Hemangiopericytoma of Buccal Mucosa: Report of a Rare Case with Review of Literature

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ABSTRACT:

Hemangiopericytoma is a rare vascular neoplasm, which arises from specialized cells (pericytes) around the walls of blood vessels. About 50% of hemangiopericytoma in the series of Stout occurred in the oral cavity and pharynx. Under the World Health Organization (WHO) classification, hemangiopericytoma and solitary tumors of the soft tissues are regarded as features of the same entity in the soft tissue fascicle. We report here a case of a 60-year-old man who presented with a painless pedunculated growth associated with right-buccal mucosa of approximately 4 cm diameter. The lesion was completely removed by wide surgical resection. Microscopic examination revealed highly packed oval cells around thin walled endothelial lined vascular channels. Neoplastic cells expressed strong immunopositivity for smooth muscle actin, CD34, CD31. These findings were consistent with the diagnosis of Hemangiopericytoma. Because of the rarity and unpredictable biological behavior of these tumors, complete follow-up is always necessary.

Key words: Hemangiopericytoma, Immunohistochemical, Vascular tumors, Sarcoma, Differential diagnosis, Treatment.

INTRODUCTION:

Hemangiopericytoma was initially described by Stout and Murray in 1942 as a soft tissue tumor derived from mesenchymal cells with pericytic differentiation.¹ Hemangiopericytoma (HPC) has been described as a variant of angiosarcoma (hemangoendothelioma) with relatively benign biological aggressiveness. It can develop at any site where there are capillaries; hence, it causes many unique problems of diagnosis and therapy. The tumor may develop over a period of months and even years and in patients of all ages. The most critical aspect of treatment is an accurate histological diagnosis separating it from other angiosarcomas and benign tumors of blood vessels such as the solitary glomus tumor.²

About 300 cases have been reported since 1942, when Stout and Murray described these tumors as ‘vascular tumors arising from Zimmerman’s pericytes’.³ Clinically, the tumor may occur at any age, with the highest incidence between the third and the sixth decades, and without any sex predilection. According to the literature, this tumor may behave benignly, being well defined, slow growing, painless and firm, and having a normal
overlying mucosa. The recurrence rate is reported to be more than 50% and metastasis ranges from 12% to more than 50%.4

The incidence of hemangiopericytoma in head and neck in all age groups ranges from 9.4% to 28%. In children the head and neck hemangiopericytoma is as frequent as 35%, while the highest frequency (46%) is found in infants. Infantile hemangiopericytoma may have a different clinical presentation, mainly multilobulated lesions located in the subcutis—usually with benign behavior. Approximately 50 cases of hemangiopericytoma in the oral cavity have been described in the literature till date, with tongue being the most common site for intraoral hemangiopericytoma.4

Disease can either be benign or malignant. Two types have been described infantile HPC and adult disease. Although Infantile HPC is usually described together with the adult type, it deserves separate consideration because of its different histological presentation and clinical behavior. Microscopic characteristics are the so-called pericytoma pattern with tightly packed cells around ramifying thin-walled and endothelial-lined vascular channels ranging from small-capillary-sized vessels to large gaping sinusoidal spaces. Distinction between low-grade and high-grade lesion is difficult on the basis of histological parameters. Combining factors such as mitotic activity, cellularity, hemorrhage and necrosis, may prove informative for assigning a grade to the tumor. Soft tissue hemangiopericytoma is a controversial pathological entity. The relative non-specificity of the characteristic branching capillary pattern and the cytological features of the constituent cells, in addition to the lack of a distinct immunohistochemical staining profile, has resulted in uncertainty and absence of consensus regarding this subgroup of tumors.1

Hemangiopericytoma assumes two histologic forms, conventional hemangiopericytoma and the lipomatous hemangiopericytoma variant. Both histologic forms share a sponge-like sinusoidal vasculature and staghorn-shaped blood vessels that are haphazardly bounded and surrounded by ovoid and short spindle shaped cells. On ultrastructural analysis the cells are largely undifferentiated, containing arrays of intermediate filaments consistent with vimentin. If ultrastructural confirmation is sought, a necessary feature is the presence of the basement membrane substance between tumor cells.5

We present here an extremely rare case of hemangiopericytoma in the buccal mucosa of an 60yr old male. The immunohistochemical analysis of neoplastic cells showed strong immunopositivity for SMA, CD31, CD34. The aim of this article is to describe a case of hemangiopericytoma in a rare site with immunohistochemical analysis that was useful in making the final diagnosis.

