CASE REPORT
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Nodular Fasciitis of the Tongue

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Abstract

Nodular fasciitis is a rare, non-malignant, rapidly growing, self-limited myofibroblastic/fibroblastic soft tissue tumor. This lesion may cause differential diagnostic problems due to the lack of specific histopathological characteristics and, mainly, due to its histological appearance that resembles mesenchymal neoplasms. A 27-year-old female sought care due to a complaint of a firm and rapid, painless swelling in the tongue. After an excisional biopsy, the histopathological evaluation using hematoxylin-eosin stain showed skeletal muscle tissue with a well-delimited lesion with rich cellularity, consisting of spindle cells, relatively uniform nuclei over a fibrous stroma. The immunohistochemistry panel was used as a complementary diagnosis procedure and included INI1, S100, EMA (MUC1), DESMIN, AE1-AE3, AML, CD34, h-Caldesmon, and β-catenin. Based on clinical, histopathological, and immunohistochemical findings, the present case was diagnosed as nodular fasciitis. Comprehensive knowledge of this entity is essential for adequate therapy to avoid unnecessary aggressive treatment.

Keywords: Nodular fasciitis, immunohistochemistry, tongue, tongue neoplasm

INTRODUCTION

Nodular fasciitis (NF) is a rare, non-malignant, rapidly growing, self-limited myofibroblastic/fibroblastic soft tissue tumor. Despite its benign nature, NF can generate confusion in the differential diagnosis due to the lack of specific histopathological characteristics and, mainly, due to its clinical and histological features that resemble mesenchymal neoplasms.[1-3] In the past, NF was also known as infiltrative fasciitis, pseudosarcomatous fasciitis, and subcutaneous pseudosarcomatous fibromatosis.[4]

The histopathology of NF may include variable cellularity of fibroblasts and myofibroblasts, intense mitotic activity, and extracellular matrix ranging from myxoid to collagenous, especially in older lesions. Areas of cystic degeneration and spindle stellate cells with a loose fascicular to storiform pattern with bland ovoid nuclei may also be identified. However, atypical figures are not a feature; scattered lymphocytes, histiocytes, and osteoclast-type giant cells are often present, and areas of extravasated erythrocytes are often present.[2,4-6] These characteristics lead to NF frequently being confused with other diseases. In this context, an accurate diagnosis is important, given the potential for initiating hazardous and incorrect treatments.[2,4-10]

Nodular fasciitis is frequently located in the deep subcutaneous region, intramuscularly, or in the fascia, and it has been reported in all age groups, although it is commonly diagnosed in the third to fifth decades of life with no gender predilection. In the maxillofacial region, NF usually presents as a rapidly growing mass, generally painless, typically firm and well-circumscribed but non-encapsulated.[2,4,-10]

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The etiology of NF has been described as uncertain, and while some authors consider it a benign tumor,[1,2,4] others classify it as a benign reactive and proliferative myofibroblastic lesion triggered by trauma that may, eventually, regress spontaneously.[5,8,9] More recently, NF has been considered a true neoplasm and not an inflammatory reactive lesion due to its consistent USP6 gene rearrangement, the most common is the MYH9-USP6 fusion.[2,3,10]

This case report explores the clinical, imaging, histopathological, and immunohistochemical features, as well as the surgical aspect of nodular fasciitis presenting deep in the tongue muscles.

CASE PRESENTATION

A 27-year-old female sought care due to a complaint of rapid, painless swelling in the tongue, which had progressed for about 2 months. On physical examination, a nodular mass was observed on the right side, at depth in the tongue muscles, with a slight increase in volume externally, without inflammatory characteristics. No history of trauma in the region was recorded. On palpation, the lesion had a well-defined and firm consistency. No pain was observed under pressure.

A contrast-enhanced soft tissue window computed tomography (CT) angiography showed a nodular and well-circumscribed image with discrete areas of peripheral enhancement, located in the paramedian region to the right of the anterior third of the body of the tongue, measuring 13 × 11 × 10 mm (Figure 1).

