

## Gingival Enlargement in Neurofibromatosis Type 1: A Case Report and Literature Review

Ajay Mahajan, BDS, MDS; Jaya Dixit, BDS, MDS; Ashu Bhardwaj, BDS, MDS

### Abstract

**Aim:** The purpose of this article is to describe a rare case of neurofibromatosis1 (NF1) of the gingiva and a review of the current literature.

**Background:** Neurofibromatosis1 (NF1) of the gingiva is an uncommon cause of gingival enlargement. The disease is clinically characterized by epidermal melanosis, nevi, and flabby skin or bone malformations; in addition, the lesions may undergo malignant transformation. Involvement of the gingiva with or without concurrent skin lesions has been reported only occasionally.

**Case Description:** A 40-year-old male patient with a history of NF1 came to us with a chief complaint of enlargement of the gums. Clinical examination revealed diffuse gingival enlargement with no signs of inflammation. The characteristic skin lesions associated with NF1 were also present. A gingival specimen was sent for biopsy.

**Results:** Based on the history, clinical, and histological findings, NF1 was established as the cause of the gingival enlargement.

**Summary:** NF1 may affect the gingival tissue; considering the neurological complications and malignant potential, NF1 must be diagnosed early and monitored regularly.

**Clinical Significance:** The clinician should be aware of clinical and histopathological findings of NF1 considering the fact that the condition has malignant potential.



**Keywords:** Gingival enlargement, neurofibromatosis, von Recklinghausen disease, literature review, case report

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### Introduction

Gingival enlargements may be multifactorial in origin: chronic inflammatory, drug induced, gingival enlargement associated with systemic conditions, neoplastic, and false enlargements.<sup>1</sup> Neoplasms account for a comparatively small

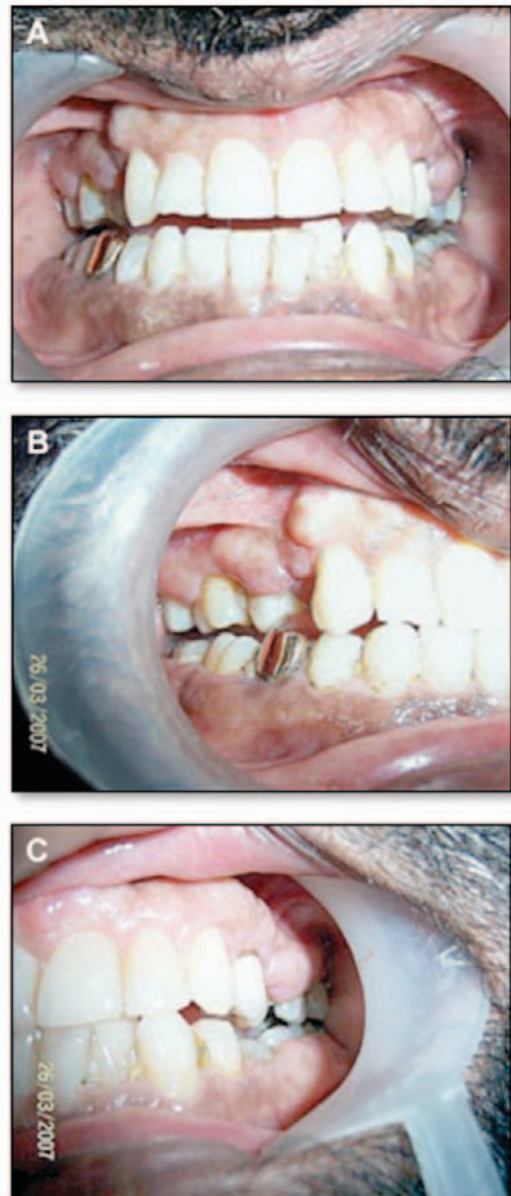


**Figure 1.** Multiple skin lesions (molluscum pendulum) on the face and hands.

proportion of gingival enlargements. In a survey of 257 oral tumors, approximately 8% occurred on the gingiva,<sup>2</sup> fibroma being the most common benign tumor of the gingiva followed by papilloma.<sup>3</sup> Neurofibromatosis1 (NF1), also known as von Recklinghausen neurofibromatosis, is an autosomal dominant inherited genetic disorder. The gene involved is a tumor suppressor gene located in the pericentromeric region of chromosome 17.<sup>4</sup> NF1 involving the gingiva also has been described but as a rare or infrequent cause of gingival enlargement.<sup>5</sup> Shapiro observed NF in only 5% of all patients with NF1.<sup>6</sup> The early diagnosis of asymptomatic neurofibromas requires a high index of clinical suspicion. Early oral lesions may not be identified due to the clinician's failure to focus attention on possible intraoral anatomical changes. Symptomatic lesions are more readily diagnosed when a patient complains of a mass or other discomfort, which will direct the clinician to the primary lesion. We report a case of NF1 resulting in generalized diffuse gingival enlargement.

