Gingival solitary Neurofibroma: mind the pitfalls! A case report

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Abstract

Background: Neurofibromas are rare benign tumors of neural origin, usually associated with Neurofibromatosis type 1, an autosomal dominantly inherited syndrome. However, they can also be solitary, and appear in the oral cavity. Gingival localization is rare and takes a hypertrophic form associated with an attachment loss that can mimic a plaque-induced periodontal disease.

Case presentation: The patient was a 52-year-old female patient. She was mistakenly referred to our department for periodontal surgical debridement, whereas she presented a symptomatic gingival solitary neurofibroma. The surgical tumour excision allowed a good periodontal healing, and no recurrence was observed after 7 years.

Conclusions: The aim of this case report was to illustrate the essential role of the dental clinician in the detection of tumoral non plaque-induced gingival diseases. Knowledge of these tumor characteristics facilitates a more comprehensive differential diagnosis approach, thus avoiding improper management or late diagnosis.

Abbreviations: NF1: neurofibromatosis type 1; EMA: epithelial membrane antigen antibody; MRI: magnetic resonance imaging

Introduction

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Introduction

Neurofibroma is a benign peripheral nerve sheath tumor, generated by the proliferation of Schwann cells, perineural cells, and endoneural fibroblasts. It may occur either as a single lesion, called solitary neurofibroma, or as part of a generalized syndrome known as Neurofibromatosis type 1 (NF1), which is a systemic disorder caused by a mutation in theNF1 tumor suppressor gene located at 17q11.2; it is also known as von Recklinghausen’s disease. Without treatment, these lesions may generate serious functional complications, and even develop into malignant tumors.

Solitary neurofibroma is uncommon in the oral cavity, and only a few cases have been reported in the literature. Clinically, oral neurofibromas are soft, sessile, asymptomatic submucosal tumors which grow slowly, and may vary in size ranging from a small nodule to a large mass. They may occur at any site in numerous oral locations such as the tongue, the palate, the cheek mucosa, the floor of the mouth, or as intra-osseous lesions. The diagnosis is confirmed by histologic examination and immunohistochemistry, essentially based on the S-100 protein detection, indicating their neural origin.

This article reports the rare and successfully treated case of a symptomatic gingival solitary neurofibroma in a female patient free of any manifestation of Neurofibromatosis type 1. This case highlights the importance of differential diagnosis, which is crucial when managing such an atypical situation, and illustrates the key role of the dental clinician in detecting isolated gingival tumors.

Case presentation

In March 2012, a 52-year-old female patient was referred to the Department of Oral Surgery and Oral Pathology of the Henri Mondor Hospital. The patient was referred to us by her dentist for periodontal surgery on the right mandibular molars, due to a recurrent severe lingual and interdental attachment loss, despite prior non-surgical root planning and debridement. The patient’s chief complaint expressed during the first appointment was gingival swelling in the lower arch, slowly developing since November 2011, and associated with moderate and intermittent irradiating pain. The patient was a nonsmoker, and with no particular medical history.

Clinical examination revealed a localized and painless hypertrophy involving the marginal and attached lingual gingiva extending from...
Magnetic resonance imaging (MRI) was then performed to exclude other tumor localizations, and to assess the local extent of the tumor. Detailed patient examination showed none of the following signs: café-au-lait spots, cutaneous neurofibroma, Lish nodule, optical pathway glioma, osseous lesion, thus excluding Neurofibromatosis type I, and allowing us to diagnose a solitary gingival neurofibroma on the lingual aspect of the right mandibular gingiva.

**Differential diagnosis**

The unusual aspect of the periodontal lesion – severe clinical attachment loss without any endodontic infection, and associated with slight bone loss – was unlikely for a common plaque-induced periodontal involvement, and required a comprehensive differential diagnosis. From the very start, the general health status and the absence of medication excluded haematological malignancy and drug-induced gingival enlargement. Moreover, we excluded all the possible etiologies associated with generalized gingival hypertrophy, such as plaque-induced gingivitis exacerbated by a risk factor, plasma cell gingivitis, vitamin C deficiency, granulomatous disease or hereditary gingival fibromatosis.

Besides these diagnostic considerations, pyogenic granuloma, peripheral ossifying fibroma and peripheral giant cell granuloma were most unlikely as the gingiva showed a normal pink color and no nodular exophytic growth (Figure 1). Furthermore, absence of calculus or focal calcification on the periapical radiograph excluded pyogenic granuloma and peripheral ossifying fibroma as potential diagnostic considerations (Figure 2). Consequently, the hypothesis of a benign gingival tumor appeared as a more credible diagnosis.

Gingival biopsy was performed and sent for histopathological analysis. The gingival sample revealed a dense spindle-shaped cell proliferation within a fibrillar stroma, associated with capillary and mast cell proliferation, showing no plexiform aspect. Immunohistochemical staining was positive for S-100 protein, EMA (epithelial membrane antigen antibody) and smooth muscle actin (Figure 3). These results were consistent with a benign gingival neurofibroma; the localization indicated that the neurofibroma originated from the lingual nerve.