Due to the uncertain nature of the lesion and tomographic appearance, an excisional biopsy of the lesion under general anesthesia was carried out. On surgical exploration, the lesion showed non-homogeneous delimitation and merging with the tongue muscles (Figure 2). The postoperative period was uneventful, with no signs of loss of tongue mobility and loss of sensitivity limited to the operated area. Sensitivity gradually returned over the follow-up period and currently shows no alteration.

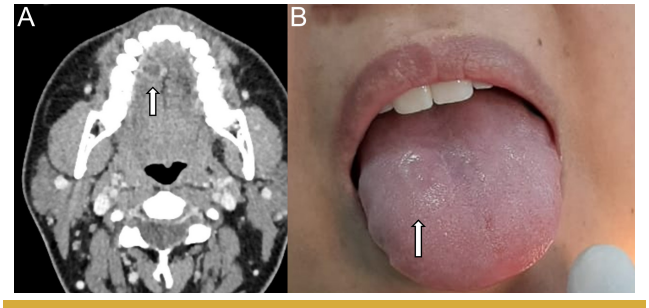

Figure 1. (A): Contrast-enhanced soft tissue window CT angiography showing a nodular image, well-circumscribed, with discrete areas of peripheral enhancement (arrow). (B): Tongue showing a light observable increase in volume (arrow). CT, computed tomography.

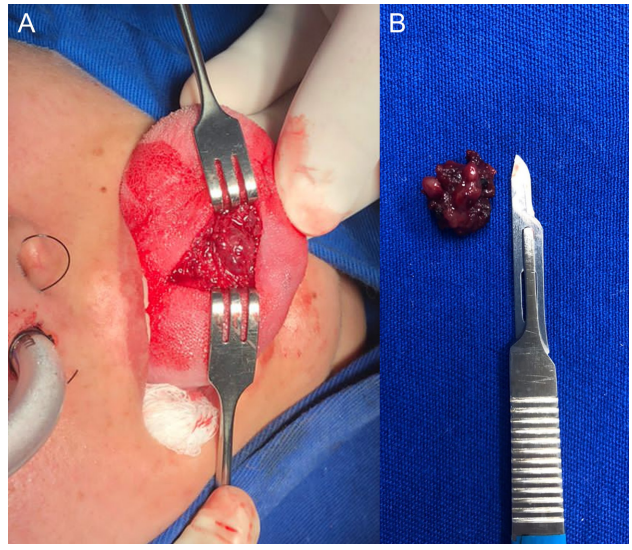

Figure 2. (A): Surgical aspect of nodular fasciitis in the tongue. (B): Specimen removed.

The histopathological evaluation using hematoxylin-eosin stain (H&E) showed skeletal muscle tissue with a well-delimited lesion, with rich cellularity consisting of spindle cells, relatively uniform nuclei amid capillaries and the presence of extravasated erythrocytes over a fibrous stroma (Figure 3). No figures of mitosis or aberrant mitosis, cellular atypia, necrosis, or vascular or perineural invasion were observed. The peripherally examined planes showed that the lesion was completely excised.

The immunohistochemistry was performed on deparaffinized, rehydrated sections obtained from a formalin-fixed, paraffin-embedded block of the case using antibody-specific epitope retrieval techniques. Immunohistochemical reactions are performed using an automated methodology (Ventana BenchMark, Roche, and Dako Autostainer Link 48, Agilent Technologies). The used antibody dilutions followed manufacturer recommendations. Positive controls were included on each slide individually according to the antigen/antibody being analyzed. Negative controls were performed by replacing the primary antibodies with the same Phosphate Buffered Saline (PBS) solution. Immunohistochemistry panel and results used as a complimentary diagnosis for NF are given as follows: (1) antigen INI1 (antibody—MRQ-27), positive result. Lack of nuclear labeling by anti-INI1 may be characteristic of malignant rhabdoid tumor. (2) Antigen S100 (antibody polyclonal), negative result. S100 is a marker of Schwann cells and melanocytes. (3) Antigen EMA (MUC1) (antibody E29), partial or focal positive result. Epithelial

