Neurofibromatosis: A case report

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Abstract

Neurofibromatosis (NF) is a Mendelian disorder which is carried as an autosomal dominant trait. Two genetically distinct subtypes have been recognized, NF type 1 (NF1) and NF2. Neurofibromatosis type 1 is a relatively common inherited disorder. Patients have a high predisposition to develop both benign and malignant tumors. Although many manifestations of neurofibromatosis type 1 affect the nervous system, other organs and tissues can also be affected. Diagnosis is mainly based on a series of clinical criteria. NF-I may present with definite oral lesions, which mandate the dental surgeons with the responsibility of accurate diagnosis.

Keywords: Neurofibromatosis, Supernumerary teeth, familial inheritance, caife au lait pigmentation.

Introduction

Neurofibromatosis (NF) is a group of autosomal dominant genetic disorders characterized by multiple cutaneous lesions and tumours of the central and peripheral nervous system.[1] NF is categorized into two genetically distinct subtypes namely, NF type-1 (NF-1) and NF type-2 (NF-2).[2] NF-1, previously called von Recklinghausen disease is the most common type of NF which affects approximately 1/3500 individuals worldwide.[1]

NF-1 occurs due to alterations of the NF-I gene (a tumour suppressor gene located in the long arm of chromosome-17 [17q11.2]).[3,4] Nearly 50% of patients affected by NF-1 have a positive family history of the disease and the remaining patients represent spontaneous mutations of the NF-1 gene.[3,5] Cutaneous light brown macules of about 10–40 mm in diameter with an ovoid shape are the classical symptoms observed in patients with NF-1. The presence of at least 6 macules is defined as strong diagnostic criterion for NF-1. Nearly 90% patients with NF-1 present with a characteristic axillary and /or inguinal freckling that commonly develops after appearance of cutaneous macules.[6,7] Development of neurofibromas around or on peripheral nerves and Lisch nodules (pigmented hamartomas of the iris) are also classical features of NF-1.[8,9]

NF-2 (referred to as central NF) occurs less frequently than NF-1 with an incidence of 1/25,000 individuals.[10] Sudden loss of hearing due to the development of

unilateral or bilateral vestibular schwannomas is often an early manifestation in patients with NF-2.[11] In contrast to NF-1 patients, tumours in NF-2 patients are smaller in size. However, these tumours may compress associated nerves and can cause considerable pain, nerve dysfunction and intracranial pressure. Furthermore, patients with NF-2 may develop nervous tissue tumours including meningiomas or gliomas.

Case Report

A 21-years-old male patient reported to the Department of Oral Medicine and Radiology with the chief complaint of pain in relation to the right upper back tooth region since 2-3 days. The pain was of sudden in onset, continuous in nature, moderate in intensity, localized and aggravates during chewing. The patient has not taken any medication. Family history revealed that his mother and sister had multiple nodular swellings over the body and face and was diagnosed as neurofibromatosis .

On general examination, the patient was moderately built and nourished, and vital signs were within the normal limits.

Clinical examination revealed the presence of multiple nodules over the body, especially prominent on the face and flexor aspects of the forearms, legs, chest and back. The nodules were sessile and pedunculated; round to oval in the shape of size varying from a few millimeters to centimeters, with a smooth surface, the skin over the nodules was normal in color. On palpation, nodules were soft to firm and nontender. Numerous brownish macules of varying diameter and smooth borders were also appreciated in the vicinity of these nodules over the chest and back region as shown in (Figure 1).

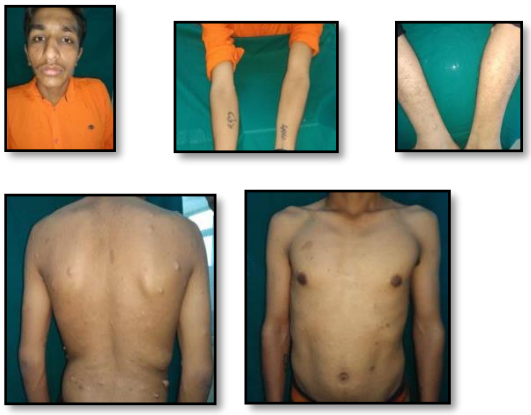

Figure 1: Showing multiple nodules on chest back hand and foot and café au lait pigmentation on chest and back.

