Primary Polymorphous Hemangioendothelioma of the Maxillary Soft Tissue: Clinical and Immunopathological Aspects of a Rare Vascular Neoplasm

ROSARIO RULLO, FRANCESCO ADDABBO, FRANCESCO RULLO and VINCENZO MARIA FESTA

Department of Stomatology, Second University of Naples, Naples, Italy

Abstract. Polymorphous hemangioendothelioma (PH) is an uncommon vascular neoplasm of borderline malignant potential characterized by a considerable variability in patterns of cellular growth. Morphologically, PH may be confused with other lesions, from benign vasoformative neoplasms and reactive inflammatory conditions to malignancies such as angiosarcoma or squamous cell carcinoma. Most occur in the lymph nodes, and to the best of our knowledge, lesions involving the maxillary soft tissue have not been described in the literature to date. A potential for local recurrence, as well as the ability to metastasize, has been for this type of neoplasm. Here we reported on a rare case of polymorphous hemangioendothelioma which presented as an asymptomatic subcutaneous mass in the right zygomatic region of a 22-year-old white female. We discuss the histopathological aspects of this tumor, with emphasis on the role of immunohistochemical analysis in differential diagnosis.

Polymorphous hemangioendothelioma (PH) is a rare neoplasm, first described in 1992 as a borderline malignant vascular tumor of endothelial cell origin. The term hemangioendothelioma was introduced to describe an uncommon vascular neoplasm of intermediate malignant potential, between hemangioma and angiosarcoma (1). PH represents a variety of the heterogeneous group of hemangioendotheliomas, which predominantly involve lymph nodes or extranodal locations such as the paravertebral region (2), mediastinum (3), and retroperitoneum (4). Although unusual clinical presentation in the sub-mandibular (5) and neck regions (6) have also been reported, lesions involving maxillary soft tissue have not been described in the literature, to date. PH is characterized by a considerable variability in patterns of cellular growth with the presence of vascular channels and endothelial cells, which make this neoplasm difficult to define histologically (5-7). A correct differential diagnosis should include the broad spectrum of vascular malformations, Kaposi’s sarcoma, angiosarcoma, hemangiopericytoma, and melanoma (6, 8). The frequent presence of a solid cellular architecture may cause diagnostic confusion with squamous cell carcinoma and the use of immunohistochemical analysis is often necessary to separate PH from these lesions (6, 7). Although the potential for local recurrence, as well as the ability to metastasize, have been reported (1, 2, 4), predictions regarding the biological behavior of PH in the oral region are not entirely possible due to lack of described cases.

The management of hemangioendotheliomas usually includes wide local surgical excision, investigation of metastatic lesions, and close clinical follow-up due to risk of recurrence (9). We report on a case of PH in the zygomatic-maxillary region of a 22-year-old woman, focusing our attention on clinicopathological and immunohistochemical features of the most common lesions encountered during differential diagnosis.

Case Report

A 22-year-old woman with no previous medical problems was referred to our Department for evaluation of an asymptomatic subcutaneous mass in the right zygomatic region, soft-elastic in consistency, and covered by normal-appearing skin. The lesion had progressively enlarged over the previous 10 months, developing a swelling in the buccal vestibule, without anatomic connections with the oral cavity and the cutaneous plane. There were no palpable locoregional lymph nodes. The provisional differential diagnosis focused on a probable mesenchymal tumor. Computed tomographic scans showed a thickening of the...
right zygomatic-maxillary region in relation to the presence of an isodense subcutaneous mass of about 2.5×1.5 cm, adjacent to the zygomatic process of the maxilla and well-dissociable from it. The radiographic appearance of the area did not demonstrate signs of bone resorption. Furthermore, a preoperative magnetic resonance imaging confirmed the presence of an oval mass, hyperintense on T2-weighted sequences, situated laterally to the anterior margin of the masseter muscle (Figure 1). The margins were well-demarcated without any evidence of infiltrative character. Under local anesthesia, an excisional biopsy was performed with surgical access through the skin, and the specimen was submitted to microscopic examinations.

Grossly, the mass measured 3.5×2.0 cm (Figure 2). Microscopic examination showed a polymorphous population of polygonal to spindle-shaped cells with low mitotic activity (Figure 3). This pattern was characterized by the presence of angiomatous areas with variably sized vascular channels lined by endothelial cells. Immunohistochemical staining revealed CD34 positivity of the lesional cells, confirming the vascular nature of the neoplasm, and the diagnosis of PH (Figure 4). Nuclei of tumour cells did not stain significantly for Ki-67 under immunohistochemistry; moreover, atypical mitotic figures, tumor necrosis, and significant nuclear pleomorphism were absent. At 1-year follow-up, no evidence of recurrence was noted, only a cutaneous scar persisted in the zygomatic region.

