A Rare Case of Intraoral Nodular Fasciitis: Diagnosis and Immunohistochemical Profile

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Nodular fasciitis is a benign, idiopathic, reactive proliferation of myofibroblasts found in the subcutaneous fascia; intraoral occurrence is very rare. An 18-year-old woman was referred to the oral diagnosis service with a 1-month history of a nodular mass in the gingiva. Clinical examination disclosed a well-circumscribed, mobile, pedunculated mass in the left mandibular gingiva. The clinical diagnoses included pyogenic granuloma. She underwent an excisional biopsy under local anesthesia through an intraoral approach. Microscopic examination showed a proliferation of spindle cells arranged in intersecting fascicles. The spindle cells exhibited plump, vesicular nuclei without significant pleomorphism. Scattered multinucleated giant cells also were present. Immunohistochemical stains showed that the lesional cells were positive for smooth muscle actin and vimentin and negative for S-100 protein. The features were those of an inflammatory, benign myofibroblastic lesion, consistent with intraoral nodular fasciitis.

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Defined by the World Health Organization as an alteration of benign proliferative fibroblasts and myofibroblasts,1,3 nodular fasciitis (NF) was first described in 1955 by Konwaler et al4 who named this entity subcutaneous pseudosarcomatous fibromatosis. Since then, it has received other denominations, such as pseudosarcomatous fasciitis, pseudosarcomatous fibromatosis, proliferative fasciitis, and infiltrative fasciitis. Before its recognition as a distinct entity, NF was often classified as some form of sarcoma, usually liposarcoma, fibrosarcoma, or rhabdomyosarcoma.3,5

Some investigators have suggested that the pathogenesis of NF may be traumatic, infectious, or inflammatory,5,6 although the role of those factors in initiating the lesion remains doubtful.5 NF is a soft tissue lesion, with about 20% of cases involving the head and neck region, especially in young patients.5,7 It rarely has an intraoral location.5,7,8 Clinically, NF presents as a well-circumscribed mass with rapid and limited growth, being related to inflammatory reactions or traumatic events.2,6 The microscopic features of a high rate of spindle cells and the presence of mitotic figures suggest that the differential diagnosis should include some benign neoplasms, such as neurofibroma and myofibroma, and some sarcomas, such as sarcomatoid carcinoma, fibrosarcoma, and leiomyosarcoma.2,5,6,8 Considering these possible diagnoses, immunohistochemical analysis represents an alternative to establish a correct and conclusive diagnosis.6,8,9

The literature suggests specific antibodies be used for the immunohistochemical elucidation of NF; the most cited among these are vimentin (fibroblasts or myofibroblasts), α-smooth muscle actin (cells of muscle origin), CD68 (macrophages), S-100 (cells of neural origin), and Ki-67 (cell proliferation).1,8,10

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This report describes a rare case of intraoral NF and presents a brief review of the literature of NF cases in the oral cavity published in the past 10 years. In addition, some important aspects regarding clinical and histopathologic aspects, immunohistochemical profile, and differential diagnosis are discussed.

Report of Case

An 18-year-old woman was referred to the Oral and Maxillofacial Surgery Clinic of the Federal University of Rio Grande do Norte, complaining of a 3-month history of painful gingival swelling. Physical examination disclosed a nodular mass with defined borders in the vestibular gingiva near the inferior left first molar. The mass was sessile, firm on palpation, presented exophytic growth, and measured approximately 1.3 cm in diameter (Fig 1). There was no history of trauma or inflammation in the region, and the medical history was noncontributory. The differential clinical diagnoses included pyogenic granuloma, inflammatory fibrous hyperplasia, and peripheral giant cell granuloma. The patient underwent an excisional biopsy (Fig 2) under local anesthesia. Microscopic examination showed a nonencapsulated, but well-demarcated reactive benign lesion consisting mainly of interlacing bundles of spindle-shaped mesenchymal cells, resembling fibroblasts. These cells displayed different sizes and were set against a myxoid background. There was a mildly lymphoplasmacytic inflammatory infiltrate scattered throughout the lesion, and rare typical mitotic figures and multinucleated giant cells were seen. Other areas

FIGURE 1. Clinical examination showed a nodular swelling in the left mandibular gingiva.

of the lesion exhibited hyalinization and hemorrhagic foci (Fig 3). An extensive ulcerated area was evident in the superficial lining of the specimen. The histopathologic characteristics suggested a diagnosis of NF.

