

Oral involvement in a patient with neurofibromatosis type I

Acometimento oral em portador de neurofibromatose tipo I

ABSTRACT

Neurofibromatosis type 1, also known as von Recklinghausen neurofibromatosis, is an autosomal dominant disorder that affects 1 in 3,000 newborns. Approximately 50% of neurofibromatosis type 1 patients have no family history of the disease. The tongue, the alveolar ridge of the buccal mucosa, gums, lips, palate, floor of the mouth, and pharyngo-maxillary fossa can be affected by tumors associated with this condition; the tongue is the most common site. We report the case of a 29-year-old female patient with neurofibroma in the tongue, highlighting the possibility of disease manifestations in the oral cavity and differential diagnoses.

Keywords: neurofibromatosis 1; neurofibroma, plexiform; neurofibroma; tongue neoplasms.

RESUMO

A neurofibromatose do tipo 1, também conhecida como neurofibromatose de von Recklinghausen, é doença autossômica dominante, que afeta 1:3000 recém-nascidos. Aproximadamente 50% dos pacientes de NF1 não apresentam história familiar da doença. Língua, rebordo alveolar da mucosa bucal, gengivas, lábios, palato, assoalho da boca e o espaço faringomaxilar podem ser acometidos por tumores em associação com NF1, sendo a língua o local mais comum. Relata-se o caso de paciente do sexo feminino, de 29 anos, apresentando neurofibroma na língua, ressaltando-se a possibilidade de manifestações da doença na cavidade oral e seus diagnósticos diferenciais.

Palavras-chave: neurofibromatose 1; neurofibroma plexiforme; neurofibroma; doenças da língua.

INTRODUCTION

Neurofibromatosis type 1 (NF1), also known as von Recklinghausen neurofibromatosis, is a dominant autosomal disease that affects 1 in 3,000 newborns. Approximately 50% of NF1 patients have no family history of the disease, 1 which is clinically characterized by the presence of café-au-lait spots, axillary ephelides, Lisch nodules, and multiple neurofibromas. It can be associated with optic gliomas, neurofibromas in peripheral and spinal nerves, neurological or cognitive deficit, scoliosis, oral and maxillofacial abnormalities, malignant nerve sheath tumors, pheochromocytoma, and vasculopathy.¹⁻⁴

Case Report

Authors:

Alceu Luiz Camargo Villela Berbert¹
Adriano Mota Loyola²
Sônia Antunes de Oliveira Mantese³
Bruno César Dornela⁴
Mabel Duarte Alves Gomides⁵

¹ Assistant Instructor of Dermatology, Universidade Federal de Uberlândia (UFU) – Uberlândia (MG), Brazil

² Associate Instructor of Dermatology, Universidade Federal de Uberlândia (UFU)

³ Dermatologist Physician; Instructor, Universidade Federal de Uberlândia (UFU)

⁴ Medical Academician da Faculdade Presidente Antônio Carlos (Unipac) – Araguari (MG), Brazil

⁵ Dermatologist Physician; Dermatology Instructor, Hospital de Clínicas da Universidade Federal de Uberlândia (UFU)

Correspondence:

Dr. Alceu Luiz Camargo Villela Berbert
Rua Tapuira 523/1002, Bairro Osvaldo
Resende, Uberlândia – MG, Brazil
Cep: 38400-436
E-mail: dermisap@yahoo.com.br

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A clinical radiological study has detected soft tissue oral manifestations in 72-92% of NF1 patients, including intraoral tumors in approximately 25% of cases. The tongue, alveolar ridge of the buccal mucosa, gums, lips, palate, floor of the mouth and pharyngeal maxillary space can be affected by tumors in association with NF1, with the tongue being the most common site.^{1,3,5}

CASE REPORT

A 29-year-old female patient, born in the city of Imperatriz (in the northeast Brazilian state of Maranhão) but then living in the city of Araguari (in the Brazilian state of Minas Gerais), with grayish-brown skin, sought care at the Dermatology Service of the Universidade Federal de Uberlândia (MG), Brazil, complaining of unsightly skin lesions that had emerged in childhood and had grown gradually. The patient reported a previous diagnosis of neurofibromatosis, having denied any family history of the disease. Dermatological examination showed papulonodular and soft tumors with a hernial ring perceptible to the touch, slightly brownish in color, and located in different areas of the skin; café-au-lait macules located in the trunk and limbs; and the presence of axillary ephelides. Intraoral examination also evidenced an erythematous, yellowish, soft, painless nodular lesion, roughly 1 cm in diameter, and located on the right lateral border of the tongue (Figures 1A, B and C).

