CASE REPORT

Neurofibromatosis Type 1 with Oral and Extra Oral Manifestations

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Abstract

The term neurofibromatosis (NF) is used for a group of genetic disorders that primarily affect the cell growth of neural tissues. At least eight forms of NF have been recognized. Neurofibromatosis type 1 (NF1) also known as von Recklinghausen’s disease of the skin is the most common type of NF and accounts for 85% to 97% of all forms of NF which is inherited as an autosomal dominant trait. NF with oral manifestations is rarely reported in the literature. We present one such rare case of 22-year-old male with recurrent plexiform neurofibroma of face, having oral and panoramic radiographic manifestations along with skeletal and cutaneous findings.

(Keywords: Neurofibromatosis type 1, Recklinghausen’s disease, plexiform neurofibroma, oral manifestation, tongue nodule)

Introduction

Neurofibromatosis (NF) is a most common neurocutaneous disorder having autosomal dominant inheritance, affecting multiple organs. At least eight different clinical phenotypes of neurofibromatosis have been identified and are linked to at least two genetic disorders. Von Recklinghausen’s neurofibromatosis or Neurofibromatosis type 1 (NF1) is the most common type of the disease characterized by multiple café-au-lait spots and the occurrence of neurofibroma along peripheral nerves. It affects all races with an estimated prevalence of 1:3500 to 1:4000. The genetic abnormality has been localized to chromosome 17, to the site of a tumor suppressor gene. In the disease process, ectodermal and mesodermal derivatives are affected due to the defect in the embryonic neural crest cells. There are clinical criteria for the diagnosis of NF1, at least two of which should be present, including:

- Six or more cafe´-au-lait macules (0.5 cm or more in pre pubertal individuals and 1.5 cm or more in post pubertal individuals)
- Two or more neurofibromas of any type, or one plexiform neurofibroma
- Freckling in the axillary or inguinal region
- Optic glioma

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- Two or more Lisch nodules (iris hamartomas)
- A distinctive osseous lesion such as sphenoid dysplasia or thinning of long bone cortex with or without pseudoarthrosis
- A first-degree relative with NF1.

The overall frequency of oral manifestations in NF1 has been generally reported to be between 4% and 7%,5-8 but some investigations9-12 that included both oral and panoramic radiographic examinations have placed the frequency at 70%8,11 or even 90%.8,9,12 The most common oral lesions are neurofibromas, enlarged fungiform papillae, intrabony cystic lesions, branched mandibular canals, and enlarged mandibular foramen and canal.13-17 The purpose of this article is to discuss a case of an young male patient of NF1 presented with recurrent plexiform neurofibroma of face having oral, skeletal, cutaneous and panoramic radiographic manifestations.

Case Report

A 22-year-old male patient reported to the Department of Oral Medicine and Radiology with the chief complaint of stains and deposits over teeth since one year. Upon eliciting the past medical history, patient revealed that he had undergone surgery thrice for a recurrent swelling in right side of the face at the region of his eye and surgery once at the region of his right shoulder and chest (Fig. 1A). On general examination, he was moderately built and nourished and vital signs were within normal limits. Patient had kyphotic deformity (Fig. 1B).

Fig. 1: Clinical picture of the patient showing (A) surgical scar at right eye, shoulder, neck and chest

Extra oral examination revealed well defined, irregular, swelling with scar tissue measuring about 6x9 cm in diameter at the region of right eye extending posteriorly up to 1 cm anterior to tragus of the right ear. (Fig. 2).

Figure 2: Plexiform neurofibroma at right eye region

On palpation, the swelling was non-tender and felt like bag of worms. The eye lashes were evident devoid of eye ball. Massive surgical scar was visible at his right shoulder, neck and chest. Nodules were present all over the body which started in childhood (Fig. 3A, 3B, 3C). They were round to oval in shape and of size varying from millimeters to centimeters, with a smooth surface, skin over the nodules being normal. On palpation they were sessile, soft to firm and non tender. Axillary freckles (Fig. 3D) and Café au lait pigmentation (Fig. 3A) were evident at lower back and at the left waist region.

Figure 3: Neurofibromas at different areas of body (A) at the back along with Café au lait pigmentation (B) over the leg (C) over the hand (D) axillary freckling
Intraoral examination revealed the presence of solitary well circumscribed nodule over the posterior mid-dorsal tongue which was measuring 2x2 mm in diameter (Fig. 4).

