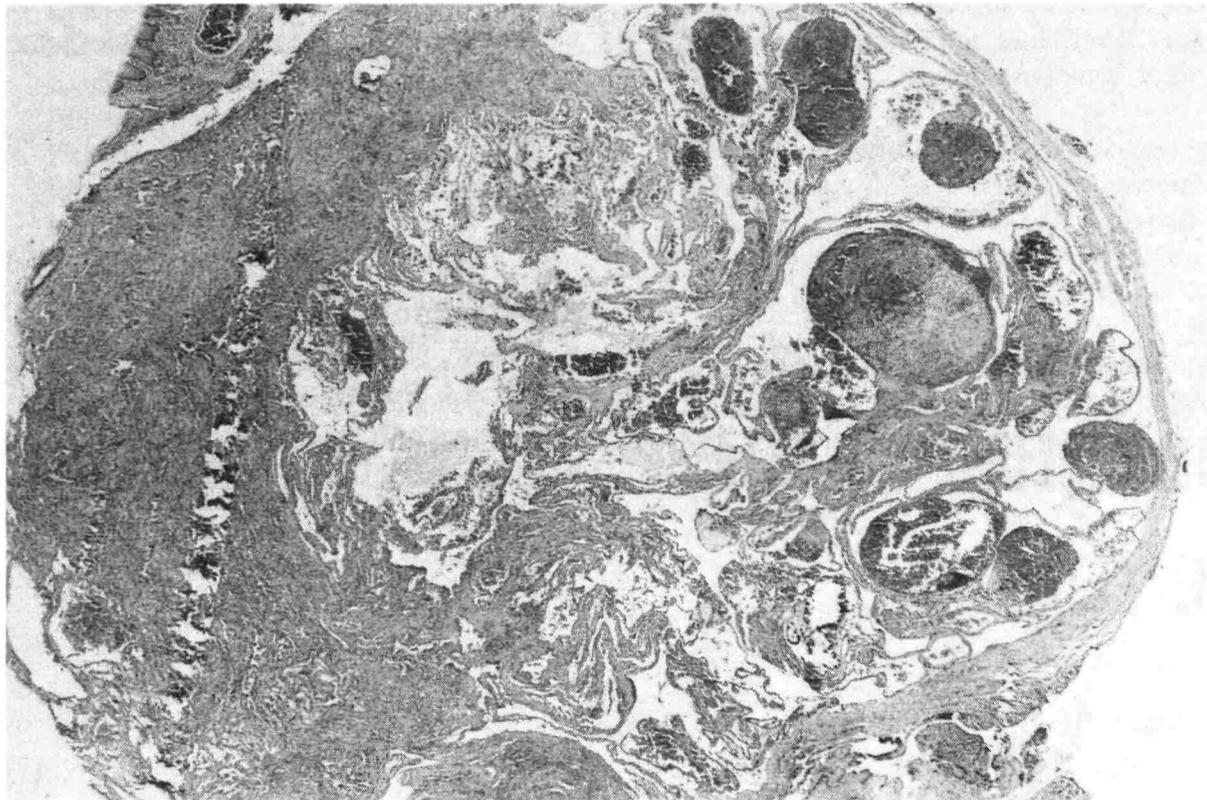


Fig. 1. Spindle cell hemangioendothelioma illustrating cavernous vascular spaces and numerous thrombi (H&E, $\times 15$).

Low-power microscopic examination revealed a nodular and relatively well-circumscribed tumor in the mucosal connective tissue, covered by thin parakeratinized squamous epithelium. Thin-walled cavernous spaces and solid cellular areas dominated the histologic pic-

ture. The vascular spaces were irregularly dilated and lined by a single layer of endothelial cells bulging into the lumen. They contained numerous thrombi at different stages of organization (Fig. 1), a few phleboliths and fibrous papillae lined by endothelial cells.