### Case Description

A 40-year-old male patient was referred to us for the treatment of nonpainful swelling of the gingiva. History revealed that the enlargement of his gums started 15 years back and initially the gingivae in relation to mandibular incisors were involved; since then there has been continuous increase in the size of gingival tissue as well as in the number of sites with gingival enlargement. There was no history of any major pain or discomfort. His medical history revealed that he was diagnosed with NF1 20 years back and no other member of his family had NF1. Except for the skin lesions



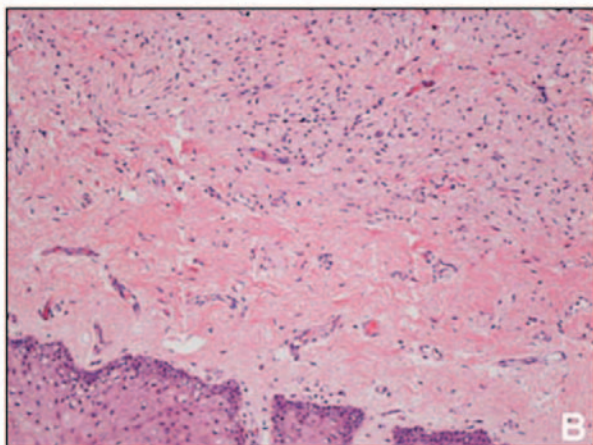
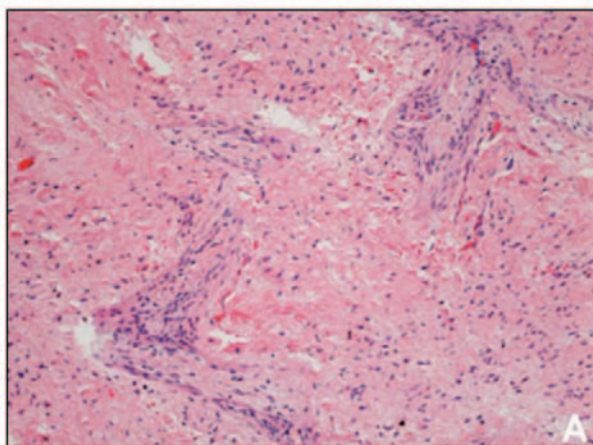
**Figure 2. A–C.** Intraoral lesions involving the gingiva.



associated with NF1, he had no other significant medical or drug history. Clinical examination revealed numerous soft tissue cutaneous nodules on the skin throughout the body, including the face and neck. Several brownish spots were also present on the trunk and arms (Figure 1).



**Figure 3.** Lesions involving the palatal mucosa.



**Figure 4.** **A.** Neurofibroma cells visible among collagen fibers. **B.** Numerous tumor cells and capillary vessels are visible beneath the oral mucosa epithelium.

On oral examination, diffuse, generalized nodular gingival enlargements were noted. The enlarged gingival tissue was fibrous and painless, and showed no signs of inflammation (Figures 2 and 3).

No other lesions or intraoral abnormalities were seen. Radiographic examination did not reveal any alteration. Based on the history and clinical findings, the diagnosis of gingival NF1 was made, and a histopathological examination of the gingival growth was advised to corroborate the diagnosis. Histological report of the gingival specimen confirmed the clinical diagnosis. The neoplasm was composed of bundles of spindle cells having elongated, wavy, and normochromatic nuclei. These cells were immersed in a stroma of delicate collagen bundles and moderate amounts of myxoid matrix (Figure 4).

## Discussion

Neurofibromatosis (NF), first described by von Recklinghausen in 1882,<sup>7</sup> comprises a group of genetic disorders that primarily affect the growth of neural tissues.<sup>8</sup> There are two forms of NF: NF1 and NF2. Despite some resemblances, these are two distinct diseases both genetically and clinically.<sup>9</sup> NF1 is the most common type of NF and accounts for about 90% of all the cases.<sup>10</sup> The estimated prevalence is about 1 in 3000 births<sup>11,12</sup> but reaches 1 in 200 for those with mental impairments.<sup>13,14</sup> There is no racial or sex predilection.<sup>15</sup> NF1 has one of the highest spontaneous mutation rates among genetic diseases in human beings. Only 50% of NF1 patients have a positive family history of the disease; the other 50% represent spontaneous mutations.<sup>16</sup>

NF1 manifests clinically in extremely variable ways, ranging from mild lesions to several complications and functional derangements.<sup>17,18</sup> The disease is a slowly evolving neurodermic dysplasia and starts at the embryonic stage before differentiation of the neural crests. After birth, the disease evolves in bursts, especially during growth, puberty, and pregnancy.<sup>7</sup> Smooth-edged yellowish to chocolate-brown macules are randomly distributed over the body; these lesions are called café-au-lait spots and the presence of more than six such spots is a pathognomic sign of NF1.<sup>7</sup> Another characteristic is the development of multiple skin neurofibromas that form either nodular or “molluscum pendulum” type tumors.<sup>6</sup>