An immunohistochemical panel was necessary to elucidate the origin of the spindle lesional cells and to exclude some benign neoplasms and sarcomas. Immunohistochemical reactions were performed with anti-vimentin (1:50; clone V9; Dako, Carpinteria, CA), anti-smooth muscle actin (1:50; clone 1A4; Dako), anti-CD68 (1:800; clone KP1; Dako), and anti-S100 protein (1:400; polyclonal; Dako). The lesional cells were positive for anti-vimentin (Fig 4) and anti-smooth muscle actin (Fig 5) and negative for anti-S100 protein (Fig 6). Some multinucleated giant cells showed positivity for anti-CD68 (Fig 7). These findings were consistent with the diagnosis of NF. After 3 months of follow-up, the patient showed no clinical evidence of recurrence (Fig 8).

Discussion

Han et al7 conducted a survey of orofacial NF cases from 1994 through 2005 and found only 8 cases reported in the literature, suggesting a low incidence of NF in this region. For the present case, a search of the English-language literature in the PubMed database regarding intraoral NF cases in the past 10 years (2004 through 2013) yielded only 15 cases (Table 1). The scarcity of publications concerning NF can be...
explained by the rarity of its occurrence or controversies in histopathologic diagnosis, because NF is an entity difficult to characterize.

NF presents a slight female predilection, affecting mainly individuals 20 to 40 years old. The most involved anatomic locations are the upper extremities, followed by the trunk, and rarely an intraoral location. When NF is located in the oral cavity, the most common site is the buccal mucosa, but it can occur in other areas, such as the gingival area, menton region, and labial mucosa. The literature does not report differences regarding clinical presentation, growth, or aggressiveness between intraoral NF and other anatomic sites of occurrence.

The main clinical features of intraoral NF include rapid nodular growth, rarely ulceration, a history

**FIGURE 4.** Immunohistochemical stain shows strong positivity for vimentin (streptavidin and biotin stain; scale bar, 100 μm).

**FIGURE 5.** Diffuse cytoplasmic positivity of the lesional spindle cells for smooth muscle actin (streptavidin and biotin stain; scale bar, 100 μm).
of days or a few months, asymptomatic, firm, exophytic, usually showing the color of the overlying mucosa, and measuring 0.5 to 3.0 cm.\textsuperscript{2,6,8,10} The clinical presentation of NF may mimic other lesions, such as benign proliferative or reaction alterations (ie, fibroma and pyogenic granuloma) or even salivary gland tumors. This clinical differential diagnosis is defined by the association of the history, clinical aspect, and location of the lesion.\textsuperscript{2,6,9,10} The present case had a history of rapid exophytic growth affecting the lower gingiva, leading to an initial diagnosis of a lesion of a reactive nature, possibly including pyogenic granuloma, inflammatory fibrous hyperplasia, or peripheral giant cell lesions.
The pathogenesis of NF remains unknown. However, it seems to be reactive or inflammatory, involving fibroblastic or myofibroblastic proliferation, rather than a true neoplasm. Some investigators have suggested that local trauma could trigger myofibroblast proliferation. Another hypothesis, based on the observation of some cases of pregnant and lactating women presenting with NF, proposes that stimulation of estrogen receptors in myofibroblasts could be a contributing factor to the proliferation of those cells.