The solid cellular areas were composed of spindle cells arranged either in interlacing short fascicles or randomly among the cavernous spaces. Most spindle cells had elongated nuclei with inconspicuous nucleoli and ill-defined cytoplasmic borders (Fig. 2A). The cells were occasionally lining slit-like spaces interspersed with red blood cells and hemosiderin deposits. Among the spindle cells were nests of plump, round or polygonal epithelioid endothelial cells, with vesicular nuclei and abundant eosinophilic cytoplasm (Fig. 2B). Round vacuolated cells resembling signet-ring cells were also observed, arranged in small clusters or lining vascular spaces (Fig. 2C). Necrosis, cytologic atypia, mitotic figures, or PAS-positive hyaline globules were absent. Some medium-sized, thick-walled vessels were seen at the periphery of the lesion.

The lining endothelial cells were highly reactive with HAM56 antibody (Fig. 3) and anti-vimentin, while variable immunoreactivity was observed for factor VIII-associated antigen in those cells as well as the round vacuolated cells. Epithelioid cells, as well as the majority of spindle cells, stained for vimentin. Anti-PCNA antibody stained

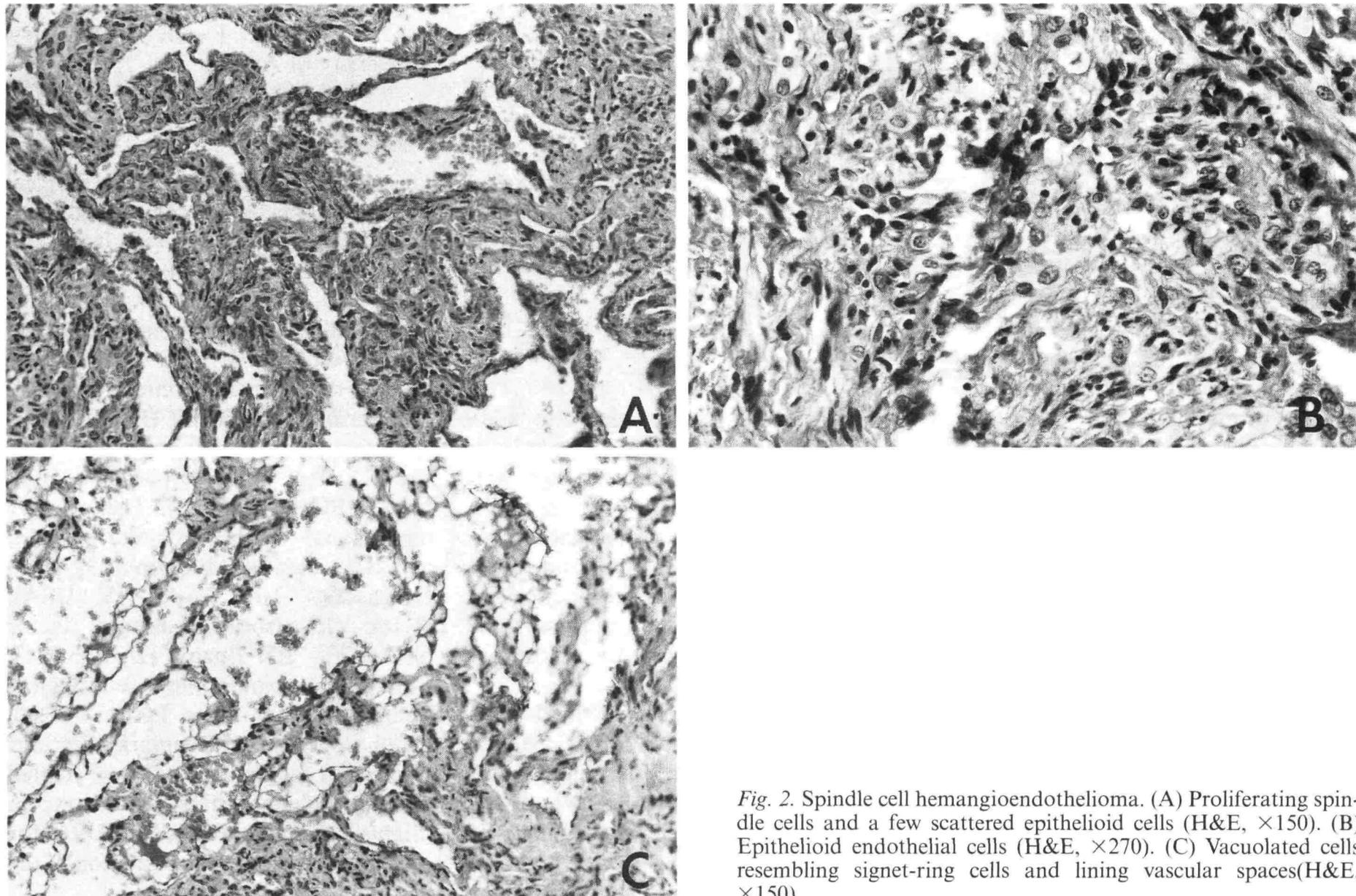


Fig. 2. Spindle cell hemangioendothelioma. (A) Proliferating spindle cells and a few scattered epithelioid cells (H&E, $\times 150$). (B) Epithelioid endothelial cells (H&E, $\times 270$). (C) Vacuolated cells resembling signet-ring cells and lining vascular spaces (H&E, $\times 150$).

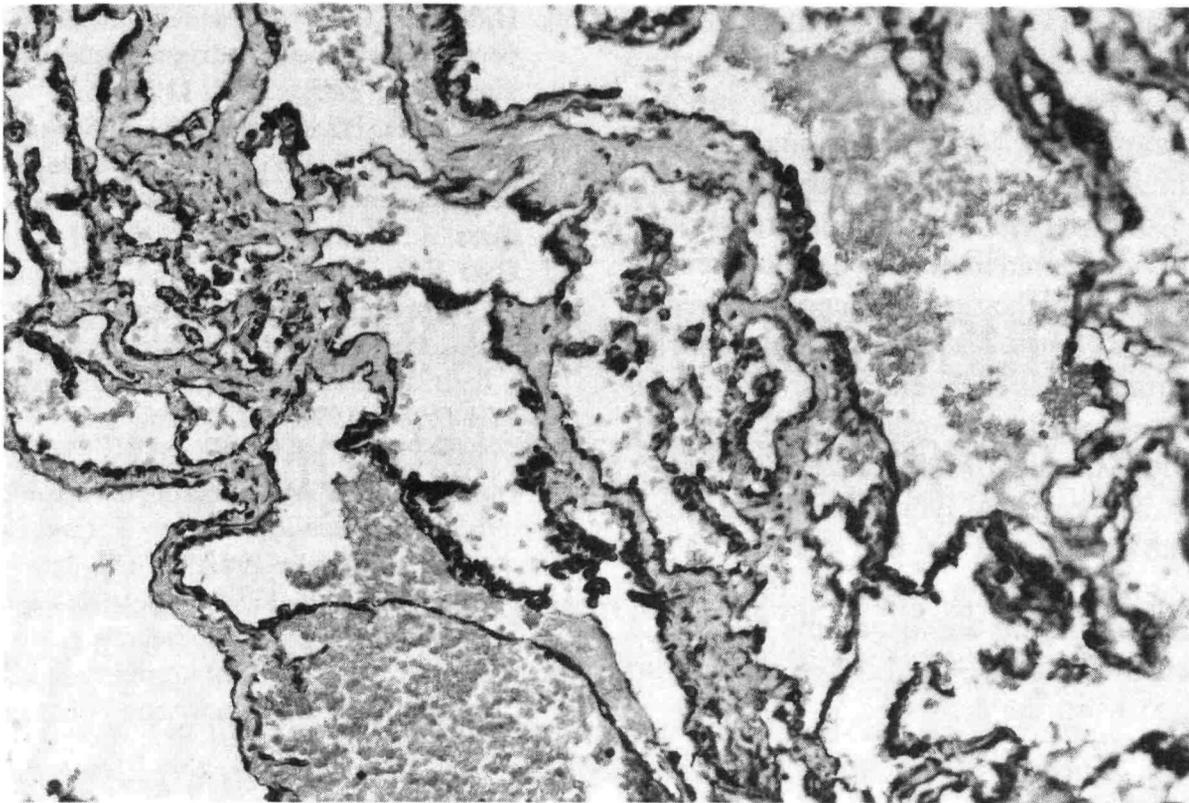


Fig. 3. Immunoperoxidase stain for HAM56 showing strong reactivity of the lining endothelial cells (ABC method, $\times 150$).

less than 3% of the tumor cells. Positive and negative controls revealed consistent immunohistochemical reactions.

