CLINICOPATHOLOGIC CONFERENCE

Tumor of the hard palate

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At the Oral Diagnosis Clinic at the Dentistry School of Universidade Federal de Minas Gerais, a 29-year-old white woman was admitted with a slow-growing, painless oral lesion that had been present for 1 year. The patient was in her eighth month of pregnancy and was receiving medical treatment for slight iron-deficiency anemia related to the pregnancy. Extraoral examination revealed no other abnormalities. One lobulated, nonulcerated lesion was evident on the right posterior hard palate. It was mainly pink with darkened, reddish and whitish areas. The lesion was well circumscribed and partially sessile with a fibrous consistency; it measured approximately 35 × 20 mm. Superficial vascularity was evident in some areas (Figure 1, A). Radiographic examination did not reveal evidence of bone involvement (Figure 1, B). Neither the dental caries on the maxillary right first molar nor the periapical lesion on the maxillary left lateral incisor appeared to be associated with the lesion.

DIFFERENTIAL DIAGNOSIS

The clinical appearance of a firm, nonulcerated, exophytic, partially pedunculated lesion with a bosselated surface strongly suggested a soft tissue neoplasm. In addition, a salivary gland neoplasm must be considered, given the clinical features and relatively high frequency in female patients.

Benign soft tissue tumors, such as neural, adipocytic, and muscle lesions, were included in the panel of diagnostic hypotheses. Among neural neoplasms, the classical descriptions for neurofibroma and neurilemroma were consistent with many features of this case.
In a Brazilian study, neurofibroma accounted for 32.2% of the oral peripheral nerve sheath tumors. Lesions were more frequently located in the palate and alveolar mucosa of young females and presented as slowly expanding, painless, smooth masses of variable size.

Neurilemmoma has been observed in 11.4% of oral peripheral nerve sheath tumors among Brazilian patients and was shown to mainly affect young adults without any race or gender predilection. This encapsulated tumor often presents in various sizes on the lips, tongue, and buccal mucosa. It can exhibit slow, smooth, solitary, painless growth. Therefore, neurofibroma was considered to be more probable among neural neoplasms because of its relatively higher frequency.

Lipoma and leiomyoma were also briefly considered. With lipoma, the lesion typically presents as a slowly growing, well-defined mass. Classical lipomas do not usually localize to the palate, but a sialolipoma could be reasonably proposed. Although leiomyoma is rarely observed in the oral mucosa and pharynx, the palate is affected in 18.9% of the cases. This class of tumor arises asymptotically with slow enlargement and has a smooth surface with a well-defined mass. Its presence is typically submucosal with a bluish to reddish color; age of onset ranges from 40 to 49 years. Considering these features, leiomyoma was included as a possible, albeit unlikely, hypothesis.

Of the types of benign minor salivary gland tumors, pleomorphic adenoma (PA) was the most probable diagnosis. PA is the most common benign salivary gland neoplasm and usually affects women between 30 and 60 years old. It presents for a variable duration as a single, slow-growing mass that is firm and painless. There is a high incidence of PA observed on the palate, but this case also has other supporting criteria for this diagnosis: the patient was female and presented with a lesion with clinical features that are characteristic of PA. Other benign salivary gland tumors, such as basal cell adenoma, myoepithelioma, and cystadenoma, were deemed to be unlikely because of their extreme rarity.

Malignant salivary gland tumors were also discussed as possible hypotheses, because these tumors occasionally present borderline clinical behaviors and characteristics that mimic benign neoplasms. Age, gender, intraoral site, evolution, and the lack of symptoms made mucoepidermoid carcinoma a plausible diagnostic hypothesis in the present case, despite the absence of some common clinical features, such as bluish color and fixed borders. Adenoid cystic carcinoma was a less probable diagnosis because of the overall characteristics of our patient’s case (i.e., her age, the absence of pain, and the partially sessile presentation of the lesion). Conversely, the classical appearance of polymorphous low-grade adenocarcinoma matches some of the characteristics of the present case (i.e., gender, painless growth, and the presence of superficial vascularity). Finally, acinic cell carcinoma presents as an asymptomatic slowly enlarging mass in female patients, but it was deemed a less probable diagnosis because it rarely arises in the palate.

