Solitary intraosseous neurofibroma of the mandible. Apropos of a case

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Abstract
Neurofibroma is a benign neoplasm derived from peripheral nerves. Most of these are associated with Neurofibromatosis but may also occur as solitary lesions. When found on the head and neck they are generally located in the soft tissue. Intraosseous location is very rare.

The following report describes a case of an intraosseous neurofibroma located in the left mandibular ramus of a 14-year-old child. The patient did not had clinical evidence of the lesion and it was found on a routine radiographic examination. Surgical excision of the lesion was scheduled and the sample was submitted to histopathological study. Representative sample cuts were studied using conventional techniques of hematoxylin-eosin and immunohistochemistry using primary antibodies anti S-100 protein, vimentin, and neuroespecific enolase.

A review of clinical, radiographic, histologic and immunohistochemical features of other cases of intraosseous neurofibromas located in the jaws together with the possible differential diagnosis of the lesion are discussed.

Our case corresponds to a intraosseous neurofibroma of controveltial diagnosis because even though it presents typical neurofibroma histomorphological features it has immunophenotype different from usual.

Key words: Neurofibroma, benign intraosseous tumor, tumor of neural origin.
Case Report
A 14-year old male patient consulted for orthodontic treatment. In the initial evaluation an orthopantomograph was taken. It revealed a unilateral radiolucency in the right mandible ramus, extending vertically up to the basal border of the mandible. Horizontally, the lesion occupied the whole width of the ramus. The radiographically boundaries of the lesion were well defined, not corticalized, with scalloped borders. The lesion was partially projected over the follicle of the 3.8 tooth. There was no vertical displacement of the mandibular canal or the tooth germ 3.8. (Fig. 1) Intraoral examination revealed no clinical changes associated with the lesion. Bone outlines were normal to palpation and the patient reported no symptoms. Based on the clinical and radiographic findings, a keratocyst, ameloblastoma and ameloblastic fibroma were proposed as provisional diagnosis. A surgical excision was planned under general anesthesia, for curetage and histopathologic study. Gross examination showed a laminar, rectangular soft tissue mass, firm and white-grayish, which measured 4x1,5x0,5 cm, with no internal calcifications. Microscopic study with hematoxilyn-eosin (HE) showed a tumour mass formed by regular spindle cells, with wavy, hiperchromatic nuclei and scanty cytoplasm, in a richly vascularized myxoide stroma, with presence of collagen fibers and connective tissue cells. There were also nerve bundles cut transversely (Fig. 2). Representative sample cuts were studied with immunohistochemistry using primary antibodies anti S-100 protein, vimentin, and neuroespecific enolase (NSE). The process was performed following the standard protocol, using positive and negative controls. Immunohistochemistry showed that tumor cells were positive for vimentin, NSE (Fig. 2) and negative for S-100 protein. The residual nerve fibers were positive for S-100 protein and NSE. Considering the tumor’s histopathological features with HE and immunohistochemistry, intraosseous neurofibroma was diagnosed., even though it might be controversial the fact that it was negative to immunostaining for S-100. It is important to considerer the differential diagnosis with other neoplasm arising from peripheral nerve sheath, such as schwannoma, perineuroma, neurofibrosarcoma and, less frequently, with mesenchymal tumor of muscular or myxoid nature.

Discussion
Nerve sheath tumors located in the jaw are extremely rare, having published only a few cases of central neurofibroma of the mandible (4). (Table 1) presents the clinical, radiographic, histological and immunohistochemistry features of the intraosseous neurofibroma of the jaws cases published. The average age is 27.5 years, ranging between 14 and 45 years old (8,9), and there is no clear evidence as to the sex distribution. In our case, it was a 14 years old man.

Ninety percent of the neurofibromas are associated with neurofibromatosis type 1 (2,3, 8-12), so the presence of a solitary case requires physical examination and family history so as to exclude the disease. In this case, there were no clinical signs or family history suggestive of neurofibromatosis. The lesion was a solitary one. As Polak et al. (5) pointed out, it is important to highlight the need to rule out the differential diagnosis of schwannoma (Antoni A and Antoni B areas) and perineuroma (pattern similar to onion bulbs), as proposed by Ide. Ide, Shimoyama and Gomez and Oliveira (6,13) also recognized that neurifibroma is composed of a complex proliferation of schwann cells, perineural cell, endoneural fibroblasts and intermediate cells. These authors distinguished three types of neurofibromas (NF type I, II, and III) based on their reactivity to different markers and ultrastructural features. This subdivision is useful and represents the variable possibility for different markers.