A provisional diagnosis of chronic generalized gingivitis and an additional diagnosis of NF1 with recurrent facial plexiform neurofibroma were given. Panoramic radiographic examination revealed the presence of bilaterally widened inferior alveolar canal and enlarged mandibular canal (Fig. 5). As the patient was not willing for any further treatment regarding recurrent facial plexiform neurofibroma, no referral was given. He was treated with oral prophylaxis and oral hygiene instructions were given.

**Discussion**

NF1 is the most common neurocutaneous disorder, inherited as an autosomal-dominant fashion having a wide range of clinical manifestations which predisposes the patient to increased morbidity and mortality. The NF1 gene is located on chromosome 17q11.2, which encodes for the protein neurofibromin. The NF1 gene has nearly 100% penetrance wherein the patient will present with clinical manifestations, but expressivity is highly variable. NF1 gene has one of the highest rates of spontaneous mutations in the entire human genome; every new case may represent the new mutation in this gene.\(^{18}\)

The systemic manifestations of this disease are widespread and variable. Most common sign on the skin is neurofibroma.\(^{19}\) Neurofibromas are arising from non-myelinating Schwann cells in the peripheral nerves system. They are of 2 types, dermal neurofibromas and plexiform neurofibromas. Dermal neurofibromas which are associated with single nerve bundles will not become malignant. They are either sessile or pedunculated, non-tender, soft tumors with well-defined borders. They arise either superficially or from deeper dermis, which may require surgical excision rarely, for pain or disfiguration. The plexiform neurofibromas are associated with multiple nerve bundles, which can cause pain, disfiguration, and neurological deficits and has a potential to turn into malignant peripheral nerve sheath tumor. Plexiform neurofibromas will require surgical excision and it may recur after surgery as seen in the present case. Our patient was unable to give precise previous history about his loss of eyeball and eyesight on right side which may be due to extensive benign or invasive plexiform neurofibroma destroying the underlying soft tissues and bony eye sockets requiring extensive surgery and removal of his right eye ball.

Café au lait pigmention is pigmented macules of varying color and sizes. In the present case the macules are of irregularly shaped and dark chocolate brown colored occupying significant body segments of lower back and left
waist. Multiple smaller macules of less than 0.5cm were present on the back of the patient. Freckles in the axillary or inguinal areas are very common in patients with NF1 and are referred to as Crowe’s sign. Our patient had axillary freckles.

Bony abnormalities in NF1 is variable, most common being scoliosis accounting up to 10% of patients which has different forms. In the present case patient had kyphotic deformity since childhood. Kyphosis is the extreme curvature of the upper back exceeding more than 50 degrees. Severe rapidly progressive form of kyphoscoliosis which develops between 3 to 5 years of age necessitates surgical correction.

Enlargement of fungiform papillae is one of the most common oral findings of NF1 which occurs in almost 50% of patients. Soft tissue neurofibroma is another common finding reported in the literature. Tongue being the most common location, it can occur in any part of oral cavity with varying numbers. Solitary nodule was present in posterior mid-dorsal tongue in the present case. Enlarged mandibular canal, mandibular and mental foramen are the observed oral radiographic findings in patients with NF1. In our case, we could view widened mandibular canal and foramen bilaterally in panoramic radiograph. If NF develops intraosseously, it will result in well demarcated unilocular, but occasionally multilocular radiolucent lesions. In these cases, teeth may become impacted, displaced or missing.

There have been many reports suggesting increased sensitivity of NF1 patients to non-depolarizing neuromuscular blocking drugs. Further, an increased, decreased or normal sensitivity to succinylcholine has been reported. Thus to prevent any complication during general surgery, a continuous monitoring of neuromuscular transmission should be done whenever neuromuscular blocking drugs are used. This is especially significant in NF1 patients with renal impairment or those on concurrent medication like anticonvulsant drugs, which may interfere with normal pharmacokinetics or pharmacodynamics of neuromuscular blocking drugs.

Every patient suffering from NF requires social and emotional support. Educating the patients and their parents regarding advances in treatment and potential complications is today’s need. The patient described here is a very typical case of NF1 with recurrent plexiform NF of face due to which the patient had lost his right eye sight. A team work between Plastic surgeon and Prosthodontist can not only aid in reducing aesthetic and functional impairment, but also boost self confidence of such patients through aesthetic rehabilitation.

References