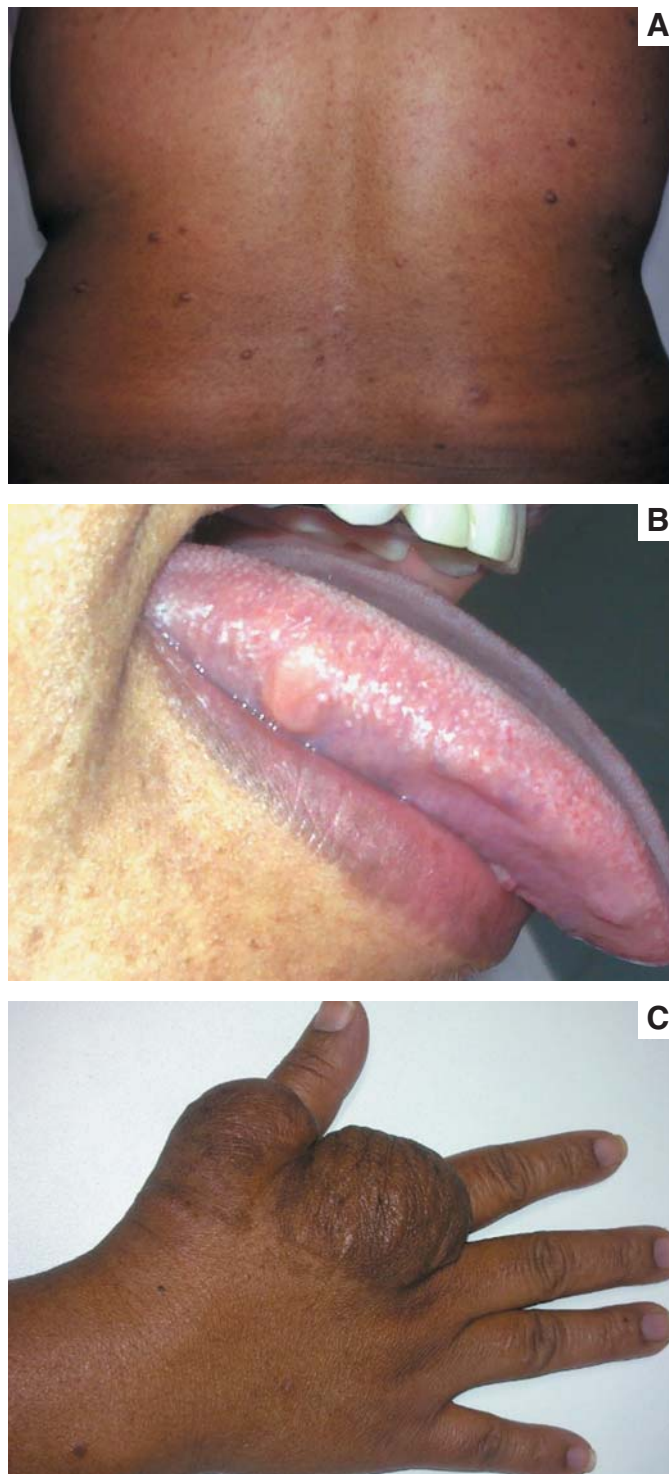
The histology of the oral lesion suggested mesenchymal nature, lined by stratified squamous epithelium, with focal areas of hyperparakeratosis, spongiosis and hydropic degeneration. Specific examination of the sections evidenced interwoven bundles of cells with elongated nuclei, distributed around nerve bundles and slightly fibrillar conjunctive tissue, with focal areas of myxoid material (Figure 2). A similar situation was found in the material collected from the lesion located on the right hand (Figure 3).

Given the clinical and histologic features presented by the patient, the diagnosis of neurofibroma was established.

DISCUSSION

NF1 is a dominant autosomal genodermatosis associated with deletions, insertions or mutations of the tumor suppressor gene NF1, located in the pericentromeric region of the chromosome 17. In general, NF1 is clinically diagnosed based on the cutaneous manifestations and family history.¹ Oral alterations of NF1 were reported to vary from four to 92% of cases, with the tongue being the most common site.^{3,4,6}

The considerable difference in oral manifestations can be attributed to the heterogeneity of the patients examined at specialized hospitals, and to differences in the investigated symptoms and research methods.¹ Early diagnosis of asymptomatic neurofibromas in the tongue requires a high index of clinical suspicion. Symptomatic oral lesions are more easily diagnosed when the tumor exerts compression or other types of discomfort. A significant positive correlation was found between the delay in the diagnosis and the oral location of lesions. The presence of discomfort is reported by most patients with lesions on the tongue, with pain being the most common complaint.¹



Figures 1 - A. Café-au-lait spots with brownish nodules (neurofibromas) present in the dorsal and lumbar regions; **B.** Presence of erythematous, yellowish nodule, 1 cm in diameter, in the right lateral border of the tongue; **C.** Brownish tumor on the back of the patient's right hand, with elastic consistency, measuring between 4 and 6 cm in diameter.