This case should be considered as a intaosseous neurofibroma of controversial diagnosis because it showed no histological or immunohistochemistry features typical
Table 1. Clinical, radiographic, histological and immunohistochemistry features of the intraosseous neurofibroma of the jaw cases.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Gender</th>
<th>Location</th>
<th>Symptomatology</th>
<th>Radiographic Features</th>
<th>Histological Features</th>
<th>Immunohistochemistry Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vivek and cols. (11)</td>
<td>39 years</td>
<td>F</td>
<td>Mandible</td>
<td>No</td>
<td>Well-circumscribed radiolucent area with continuity loss of the mandibular canal</td>
<td>Spindle cells with wavy nuclei arranged in the form of booklets</td>
<td>Anti S-100 Positive</td>
</tr>
<tr>
<td>Larsson and cols. (2)</td>
<td>46 years</td>
<td>M</td>
<td>Mandible</td>
<td>Intermittent pain</td>
<td>Bone destruction with slightly radiopaque areas</td>
<td>Spindle cell with elongated or oval nuclei forming cords</td>
<td>Not performed</td>
</tr>
<tr>
<td>Larsson and cols. (2)</td>
<td>25 years</td>
<td>F</td>
<td>Mandible</td>
<td>No</td>
<td>Extensive bone resorption</td>
<td>Irregular nerve fiber strands intermingled with collagen fibers and abundant cells</td>
<td>Not performed</td>
</tr>
<tr>
<td>Polak and cols. (5)</td>
<td>60 years</td>
<td>M</td>
<td>Mandible</td>
<td>No</td>
<td>Unilocular radiolucency</td>
<td>Cords of fusiform or ovoid cells intermixed with a fibrillary stroma</td>
<td>Anti S-100 Positive Anti-Lai 7 Positive</td>
</tr>
<tr>
<td>Sharma and cols. (8)</td>
<td>5 months</td>
<td>F</td>
<td>Maxilla</td>
<td>No</td>
<td>No</td>
<td>Cords of dense collagen fibers intermixed with strands of nerve tissue with wavy nuclei</td>
<td>Anti S-100 Positive EMA Negative</td>
</tr>
<tr>
<td>Mori and cols. (3)</td>
<td>18 years</td>
<td>F</td>
<td>Maxilla</td>
<td>Tooth mobility</td>
<td>Well-circumscribed multilocular radiolucency</td>
<td>Growth of wavy-like tumor cells in a myxomatous matrix</td>
<td>Anti S-100 Positive</td>
</tr>
<tr>
<td>Skouteris and cols. (9)</td>
<td>16 years</td>
<td>F</td>
<td>Maxilla</td>
<td>No</td>
<td>Poorly-defined radiolucency</td>
<td>Spindle cells and abundant myxomatous stroma</td>
<td>Not performed</td>
</tr>
<tr>
<td>Apostolidis and cols. (4)</td>
<td>67 years</td>
<td>F</td>
<td>Mandible</td>
<td>Paresthesia and hyperesthesia</td>
<td>Circumscribed elliptical radiolucency with expansion of the mandibular canal</td>
<td>Numerous spindle cells in a myxoid matrix</td>
<td>Not performed</td>
</tr>
<tr>
<td>Poupard and cols. (12)</td>
<td>14 years</td>
<td>M</td>
<td>Maxilla</td>
<td>Poorly defined radiolucency</td>
<td>Spindle and estellate cells with a mucoid extracellular material with some condensation of fibrous tissue</td>
<td>Anti S-100 Positive</td>
<td></td>
</tr>
</tbody>
</table>

F: female, M: male.
Intraosseous Neurofibroma

of NF. Although positivity for neurospecific enolase shows the presence of nerve tissue, negativity for S-100 protein rules out the neural origin of cells observed in the tumor. This may be because the cells have a maturity level in which do not reflect the characteristics immunophenotype of neural origin cells (6). Despite the above and considering the histomorphological architecture of the lesion, the anatomic area (periphery of the inferior alveolar nerve), the delimitation and biological behavior, supported by the opinion of several pathologists, we confirm the diagnosis of neurofibroma.

It is important to consider that the solitary intraosseous neurofibroma may be the first manifestation of neurofibromatosis (3, 12). It is also necessary to conduct a clinical and radiographic follow-up, since recurrence and malignant changes have been reported (3).

References