**Treatment**

The treatment consisted in surgical excision. Following patient information of a potential postoperative lingual nerve injury and her signed informed consent; the surgery was performed under local anaesthesia, using a 4% articaine solution with 1/200000 epinephrine. The gingival lesion was carefully dissected and excised including surgical margins, using Metzenbaum scissors and a CO2 LASER (Figure 4). The surgical site was protected using collagen absorbable sponges and a periodontal dressing. The patient was sent home with a prescription of amoxicillin, prednisolone, acetaminophen + codeine, chlorhexidine mouth rinse and topical disinfectant.
Neurofibromas are the most frequent benign neoplasms originating from the peripheral nerve sheath which may occur either as solitary or multiple tumors when related to Neurofibromatosis type 1 (NF1) [1-8]. The lesions most often appear on the skin; however, many organs can be involved including the stomach, intestines, kidneys, bladder, larynx and heart. Neurofibromas can be present at birth or develop anytime during life: they often affect adults and children ranging from 9 to 50 years of age, with a mean age of 31.2 years old [9-11]. Some studies have reported a female predominance [9,11-13] whereas other studies have shown no gender predominance for this lesion [10].

Histologically, neurofibromas are non-encapsulated tumors formed by a complex proliferation of Schwann, perineural, endoneural fibroblastic and intermediate cells [1,3,16,17,20-22]. Subsequently, they present a large microscopic cell heterogeneity [4,12,13,23]. Generally, they are well-circumscribed tumors characterized by intermingled sheaves of elongated spindle-shaped cells with wavy or comma-shaped nuclei, within a myxoid matrix consisting of scattered delicate collagen fibers, and a variable number of mast cells [24]. In older lesions, hyaline changes may occur, although edematous changes are more likely, especially in the plexiform variety [25].

Malignant transformation of neurofibromas has been a well-established phenomenon for decades [26,27], and their incidence is 3 to 5 % [1,28]. Identified as a malignant peripheral nerve sheath tumor, it often occurs in association with large diffuse neurofibromas, especially in NF1 patients [29]. Rapid enlargement of the neurofibroma and the presence of pain must suggest malignant transformation [14,30]. Once a malignant change has occurred, the lesions have a poor prognosis [31].

In the head and neck region, the most commonly affected sites are the scalp, cheek, neck and oral cavity. Nevertheless, oral neurofibromas remain quite uncommon [31,32], especially when not related to NF1 [11,31,33]; past literature reports that the frequency of solitary neurofibromas in the oral cavity is around 6.5%.

All the hard and soft oral tissues have been reported to be involved in these tumors [34]. However, the majority of oral neurofibromas occur in the tongue, oral mucosa and the lips [1,3,12,13,32]. Other less frequent sites include the gingiva [13,35] and the palate [11,36].

Their clinical aspect is not specific and does not much differ from cutaneous neurofibromas; solitary oral neurofibromas resemble localized nodules matching the color of the surrounding mucosa, and are usually asymptomatic [19,21,31,37]. The lesions are often diagnosed late due to their slow and painless growth, causing few symptoms [38]. However, when adjacent to cranial nerves, they can impair motor functions of facial/hypoglossal nerves or the sensitivity of trigeminal nerves [21,37]; they may even affect speech [39]. In case of gingival involvement, neurofibromas also cause tooth malposition or impaction [19].

Gingival neurofibromas are rare [37], most cases occurring in NF1 patients (5 % of cases) [40,41] (Figure 6). Within the limits of our research, few cases of solitary gingival neurofibromas have been fully described in the English literature (Table 1).

When compared to former reported cases of solitary gingival neurofibromas, our case is peculiar in its clinical expression. Whereas
most solitary gingival neurofibromas have been described as painless, localized, sessile or pedunculated exophytic gingival enlargements, our patient presented a painful and diffuse gingival lesion, mimicking periodontal pockets around the mandibular molars. Such clinical signs indicate the need for a well-conducted clinical evaluation, in order to establish proper differential diagnosis. In this particular case, the atypical feature may explain the initially delayed diagnosis.

Treatment of solitary neurofibromas consists in surgical excision, in order to solve a functional or esthetic disorder, or to avoid chronic traumatism, considering that a malignant transformation may occur. It is recommended to perform total tumor resection including 1 cm of surgical margins in order to reduce the risk of recurrence [19,21,28,37]. This approach seems to be the treatment of choice for small and accessible tumors as for this clinical case. To our knowledge, our case is the only one reported with a 7-year postoperative follow-up. Generally, sporadic neurofibromas are histologically identical to those encountered in NF1.

In conclusion, the present case report emphasizes the fact that neurofibromas may occur as sporadic lesions, without any NF1 characteristics and no family history. Their location and clinical features can be misleading, thus highlighting the need for histological examination as the gold standard to reach a definite diagnosis.

These neurofibromas may be the first manifestation of Neurofibromatosi type I; to our knowledge, at least one case has been reported in which the diagnosis of an oral neurofibroma led to the diagnosis of NF1. This points out the importance of a careful diagnostic approach when dealing with such lesions.

Considering the possible local complications and malignant transformation, it is crucial that dental clinicians and oral pathologists, conduct long-term follow-ups after surgical excision of such lesions, especially in NF1 patients [54] (Supplementary File).

Declarations

Ethics approval and consent to participate: not applicable

Consent for publication

Written informed consent was obtained from the participants.

Availability of data and materials

Not applicable.

Competing interest

The authors declare that they have no competing interests.

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