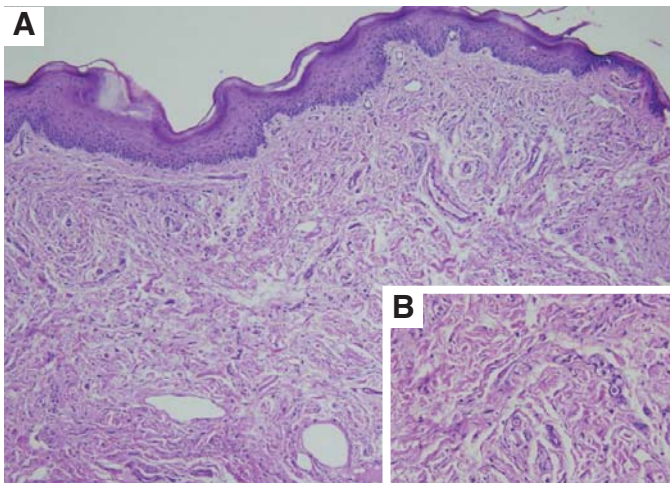


Figure 2 - Histological examination of the material collected from the lesion on the tongue, showing: **A.** Peripheral nerve sheath cell neoplasm with imprecise limits, the presence of elliptical, fusiform, and ovoid cells, permeating the fibrillary stroma and forming fairly organized bundles (HE, 10xmagnification); **B.** Tumor in greater detail (HE, 40x magnification).

Lesions located on the tongue develop slowly. Nevertheless, tumor growth can be accelerated by puberty, pregnancy and growth, with the clinical and histological findings being key to distinguishing between neurofibromas and other soft tissue tumors.

The differential diagnosis of tumors located in the tongue includes plexiform neurofibroma, lipoma, angiolipoma, chondroid lipoma, myolipoma, hamartoma, schwannoma, lymphangioma, granular cell tumor, leiomyoma, hemangioma, rhabdomyosarcoma, neurofibroma and localized amyloidosis.^{1,5,6}

A thorough histological analysis, assisted by the use of immunohistochemistry is essential for the correct diagnosis of soft mouth tumors. S100 protein, type IV collagen and the molecule CD34 are useful biomarkers in the analysis of NF1 with oral manifestations.¹

Partial or total surgical exeresis of tumors can be carried out to resolve aesthetic and functional problems. However, waiting for the end of a tumor's growth cycle is recommended in order to reduce the risk of recurrence, always keeping in mind the possibility of malignant degeneration (occurring in one to 29% of cases) with the appearance of peripheral nerve sheath malignant tumors.¹

Such tumors are not radiosensitive and, given their slow growth rate, limited benefit has been seen with the use of chemotherapy. Alternatives to surgical treatment of plexiform neuromas are still largely experimental, but include: retinoic acid, ketotifen fumarate, antiangiogenic drugs (alpha-interferon), thalidomide, pirfenidone (drugs with antifibrotic action) and tipifarnib (a farnesyl transferase inhibitor, since high levels of that enzyme are found in plexiform neuromas). Nonetheless, evidence of the efficacy of each of these treatments remains limited. Additional research with pharmaceutical alternatives should improve survival rates and quality of life for patients with plexiform neuromas.⁶

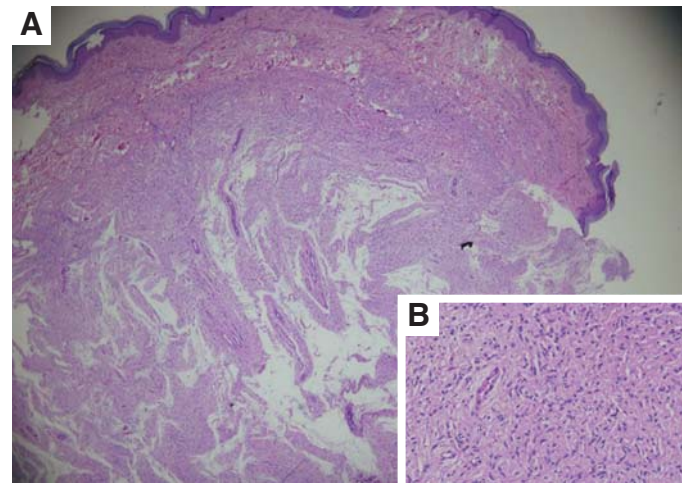


Figure 3 - Histological examination of a skin lesion fragment originating from a lesion on the dorsum of the right hand: **A.** Tumoration present in the dermis (HE, 4x magnification); **B.** Detail showing the presence of elliptical, ovoid, and spindle-shaped cells in bundles (HE, 40x magnification).

CONCLUSION

Searching for oral lesions in patients with NF1 is of paramount importance, and given that the examination of mucous membranes is increasingly relevant in the daily routine of dermatologists, it provides new tools for the elaboration of diagnostics. It is therefore necessary that the specialist dermatologist be familiarized with the different types of lesions that may be found in the various genodermatoses. ●

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