At least two major types of NF1 have been described on the basis of clinical presentation. Discrete, which arises from a single site along a peripheral nerve and presents as a focal mass with well-defined margins, is the most common type and tends to increase with age.<sup>10</sup> In the plexiform type, a peripheral nerve sheath tumor extends along the length of the nerve and may involve multiple nerve branches; the cranial nerves CN V, CN IX, and CN X are most frequently involved.<sup>19</sup> Several such discrete café-au-lait spots were present in our patient; also the patient reported a continuous increase in the incidence of such lesions with his age. The central and peripheral nervous system and skeletal system are also frequently involved in patients with NF1.<sup>20</sup> Bone malformations such as kyphoscoliosis or pseudoarthrosis may be present and can affect the temporomandibular joint.<sup>21</sup> Although various neurological disorders like hamartomas of the iris, neurinomas of the acoustic nerve, gliomas, glioblastomas, and mental deficiencies also may be associated with NF1,<sup>21</sup> though none of these conditions were noted in our case.

The overall frequency of oral manifestations have generally been reported to be between 4% and 7%, but recent investigations that included both oral and panoramic radiographic examinations have placed the frequency at 70% to 90%.<sup>20</sup> Lesions of the soft tissues of the oral cavity are present in up to 10% of the cases.<sup>7</sup> The most common oral lesions are enlarged fungi-form papillae of the tongue that occur in about 50% of the cases,<sup>15</sup> intrabony cystic lesions, branched mandibular canals, and enlarged mandibular

foramen and canal.<sup>20</sup> Other less frequent sites for neurofibromas are the gingiva,<sup>22</sup> palate,<sup>23</sup> cheeks, lips, floor of the mouth, and pharynx.<sup>7</sup> Most of the soft tissue lesions were present in our patient, but radiographic findings were normal. Despite the advances of molecular biology, the diagnosis of NF1 is still based on clinical criteria (Table1).

In our case, previous diagnosis of NF1 of the skin and the associated clinical findings in the gingiva helped us to differentiate this enlargement from the other types of gingival enlargements. Since there is no cure for NF1, the treatment is aimed towards prevention and control of complications. Although the rate of malignant transformation is low (3–5%),<sup>8</sup> these neoplasms may result in aesthetic and functional problems. Despite earlier beliefs that surgery favors malignant transformation, there is not enough evidence in support of the same.<sup>9</sup> Surgical treatment is not always advised as the total removal of the lesions is difficult; partial removal of the tumors can be performed for resolving the aesthetic and functional problems associated with large lesions.<sup>7</sup> The NF1 patient must receive genetic counseling as the probability of transmitting the disease to each offspring is 50% in both sexes, and the same protocol was followed by us in the present case; also the patient was put on a regular recall visit to interrupt any neurological complication or sarcomatous evolution at the earliest possible stage.

## Summary

Although infrequent, the possibility of NF1 involving the gingiva cannot be ruled out. NF1 may result in

**Table 1. Diagnostic criteria for neurofibromatosis type NF1.**

<p><b>At least two of the following criteria are needed for diagnosis:</b></p> <ul style="list-style-type: none"> <li>• Six or more café-au-lait spots, &gt;5 mm in diameter in prepubertal patients and &gt;15 mm in diameter in postpubertal patients.</li> <li>• Two or more neurofibromata of any type, or one plexiform neurofibroma</li> <li>• Auxiliary or groin freckling</li> <li>• Optic glioma</li> <li>• Two or more Lisch nodules: pigmented hamartomas, often bilateral, appearing as domed-shaped elevations on the surface of the iris upon slit-lamp examination</li> <li>• A distinctive bony lesion, dysplasia of the sphenoid bone, dysplasia or thinning of the long bone cortex</li> <li>• First-degree relative with NF1</li> </ul>
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diffuse generalized gingival enlargement, which, besides causing local discomfort, has a potential for neurological complications and malignant transformation.

## Clinical Significance

It is important that dentists be aware of the clinical and histological features of NF1. Any sudden increase in the size of the lesion and presence of pain must raise the suspicion of malignant transformation and an immediate biopsy of the lesion should be advised.

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## About the Authors

### Ajay Mahajan, BDS, MDS (Corresponding Author)



Dr. Mahajan is a senior lecturer in the Department of Periodontics at H.P.G.D.C. in Shimla, Himachal Pradesh, India.

e-mail: [julius05@rediffmail.com](mailto:julius05@rediffmail.com)

### Jaya Dixit, BDS, MDS



Professor Dixit is dean of dental studies and the head of the Department of Periodontics at KGMC (CSMMU) in Lucknow, U.P., India.

### Ashu Bhardwaj, BDS, MDS



Professor Bhardwaj is dean of dental studies and the head of the Department of Periodontics at H.P.G.D.C. in Shimla, Himachal Pradesh, India.