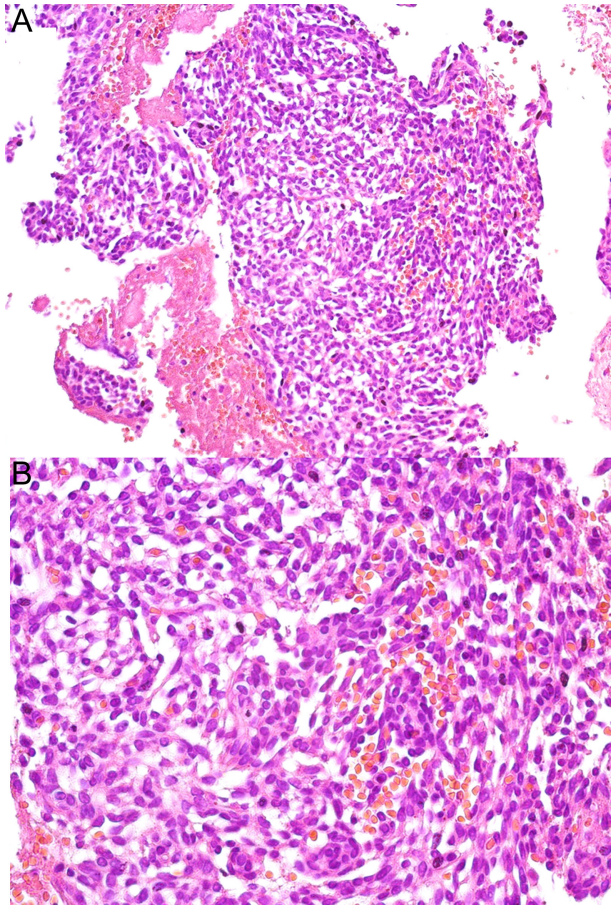

Figure 3. (A/B): Histopathological features of nodular fasciitis stained by hematoxylin-eosin (H&E) showing a rich cellularized tumor consisting of spindle cells, with relatively uniform nuclei over a fibrous stroma (A: H&E, 20×; B: H&E, 40×).

membrane antigen (EMA) or MUC1 is expressed in most normal and epithelial neoplastic cells. Epithelial membrane antigen is also expressed in plasma cells, anaplastic large cell lymphoma, malignant histiocytosis, and erythroleukaemia. (4) Antigen desmin (antibody DE-R-11), negative result. Desmin is a marker for neoplasms with myogenic differentiation including rhabdomyosarcoma, rhabdomyoma, leiomyosarcoma, leiomyoma, smooth muscle, and rhabdomyoblastic elements in other tumors. (5) Antigen AE1-AE3 (antibody AE1/AE3/PCK26), negative result. This is also known as "Keratin cocktail" or "pankeratin" that detects CK1-8, 10, 14-16, and 19. It is used to confirm or rule out the epithelial nature of tissue, tumors, or components of tumors. (6) Antigen AML (antibody HUC1-1), positive result. Anti-muscle-actin is a pan muscle actin that reacts with tumors arising from smooth muscle as well as skeletal muscle. (7) Antigen CD34 (antibody QBEnd10), negative result. It is a commonly used marker of hematopoietic progenitor cells and endothelial cells. (8) h-Caldesmon (hHCD), negative result. Immunohistochemical detection of h-caldesmon is used to distinguish smooth muscle tumors, such as leiomyoma and leiomyosarcoma from myofibroblastic lesions, such as inflammatory myofibroblastic tumors and fibromatoses. (9) β-Catenin (antibody E-5) negative result. Mutations and overexpression of β-catenin are associated with various carcinomas, including colon, thyroid, and uterus.

The present case diagnosis of NF was based on clinical appearance and follow-up, histopathological, and immunohistochemical findings and corroborates the general characteristics reported in the literature. To date, after 18 months of follow-up, no recurrence was observed and the patient is still under follow-up.

Appropriate written informed consent and permission were obtained from the patient described in this article.