CASE REPORT:

A 60-year-old man came for evaluation of a gradually enlarging asymptomatic mass in his right buccal mucosa area of 1.5 months’ duration (Fig. 1). His past medical history was unremarkable. The mass measured 4 × 3 cm approximately was well circumscribed, mucosally covered, and pedunculated on a broad-based stalk. The overlying mucosa was covered with dilated vascular channels. The mass was rubbery in consistency.

An excisional biopsy was performed under local anesthesia. The specimen was fixed in formalin, paraffin embedded and stained by hematoxylin and eosin. The patient had a normal postoperative course of healing.

Microscopic examination revealed cellular connective tissue composed of numerous dilated large and small endothelial lined blood vessels. The blood vessels on their outer aspect are surrounded by densely and loosely packed round to oval cells with dark nuclei and indistinct cytoplasm. The lesional tissue is covered by stratified squamous epithelium which appears to be stretched out due to loss of rete ridges. (Fig 2 & Fig 3)

On Immunohistochemical analysis, neoplastic cells expressed strong immunopositivity for smooth muscle actin [SMA], CD31, CD34. These findings were consistent with the diagnosis of hemangiopericytoma. (Fig 4, Fig 5 & Fig 6 respectively)

DISCUSSION:

Among vascular tumors, the diagnosis of hemangiopericytoma (HPC) is one of the most controversial. Doubt has even been raised as to its existence as a specific tumor type. Initially described by Stout and Murray in 1942,6 it was thought to represent a neoplasm of the pericytes of Zimmerman. Hemangiopericytoma is included in an authoritative classification of soft tissue tumors, but it is likely over-diagnosed.7 Histologic confusion with other soft tissue tumors, such as solitary fibrous
Hemangiopericytomas have been described in all age groups; with more than 40% occurring in the fifth and sixth decades. This tumor has no sex predilection. Clinically the lesion is firm, apparently circumscribed and often nodular, and may not exhibit redness indicative of their vascular nature. A painless enlarging mass is the general mode of presentation, as seen in this case. Majority of tumors grow rapidly and are therefore of short duration.

Hemangiopericytoma consists of numerous vascular channels with plump endothelial nuclei and a surrounding, tightly packed proliferation of oval and spindled cells with dark nuclei and a moderate amount of cytoplasm. Areas with more spindled pericytes may show an interlacing pattern of cells but usually there is a medullary tissue pattern, sometimes with palisading of cells, reminiscent of a neural tumor. Older, less aggressive lesions tend to have less cellularity and may have a largely mucoid interstitial appearance, which can be mistaken for myxoid lipoma or myxoid liposarcoma. Focal cartilage production may rarely be seen and such lesions must be differentiated from mesenchymal chondrosarcoma. The number of mitotic figures is variable and of prognostic significance, with lesions showing fewer than 2-3 mitotic figures per high-power field having a slower growth, lesser recurrence rate and fewer metastases than lesions with four or more mitotic figures per high power field. Lesions with pleomorphic cells and areas of necrosis or hemorrhage usually have a more aggressive behavior than those without these features.

Reticulin staining will demonstrate lesional vessels lined by a single layer of endothelial cells, with the pericytes lying outside the basal lamina, although they are often individually surrounded by reticulin and collagen fibers. Lesional cells are immunoreactive for vimentin (variable intensity), factor XIIIa antigen, HLA-DR antigen and QBEND10 (CD34). They do not stain for or react with factor VIII-related antigen, Ulex europaeus I lectin, alpha-smooth muscle actin, desmin, myoglobin, low-molecular weight cytokeratin, high-molecular weight cytokeratin, or epithelial membrane antigen. Prior to the routine use of immunohistochemistry in the diagnosis of HPC, misinterpretation for synovial sarcoma was common. However, unlike HPC, synovial sarcomas are often immunoreactive for both keratins and epithelial membrane antigen (EMA). Electron microscopy is also helpful in separating the two tumors, as epithelial differentiation is identified in some synovial sarcomas studied ultrastructurally but not in examples of HPC. Basement membrane substance may be found in both HPCs and synovial sarcomas. Yet it is the presence of basement membrane in HPCs that allows distinction from SFT, a tumor of fibroblasts, composed of cells devoid of a basement membrane lining.