Discussion

Spindle cell hemangioendothelioma is a rare vascular lesion with only 80 cases, including the present one, reported in the literature (1–5, 8–19). Cases 2 and 4 of SCOTT & ROSAI (2) were reported by WEISS & ENZINGER (1) and LAWSON & SCOTT (10), respectively, and a case seen in consultation by Weiss and Enzinger (1) was later described in detail (8). Five cases of SCH mentioned by ALLEN *et al.* (20) are excluded, as well as three cases of spindle- and epithelioid-cell vascular lesions that are not unequivocal examples of SCHs (21, 22, 23).

Upon review of the reported cases, there were 43 females and 37 males affected. The age range is broad-extending from birth (4) to 76 years (16). However, the first onset of the lesion is usually in the second, third, or fourth decade. The longest recorded duration is 50 years (16), with solitary lesions being of shorter duration. The size of the tumors ranges from a few millimeters in the majority of cases, to 11 cm (4). Forty-four lesions were solitary and 37 multiple. It is reported that solitary types tend to show multifocality (6), but definite progression from a solitary to multiple lesions is documented in four out of 17 cases (1). The superficial soft tissues of the lower and upper limbs are most frequently involved, followed by various trunk sites, vulva, penis, and

ear. No case has been previously reported in the oral region.

SCH has been seen in association with other pathologic conditions, including Maffucci's syndrome and Ollier's disease (1, 10, 19). One patient with Maffucci's syndrome had a history of acute myelomonocytic leukemia and von Willenbrand's disease, while another developed a high-grade angiosarcoma (1, 10). Three patients with SCH had chronic lymphedema, described as Milroy's disease in two of them (1, 4, 8). One of the patients with chronic lymphedema presented extensive venous malformation of the affected limb (4) and another had a recurrent epithelioid hemangioendothelioma (8). There is also a case of multiple SCHs, similar to epithelioid hemangioendotheliomas, associated with probable chronic lymphedema and a well-differentiated angiosarcoma (4). Finally, there are single case reports of SCH associated with varicose veins (4) and Klippel-Trénaunay syndrome (4). Nearly all patients with an associated disease present with multiple SCHs. No other pathologic condition affected our patient.

The pathogenesis of SCH is unknown. Originally SCH was defined as a low-grade angiosarcoma or vascular neoplasm of intermediate malignancy on the basis of its tendency to affect large areas of the body progressively (1). Malignancy, however, is disputed by the lack of distant metastases, long clinical course and multifocality of the lesions (4, 16, 24). Microscopic features of SCH that are not consistent with a

malignant phenotype are the lack of cellular atypia, the identification of multiple cell-types including dendritic macrophages, the presence of cavernous spaces with organizing thrombi (5, 16, 24), and the diploidy of the tumor cells (15). The proliferative activity of tumor cells is low, as indicated by the lack of mitoses (5, 4, 16) and the scant PCNA positivity observed in our case.

