Gingival solitary Neurofibroma: mind the pitfalls! A case report

Dridi Sophie-Myriam1, Bontemps Lea2, Moreau Nathan3, Le Pelletier de Glatigny François4, Gogly Bruno5 and Gaultier Frederick6

1 UFR of Odontology, Department of Periodontology, Saint Roch Hospital, University of Nice Sophia Antipolis, France
2 Faculty of Dental Surgery, Department of Periodontology, Henri Mondor Hospital, University of Paris Descartes, France
3 Faculty of Dental Surgery, Dpts of Oral Medicine, Oral Surgery, Bretonneau Hospital, University of Paris Descartes, France
4 Faculty of Medicine, Department of Pathology, Pitié Salpêtrière Hospital, University of Pierre and Marie Curie, France
5 Faculty of Dental Surgery, Departments of Oral Medicine, Oral Surgery, Henri Mondor Hospital, University of Paris Descartes, France
6 Faculty of Dental Surgery, Departments of Oral Medicine, Oral Surgery, Henri Mondor Hospital, University of Paris Descartes, France

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

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 the NF1 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.

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 anesthesia, 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].

Based on clinical observation and medical history of the lesions, neurofibromas can be divided into two major categories, localized and plexiform [14]: localized neurofibromas which develop from a single site along a peripheral nerve, and depict a focal mass with well-defined margins; plexiform neurofibromas extend along a peripheral nerve and may involve multiple nerve branches [1,15]. They represent a major source of morbidity associated with NF1, mainly due to their tendency to grow and reach large sizes, thus causing disfigurement. The most involved cranial nerves in plexiform neurofibromas are the V, IX and X.

Neurofibromas are clinically characterized by slow growth, lack of pain, superficial location [16,17] and variable size [18] During puberty or pregnancy, their development may be accelerated due to intense hormonal disorders [19]. They are most often unilateral and nodular lesions [19].

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].

Histological examination alone is not sufficient for a final diagnosis of neurofibroma, which also requires immunohistochemistry. More specifically, a panel of immunoreactions including S100 protein, type IV collagen, CD34, EMA and neurofilament or neuron-specific tubulin (TUBB3) can be implemented [13].

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 Neurofibromatosis 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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Table 1. Reported oral neurofibromas in the literature

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Location</th>
<th>Neurofibroma</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bruce</td>
<td>Male</td>
<td>36 y.o.</td>
<td>Mandibular posterior alveolar ridge</td>
<td>Localized</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Richards</td>
<td>Female</td>
<td>55 y.o.</td>
<td>Buccal maxillary anterior gingival papilla</td>
<td>Localized</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Alatli, et al.</td>
<td>Female</td>
<td>37 y.o.</td>
<td>Buccal mandibular posterior gingiva and mucosa</td>
<td>Plexiform</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Sinha, et al.</td>
<td>Female</td>
<td>50 y.o.</td>
<td>Soft palate</td>
<td>Localized</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Marocchio, et al.</td>
<td>Female</td>
<td>24 y.o.</td>
<td>Cheek mucosa</td>
<td>Localized</td>
<td>Biopsy S-100 positivity</td>
<td>Excision</td>
</tr>
<tr>
<td>Deprich, et al.</td>
<td>Male</td>
<td>64 y.o.</td>
<td>Lingual mandibular gingiva and mouth floor</td>
<td>Localized</td>
<td>Biopsy S-100 positivity</td>
<td>Excision</td>
</tr>
<tr>
<td>Ohno, et al.</td>
<td>Female</td>
<td>32 y.o.</td>
<td>Buccal mandibular gingiva</td>
<td>Localized</td>
<td>Biopsy S-100 positivity</td>
<td>Excision</td>
</tr>
<tr>
<td>Suranya, et al.</td>
<td>Female</td>
<td>57 y.o.</td>
<td>Buccal maxillary anterior gingival papilla</td>
<td>Plexiform</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Borges, et al.</td>
<td>Male</td>
<td>12 y.o.</td>
<td>Labial mucosa</td>
<td>Localized</td>
<td>Biopsy S-100 positivity</td>
<td>Excision</td>
</tr>
<tr>
<td>Koidyi, et al.</td>
<td>Male</td>
<td>40 y.o.</td>
<td>Soft palate</td>
<td>Localized</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Pawar, et al.</td>
<td>Female</td>
<td>25 y.o.</td>
<td>Buccal maxillary posterior gingiva</td>
<td>Localized</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Mahalle, et al.</td>
<td>Female</td>
<td>37 y.o.</td>
<td>Labial mucosa</td>
<td>Plexiform</td>
<td>Biopsy</td>
<td>Excision</td>
</tr>
<tr>
<td>Mahmud, et al.</td>
<td>Female</td>
<td>73 y.o.</td>
<td>Tongue</td>
<td>Localized</td>
<td>Biopsy S-100 positivity</td>
<td>Excision</td>
</tr>
<tr>
<td>Sekhar, et al.</td>
<td>Female</td>
<td>55 y.o.</td>
<td>Hard palate</td>
<td>Localized</td>
<td>Biopsy S-100 positivity</td>
<td>Excision</td>
</tr>
</tbody>
</table>

**NS= not specified**

Figure 6. Gingival neurofibroma in the context of neurofibromatosis type I. The syndromic diagnosis was clinical, based on the presence of multiple cutaneous neurofibromas, cutaneous “café-au-lait” spots, and the history of a positive diagnosed mother. The diagnosis of gingival neurofibroma was confirmed by the biopsy.
Authors’ contributions
- Concept and design: SMD, LB
- All authors performed the acquisition, analysis, and interpretation of data
- Drafting of the manuscript: SMD, LB
- All authors read and approved the final manuscript

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Conflict of interests
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