Hemangiopericytomas are immunopositive for alpha smooth muscle actin, CD31, CD34. The most accepted hypothesis is that pericytes contribute to the regulation of microvascular blood flow through contractile activity, which is supported by morphological observations showing similarity between pericytes and smooth muscles cells. Previous studies have demonstrated that pericytes contain proteins essential for contraction and confirm the close relationship between pericytes and vascular smooth muscle cells. The expression alpha smooth muscle by pericytes is found to be useful in evaluating the histogenesis of tumors considered to be of pericytic origin such as hemangiopericytoma. Alpha smooth actin is mainly located in that portion of cytoplasm of pericytes which is facing the endothelial cells.

CD-31 is normally found on endothelial cells, platelets, macrophages and Kupffer cells, granulocytes, T/NK cells, lymphocytes, megakaryocytes, osteoclasts, neutrophils. In immunohistochemistry, CD31 is used primarily to demonstrate the presence of endothelial cells in histological tissue sections. This can help to evaluate the degree of tumour angiogenesis, which can imply a rapidly growing tumour. Malignant endothelial cells also commonly retain the antigen, so that CD31 immunohistochemistry can also be used to demonstrate both angiomas and angiosarcomas. Cells expressing CD34 are normally found in the umbilical cord and bone marrow as hematopoietic cells, a subset of mesenchymal stem cells, endothelial progenitor cells, endothelial cells of blood vessels but not lymphatics (except pleural lymphatics), mast cells, a sub-population dendritic cells (which are factor XIIIa negative) in the interstitium and around the adnexa of dermis of skin, as well as cells in soft tissue tumors like...
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Hemangiopericytoma is somewhat less than 50%. Metastasis is usually to the lungs and bones; lymph node metastasis is uncommon. Most recurrent tumors will eventually demonstrate metastasis. The overall five-year survival rate for this tumor during the first five year postoperative period varies from 17-56%, and metastasis occasionally occurs up to 10 years after surgery. Metastases are usually to the lungs and bones; lymph node metastasis is uncommon. Most recurrent tumors will eventually demonstrate metastasis. The overall five-year survival rate for the microscopically dysplastic hemangiopericytoma is somewhat less than 50%. The infrequent exposure of pathologists to vascular neoplasms coupled with overlapping histologic patterns can often make diagnosis challenging as undifferentiated malignant neoplasms are a daunting diagnostic problem for anatomical pathologists, calling for a tour de force in morphological skill, clinicopathologic correlation, and application of adjunctive laboratory studies. Early and accurate diagnosis followed by radical treatment is of utmost importance for improving the prognosis of these tumors. Given the limitations of histopathologic examination in precisely predicting the clinical behavior and prognosis of vascular tumors, identification of new molecular markers emerges as a necessity. It will also enhance our understanding of the pathogenesis of HPC, hopefully leading to the development of novel therapeutic approaches.

CONCLUSION:

The infrequent exposure of pathologists to vascular neoplasms coupled with overlapping histologic patterns can often make diagnosis challenging as undifferentiated malignant neoplasms are a daunting diagnostic problem for anatomical pathologists, calling for a tour de force in morphological skill, clinicopathologic correlation, and application of adjunctive laboratory studies. Early and accurate diagnosis followed by radical treatment is of utmost importance for improving the prognosis of these tumors. Given the limitations of histopathologic examination in precisely predicting the clinical behavior and prognosis of vascular tumors, identification of new molecular markers emerges as a necessity. It will also enhance our understanding of the pathogenesis of HPC, hopefully leading to the development of novel therapeutic approaches.

REFERENCES:

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13. Available at: http://www.enwikipedia.org/wiki/CD31
FIGURE 1: Pedunculated growth associated with right-buccal mucosa

FIGURE 2: Blood vessels surrounded by densely packed round to oval cells (10x)

FIGURE 3: Blood vessels surrounded by densely packed round to oval cells with dark nuclei and indistinct cytoplasm (40x)

FIGURE 4: Neoplastic cells expressed strong immunopositivity for CD 31(10x)

FIGURE 5: Neoplastic cells expressed strong immunopositivity for CD 34(10x)

FIGURE 6: Neoplastic cells expressed strong immunopositivity for smooth muscle actin(10x)