FLETCHER *et al.* (4) were the first to investigate the possible non-neoplastic nature of SCH. They suggest that SCH arises in association with an acquired or congenital focal abnormality of blood flow at the affected site or field, with thrombosis arising secondarily (4). They support their theory by the presence of clusters of large malformed vessels close to the lesion that are highly reminiscent of an arteriovenous shunt. We also found some thick-walled vessels at the periphery of the lesion but no evidence of arteriovenous anastomoses. IMA YAMA *et al.* (5) noticed that the endothelial cells of SCH tend to attach to each other by numerous tight junctions. They hypothesize that this abnormal cellular behavior could produce repeating vascular obstructions initiating a process of thrombosis and endothelial proliferation for the recanalization of the thrombi. In accordance with a previous report (16), we found that the endothelial cells of SCH were strongly positive for vimentin and the histiocytic marker HAM56, and that they present variable or multifocal reactivity for factor VIII-associated antigen. This immunoreactivity is reminiscent of that of endothelial-like cells seen in conventional intravascular organizing thrombi and in intravascular papillary endothelial hyperplasia considered to be an exuberant form of organizing thrombi (25). The ability of the vessels of the SCH to reproduce different segments of the normal microvasculature also supports a reactive origin (5, 4, 16).

Injury is considered as a possible initiating factor because lesions occur frequently on the distal extremities (5). Furthermore, there are reports of SCH occurring on the precise site of repeated injections or surgical excisions (4, 9, 19). Although a history of injury was not provided in our case, it should be noticed that the mandibular-buccal fold is a frequently traumatized area.

The origin of spindle cells in SCH remains obscure. Ultrastructural (1, 2, 4, 5, 12, 16) and immunohistochemical studies (1–5, 8, 10, 12, 16, 19) have identified various cell types in the peri-

vascular and interstitial spaces of SCH. Thus, it has been suggested that spindle cells constitute a population of heterogeneous cell types, consisting mainly of fibroblasts admixed with smooth-muscle cells, pericyte-like cells, macrophages and primitive mesenchymal cells (5, 16). The immunophenotype of epithelioid and vacuolated cells is variable but generally similar to that of the endothelial cells (1, 2, 16). The cytoplasmic vacuolation that may be so extensive as to produce the "signet-ring" appearance seen in our case is regarded as an indication of primitive lumen formation (1, 16).

The differential diagnosis of SCH includes Kaposi's sarcoma, cavernous hemangioma, papillary endothelial hyperplasia (PEH), epithelioid hemangioendothelioma, disseminated lobular capillary hemangioma (DLCH) and epithelioid angiomatosis (2, 10). SCH resembles Kaposi's sarcoma, apart from the microscopic features in the clinical manifestations – namely, acral location and multifocality (1). However, cavernous spaces with thrombi and phleboliths, epithelioid endothelial cells, some of them vacuolated, as well as the lack of hyaline globules distinguish the two entities (26). Cavernous hemangioma can be easily ruled out due to the presence of spindle-shaped and epithelioid cells (3, 12).

PEH, or Masson's pseudoangiosarcoma, is usually a solitary intravascular tumor, while only five SCHs were confined within the lumen of a vessel (1, 2, 4). Furthermore, SCH does not feature spindle and epithelioid endothelial cells, and the core of the papillae typically consist of collagenized connective tissue. SCH and epithelioid (histiocytoid) hemangioendothelioma share many features (20) but the latter shows a more solid growth pattern, without cavernous spaces, thrombi and phleboliths or discrete spindle-cell areas.

DLCH and epithelioid angiomatosis are both multifocal vascular lesions. The former has the microscopic appearance of a typical capillary hemangioma and the latter of a histiocytoid hemangioma underlying a lobular capillary hemangioma (2). Both lesions lack dilated vascular channels and spindle cells. Furthermore, epithelioid angiomatosis may involve internal organs and exclusively affects patients with ARC or AIDS, while no patient with SCH has yet tested positive for HIV (2, 8, 13).

Wide local excision for solitary or multiple adjacent lesions is usually ade-

quate (1), and thorough angiographic examination is advised for the detection of a possible clinically occult vascular abnormality (4). Intralesional vinblastin injection was tested unsuccessfully in one patient, and radiotherapy possibly contributed to the development of an angiosarcoma (2). Reported "recurrences" most likely represent separate primaries, as they tend to develop in adjacent previously uninvolved tissue and not at the site of a former excision (1, 4, 5). The regional lymph node metastasis that developed in one patient (1) is thought to be a radiation-induced or post-radiation angiosarcoma and not a true metastatic SCH (2). No patient has died from the disease.

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