Palatal involvement by non-Hodgkin’s lymphomas has been reported, but mainly in the context of human immunodeficiency virus infection. Given its rarity in the oral cavity and its usual presentation (rapid enlargement into a fixed, poorly defined mass), non-Hodgkin’s lymphoma was not proposed as a potential diagnosis.

Reactive processes were also contemplated. Pyogenic granulomas are typical reactive lesions, which can arise with pregnancy. These lesions exhibit smooth or lobulated exophytic swellings that progress slowly and are generally red in color with a pedunculated or sessile base. Ulceration with recurrent bleeding and occasional pain may occur as well. The palate may be affected, but large lesions are not common. Despite its frequency, some features of the current case did not support this hypothesis, such as the size and location of the patient’s lesion, the absence of inflammation, and the absence of local etiologic factors. Follicular lymphoid hyperplasia is a very uncommon pathosis of the oral mucosa, although when present frequently affects the palate. Follicular hyperplasia often occurs in older female patients as a firm, painless, nonulcerated, nonfluctuant mass. These lesions grow slowly without bone involvement. Thus, despite its relatively low occurrence, follicular hyperplasia shares many clinical features with the present case. Finally, adenomatoid hyperplasia of the minor salivary glands was considered, but it is a rare lesion that typically occurs on the hard palate of patients who are 40 to 60 years old.

Based on the clinical features of this patient’s tumor, demographic data, and the prevalence of the lesions described previously, benign soft tissue tumor was endorsed as our major diagnostic hypothesis; however, the different types of lesions discussed in this section were deemed relevant possibilities.

**DIAGNOSIS AND MANAGEMENT**

An incisional biopsy was performed under local anesthesia, and a highly fibrous lesion was noted during the surgical procedure. Hematoxylin and eosin (H&E)-stained histologic sections revealed a mucosal fragment covered by parakeratinized stratified squamous epithelium with hyperplastic and atrophic areas. Pseudoepitheliomatous hyperplasia was not observed. In the subjacent connective tissue, a solid lesion formed by fusiform and polygonal cells was observed. The cells showed fibroblast and histiocyte-like characteristics.
and were arranged in syncytial and storiform patterns that were intermixed with short collagen bundles (Figure 2, A and 2B). At a higher magnification, the cells had indistinct borders and abundant eosinophilic granular cytoplasm with round or oval vesicular nuclei (Figure 2, C). Blood vessels and a few inflammatory cells were present, mainly at the peripheral areas, but neither calcification nor giant multinucleated cells were observed. Scarce mitotic figures and a few slightly pleomorphic cells were visualized.

Diagnosing oral lesions with granular cells is challenging because these cells are found in many types of oral tumors, including granular cell tumors, congenital epulides, and odontogenic tumors. In the present case, cytoplasmic granules, which were the most noticeable cellular feature, were positive for periodic acid-Schiff (PAS) staining and were diastase resistant (Figure 2, D). Tumor cells were immunopositive for vimentin and factor XIIIa. These cells were also focally positive for CD68, calponin, neuron-specific enolase (NSE), and α-smooth muscle actin (α-SMA), which showed a weak positivity (Figure 3). Negativity for S-100 protein, HHF-35, CD1a, CD56, CD57, glial fibrillary acidic protein, calretinin, α-inibin, AE1/AE3, epithelial membrane antigen, CD34, and HMB-45 was observed.

Considering the morphologic and immunohistochemical results for this case, benign fibrous histiocytoma rich in granular cells was the diagnosis.