The histopathologic features of NF are nonspecific; this hampers the characterization and diagnosis of this lesion. Histologically, there are 3 subtypes of NF according to the plane of the tissue involved: subcutaneous, intramuscular, and fascial. The most common presentations are the subcutaneous and facial subtypes, although, in general, all exhibit numerous lesional spindle-shaped cells of prominent ovoid nucleoli arranged in a storiform pattern or a haphazard manner in a myxoid fibrous stroma. Scattered chronic infiltrate and red blood cells are frequently evident within the background. Usually the lesion is well delimited, but nonencapsulated, and some cases with high cellularity exhibit abundant mitotic activity, but no cellular atypias are seen. In addition, some lesions display multinucleated giant cells and entrapment of adjacent skeletal muscle. The findings of the present case corroborate the general histopathologic characteristics reported in the literature, suggesting a diagnosis of NF. However, owing to the rapid growth associated with spindle cells resembling fibroblasts, abundant cellularity, presence of occasional mitoses, and the intraoral site of development, neoplasms, such as myofibroma, neurofibroma, schwannoma, sarcomatoid carcinoma, fibrosarcoma, and leiomyosarcoma, need
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Abbreviations: DC, dermoid cyst; F, female; IFH, inflammatory fibrous hyperplasia; M, male; NM, not mentioned; PG, pyogenic granuloma; PGCG, peripheral giant cell granuloma; SGT, salivary gland tumor.

<sup>*</sup> Han et al<sup>7</sup> cited the existence of 2 more cases of nodular fasciitis in the intraoral region, one in the gingival area and the other in the mandibular body, but did not describe the clinical appearance of these cases.

to be included in the histopathologic differential diagnosis.\textsuperscript{1,2,6-9} Very few neoplasms can be distinguished from NF based only on cell appearance. For example, the stroma of schwannoma consists of 2 types of cellular arrangement, Antoni A and B, and these are not present in NF.\textsuperscript{1,6} Most NF cases, including the present case, display a cellular morphology and organization similar to those of other neoplasms and require a more thorough investigation with immunohistochemical analysis to elucidate the nature of the lesional spindle cells.\textsuperscript{1,3,6,7,10} The immunohistochemical profile of NF includes positive expression for vimentin, α-smooth muscle actin, and muscle-specific actin, indicating myofibroblastic differentiation of spindle cells.\textsuperscript{6,7,9} A complementary differential expression is exhibited by the negative reaction of antibodies directed against muscle-specific actin, cytokeratins, desmin, and S-100 protein.\textsuperscript{1-9} Staining with antibodies for CD34, CD99, and bcl-2 aid in excluding solitary fibrous tumor. Moreover, anti-CD68 antibody can be used to confirm the presence of giant cells.\textsuperscript{9} Although immunohistochemistry can help differentiate other benign or sarcomatous lesions, this technique does not appear to be as effective when trying to distinguish NF from lesions with a proliferation of fibroblasts and myofibroblasts (ie, inflammatory myofibroblastic tumor), because they also can exhibit positive staining for α-smooth muscle actin and muscle-specific actin.\textsuperscript{2,3,8}

Anti–Ki-67 and antiproliferating cell nuclear antigen have been suggested to assess the proliferative activity of the lesion.\textsuperscript{1,6} Although some investigators have reported that NF can present high proliferative activity,\textsuperscript{1,6,7} in the present case, only a few mitotic figures were observed. The immunohistochemical panel and the clinical and histopathologic findings led to a definitive diagnosis of NF for the case in question.

The treatment for NF consists of conservative surgical excision,\textsuperscript{10} although Carli et al\textsuperscript{2} reported a case of spontaneous regression of NF with a considerable decrease in size after the completion of an incisional biopsy, which allowed a new but less aggressive surgical intervention. Regression or shrinking of NF can occur from a gradual transition from a loose myxoid component to a more fibrous and compact component.\textsuperscript{2,3}

This case was surgically treated and no recurrence occurred during the 3-month follow-up, confirming other reports that have shown the absence of recurrence in periods ranging from 3 months to 9 years.\textsuperscript{2,7}

This report emphasizes that NF is rare in the intraoral region and highlights the importance of including this lesion in the differential diagnosis for other entities involving this area, particularly those with rapid growth, such as reactive proliferative lesions and some malignant neoplasms. This can avoid misdiagnosis and inappropriate treatment. Therefore, the correlation of clinical and histopathologic features and the immunohistochemical profile of cellular components are extremely important for the diagnosis of NF.

References