DISCUSSION

Nodular fasciitis is a rare benign, proliferative neoplasm that can appear in any body area, while the intraoral presentation is extremely unusual.[7-9] The diagnosis of NF is often a challenge and the correlation of clinical and histopathologic features together with the immunohistochemical profile of the lesion is extremely important for its diagnosis. For differential diagnosis, it may take into account the position and clinical features of the lesion as well as the histological and immunohistochemical features so this may encompass lesions with different origins, from reactive proliferations to several soft tissue mesenchymal neoplasms.[8,9]

Imaging studies, such as ultrasound and magnetic resonance imaging (MRI), may help to identify the benign features of this lesion. On ultrasound, the lesions have been described as predominantly hypoechoic or with mixed echogenicity and poorly defined margins. On MRI, T1, T2, and T2 fat-saturated sequences were utilized resulting in images that may vary from well-defined to poorly-defined borders.[1,10] The present study used a contrast-enhanced soft tissue window CT angiography which showed a non-vascularized and well-circumscribed lesion and these features helped to characterize and emphasize the benign aspect of the lesion and also, helped in the surgical planning, considering that the lesion was located deeply in the tongue muscles.

Immunohistochemistry is mandatory to confirm the NF diagnosis and elucidate the origin of the spindle lesional cells. Moreover, it is relevant to exclude some benign neoplasms and sarcomas. On immunohistochemical analysis, it has been reported that NF may express vimentin (a fibroblast marker),[6,8,9] smooth muscle actin, and muscle-specific actin,[1,6,7,10] CD10,[1] Ki67,[10] and more recently, USP6, p16, p27, TRAIL, and IFNB.[3] The reactivity for vimentin, smooth muscle actin, and muscle-specific actin may indicate myofibroblastic

differentiation of spindle cells. Although these markers can help differentiate other benign or sarcomatous lesions, they do not help to differentiate NF from lesions with a proliferation of fibroblasts and myofibroblasts.[9]

Desmin,[6,7] keratin,[6,10] S-100 protein,[6,7,9] cytokeratin AE1-AE3,[1,7] CD34,[1] CD99, ALK, MyoD1, myogenin,[10] melan-A, factor VIII, CD31, cytokeratin, and β-catenin have been reported as negative for NF in immunohistochemistry analysis.[1] Staining with antibodies for CD34, CD99, and bcl-2 may aid in excluding solitary fibrous tumors and, whenever present in the lesion, multinucleated giant cells may show positivity for anti-CD68.[9] In this myriad of makers available for immun ohistochemistry, our results are compatible with the already reported negative for NF as CD34, desmin, and cytokeratin AE1-AE3, as well as the positivity for AML which is already been reported in the literature.[1,6,7,10] However, this present study included EMA (MUC1), h-Caldesmon, β-catenin, and HUC1 as negative as well, and also, as excluding criteria for malignant rhabdoid tumor, the positivity for INI1.

The most recommended treatment for NF is surgical resection of the lesion; however, intralesional injection with triamcinolone has also been reported.[3,6,9,10] Spontaneous regression has been reported, which reinforces the recommendation of non-intervention based on the self-limiting nature of the lesion; however, this conduct must be based on an accurate diagnosis.[1,5] Comprehensive knowledge of this entity is mandatory for adequate therapy and avoids more aggressive treatment strategies. Recurrences are rare for NF. However, when they do occur, they are usually related to incomplete tumor resection and, in this context, it is relevant that the original diagnosis is revised to rule out neoplasms of mesenchymal origin.[4,5]

Nodular fasciitis is a rare benign soft tissue tumor that may create confusion in the differential diagnosis due to its similarities with mesenchymal neoplasms. Clinical, histopathological, and immunohistochemical findings are mandatory for the proper diagnosis of NF. Comprehensive knowledge of this entity is essential for adequate therapy, avoiding unnecessary aggressive treatment.

Ethics Committee Approval: Ethical committe approval was received from the Ethics Committee for Human Research of the State University of Ponta Grossa under number 5.510.219.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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