**DISCUSSION**

Fibrous histiocytoma (FH) usually involves the skin and is composed of a group of lesions with different clinical behaviors. It is classified into benign, atypical, and malignant subtypes. When located in the head and neck region, benign FH tends to be a painless, well-circumscribed lesion. It exhibits solitary and slow growth that varies in size. Age of onset differs substantially, with an apparent predilection toward women (2.5:1.0). Oral lesions are uncommon and might arise in the buccal mucosa, gingiva, lips, and floor of the
mouth. In some instances, these lesions cause dysphagia, dyspnea, and snoring.\textsuperscript{13-15} Benign FH is characterized microscopically by a mixture of fibroblastic and histiocytic cells arranged in a storiform pattern but typically without atypia. Mitotic figures are scarce, and multinucleated giant cells can be observed.\textsuperscript{15,16} Its immunoprofile can vary, but is commonly positive for vimentin and factor XIIIa and negative for S-100 protein and CD34; results for CD68 vary.\textsuperscript{14-16} Benign FH has an excellent prognosis after surgical resection, and recurrences are rare; however, follow-up is recommended owing to the lingering uncertainty over the pathogenesis and long-term clinical behavior of these lesions.\textsuperscript{16}

One of the most interesting attributes of this case was its challenging histopathological diagnosis, because granular cells in oral lesions are commonly observed. Even with this information, benign FH was not considered as a clinical hypothesis. To establish the correct diagnosis for this lesion, we carefully analyzed the microscopic presentation and immunohistochemical profile of the case, which was not fully consistent with any previous description of a lesion with granular cells.

Granular cell tumor (GCT) was proposed as a reasonable scenario for this case, including atypical GCT subtypes, such as the S-100 negative variant. Although GCT is a very common oral lesion, occurring mainly in the tongues of middle-aged or older women, its origin has been extensively discussed but not well established. It is composed of polyhedral or round cells with small, eccentrically placed, rounded nuclei and a large, granular eosinophilic cytoplasm with indistinct cell borders. These granular cells are usually arranged in cords or clusters, and the over-

Fig. 3. Immunohistochemical features. Lesion was positive for (A) vimentin, (B) factor XIIIa, (C) NSE, and (D) calponin. There was (E) weak staining for CD68 and (F) focal and weak positivity for α-SMA (streptavidin-biotin; A, B, C: original magnification ×200; D, E, F: original magnification ×400).
lying epithelium may exhibit pseudoepitheliomatous hyperplasia, which was absent in the present case. Moreover, these cells usually show strong and diffuse S-100 immunostaining, which is the most widely used marker for GCT.\(^\text{17}\) In addition, GCT cells immunostain for NSE and are PAS-positive with diastase-resistant granules.\(^\text{18}\) Immunostaining for CD68, vimentin, calretinin, α-inhibin, CD57, α-1-antitrypsin, and CD34 has also been described in GCT.\(^\text{17,19}\) CD68 expression might be considered as a marker for degeneration linked to the presence of lysosomes rather than a marker of histiocytic derivation because trauma has been reported to play a role in degenerative processes involving granular cell changes.\(^\text{20}\) In our case, no history for local trauma was reported, although the clinical appearance and behavior of the lesion were compatible with a proliferative, non-neoplastic lesion. Therefore, GCT was excluded because of the noteworthy storiform arrangement of the cells in the present case, which has not been previously described for GCT.

The diagnosis of fibrous hyperplasia with xanthomatos alterations could be possible, but the granular cells would need strong expression of CD68. This characteristic was not observed in the present case. Another possibility was perivascular epithelial cell tumor, but the lesion was negative for HMB-45, which does not support this diagnosis.\(^\text{21}\) Alternatively, granular cell leiomyoma is a potential hypothesis, but α-SMA staining in the present case was weak. This case appears to be more similar to a myogenic differentiation of FH than a smooth muscle neoplasm.\(^\text{22}\)

Thus, considering the collective features of the present lesion, namely the prominent storiform pattern, xanthomatos aspect of the granular cells, and focal positive staining for CD68 and factor XIIIa, the final diagnosis was benign fibrous histiocytoma rich in granular cells. It is important to emphasize that the immunohistochemical profiles of FH, GCT, and dermatofibroma with granular cells demonstrate significant overlap.\(^\text{15,17,19,20,23,24}\) FH has been described previously in the mouth, but this case appears to be the first that microscopically mimics a granular cell tumor that closely resembles lesions described previously in skin as dermatofibroma with granular cells.\(^\text{20,23,25}\)

**REFERENCES**


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