Discussion
Among the wide spectrum of vascular neoplasms, ranging from benign hemangioma to metastasizing angiosarcoma, PH represents a rare tumor of borderline malignant potential, characterized by a complex variety of growth patterns (1). PH is currently categorized as borderline neoplasm of vascular origin exhibiting histological features and clinical behavior intermediate between hemangioma and angiosarcoma (1, 8). The adjective “polymorphous” has been used to denote the typical architectural variability of solid, primitive vascular, and angiomatous endothelial areas, which make this neoplasm
difficult to recognize histologically (5, 6). Usually, PH predominantly involves lymph nodes, and only few cases of primary occurrence in extranodal soft tissues have been described in literature (2, 5). Polymorphous hemangioendothelioma showed tendency to recur locally, as well as to metastasize; however, it seems reasonable that the neoplasm should be able to present distant metastasis only after malignant transformation (2, 3, 4, 7). Nowadays, because of the small number of cases reported the etiology is still unknown, and no consistent clinical or histological criteria for predicting the biological behavior of this vascular tumor in the maxillofacial region have yet been identified. Nevertheless, some features considered suggestive of a more aggressive phenotype with recurrence and regional or distant metastasis, include the presence of an increased number of mitotic figures, cellular atypia, and areas of focal necrosis (10).

The case reported here illustrates a low-grade vascular neoplasm with no relevant cellular atypia or mitotic activity, which suggest a generally good prognosis. Microscopically, PH is typically characterized by a remarkable variety in patterns of growth of a polymorphous population of polygonal to spindle-shaped cells. This complex cellular mixture is completed by the presence of vascular channels lined by endothelial cells as well as ectatic vessels (5-7). Because of the presence of a conspicuous polymorphous solid component, the vascular nature of PH can be difficult to recognize microscopically without immunohistochemical analysis, and a complete differential diagnosis should include lesions such as squamous cell carcinoma, angiosarcoma, melanoma, Kaposi’s sarcoma, and hemangiopericytoma (6-8). In the maxillofacial region, hemangioendotheliomas can clinically mimic benign vasoformative neoplasms, and reactive inflammatory conditions, including pyogenic granuloma, peripheral giant cell granuloma, fibroma, peripheral ossifying fibroma, and inflammatory fibrous hyperplasia (11, 12). Misdiagnosis of PH as a pure benign lesion acquires relevance when the neoplasm shows intermediate or malignant biological behavior (2, 8). In such cases, histomorphological analysis and immunohistochemical stains are very useful to resolve any doubt and to guide the

Figure 2. Gross appearance of the lesion: a well-circumscribed hemorrhagic nodule of about 3.5×2.0 cm.
Figure 3. High-power field showing angiomatous areas composed of ovoid, polygonal, and spindle cells, with low mitotic activity (hematoxylin and eosin, ×400).

Figure 4. Immunohistochemical staining showing the neoplastic endothelial cells reactive for CD34, confirming the vascular nature of the tumor (original magnification, ×200).
clinician in the differential diagnosis. Moreover, the presence of polygonal cells arranged in a cord-like pattern may lead to misinterpretation of a metastatic carcinoma; therefore, to rule-out this malignancy, immunohistochemical assessment for cytokeratins and epithelial markers such as epithelial membrane antigen, usually lacking in PH, would be beneficial (1, 10). Furthermore, stains for endothelial markers, such as lectin from Ulex europaeus, factor VIII-related antigen, CD34, and CD31 are negative in squamous cell carcinoma. The presence of fibrosarcoma-like spindle cells along with positivity for Human Herpesvirus 8, may help differentiate Kaposi’s sarcoma from PH. Hemangiopericytoma can imitate hemangioendothelioma in routine hematoxylin and eosin staining with its tightly packed round-to-fusiform cells arranged around an elaborate vasculature, but silver reticulin stain can differentiate these two lesions, showing characteristic tumor cells of pericyte origin outside the reticulin network that encloses the vessels (10, 13, 14). The distinction from angiosarcoma or other neoplasms such as melanoma, metastatic carcinoma and adenocarcinoma remains a crucial issue. In this perspect, the microscopic lack of cytological atypia, necrosis, and mitotic activity, are useful to separate PH from other malignancies (10). Finally, CD34 immunoreactivity can easily be used to identify the primitive vascular nature of PH, and the histological demonstration of a non-infiltrative growth of a polymorphous population of polygonal to spindle-shaped cells confirms its diagnosis.

The particular histopathological and immunohistochemical features of PH require for careful evaluation to recognize and treat this entity properly. Our rare case of PH with good prognosis was treated only by local excision. Nevertheless, considering the spectrum of lesions included in the differential diagnosis, the clinician must take into account that mis-diagnosis as a malignancy can cause significant treatment errors. Because the number of reported cases of PH is very small in literature, the ideal treatment for these tumors, and a definitive prognosis, are still not established. Further studies are necessary to clarify the possible malignant biological behavior of the neoplasm and to define the most appropriate clinical management.

References