Intraoral examination revealed supernumerary teeth in relation to 16 and 17 in the right back region of mouth. IOPA reveals carious supernumerary teeth in relation to 16 and 17 (Figure 2). A provisional diagnosis of neurofibromatosis was made.

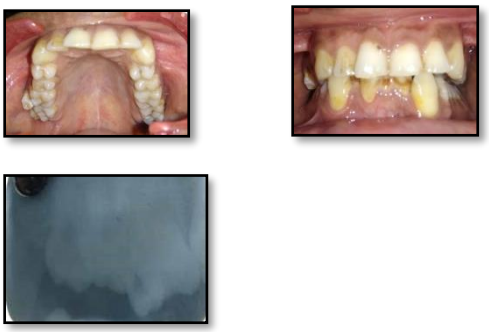

Figure 2: Showing supernumerary paramolar with 16 and 17.

Discussion

NF is a group of autosomal dominant genetic disorders characterized by multiple cutaneous lesions.[12] It mainly encompasses two clinical forms: Peripheral - NF-I and central - NF-II, of which Von Recklinghausen's disease (NF-I) is the most common type which accounts for about 90% of all cases.[13,14] NF-II occurs less frequently than NF-I with an incidence of 1/25,000 individuals. An early manifestation of NF-II is the sudden loss of hearing due to the development of unilateral or bilateral vestibular schwannomas.[15] In contrast to NF-I patients, tumors in NF-II patients are smaller in size, however, these tumors may compress associated nerves and can cause considerable pain, nerve dysfunction, and intracranial pressure. Moreover, patients with NF-II may develop nervous tissue tumors including meningiomas or gliomas.[16,17]

The diagnosis of NF-I and NF-II are still based on clinical criteria regardless of the advances in molecular biology (Tables 1 and 2). The National Institute of Health Consensus Development Conference established the diagnostic criteria for NF-I in 1987 as reported.[14,15] Two or more of the below criteria are required to designate the patient as NF-I individual, and the case reported here fulfilled 3 criteria, that is, (1) Numerous *café au lait* spots over face and the hands, (2) Multiple neurofi bromas, and (3) First-degree relatives (patient's father and brother) with NF-I.

Table 1: Clinical criteria for the diagnosis of NF-I

- At least two of these clinical criteria are needed to diagnose NF-I
- Six or more *cafe au* lait spots, >0.5 cm diameter in prepubertal ageand >15 mm diameter in postpubertal age
- Two or more neurofi bromas of any kind or a plexiform neurofi broma
- Axillary or inguinal freckles - Crowes sign
- Optic glioma
- Two or more Lisch nodules: Pigmented bilateral hamartomas, that appear as copular elevations on iris surface
- Distinctive bone lesion, sphenoidal dysplasia, dysplasia or thinning of long bones cortical
- Relatives in fi rst degree with NF-I

Table 2: Diagnostic criteria for NF-II

- The criteria are met by an individual who satisfies condition 1 or 2
- Bilateral vestibular schwannomas (VS) or
- Family history of NF-II (fi rst-degree family relative) plus
- Unilateral VS <30 years or
- Any two of the following: Meningioma, glioma, schwannoma, juvenile posterior subcapsular lenticular opacities/juvenile
- cortical cataract

The manifestations of NF1 are widespread and affect many of the body systems:

The skin: Cafe´ au lait patches and skin-fold freckling do not usually cause complications; however, some patients are distressed by the appearance of this pigmentation and may be helped by skin camouflage advice. There is no evidence to support the routine use of laser treatment for cafe´ au lait patches. Hypopigmented macules may coexist with café au lait spots in NF1 and are found in a similar distribution.[18]

Neurofibromas: Neurofibromas are benign peripheral nerve sheath tumours that are focal cutaneous or subcutaneous, or diffuse or nodular plexiform lesions. Cutaneous neurofibromas are found in the majority of NF1 individuals, usually develop in the late teens or early twenties but occasionally emerge in early childhood. Initially, some lesions have a purplish tinge and may become pedunculated as they grow. The number of neurofibromas varies between individuals and within families.[19,20]

Malignant peripheral nerve sheath tumours: There is an 8–13% lifetime risk of developing MPNST in NF1, predominantly in individuals aged 20–35 years. These cancers are hard to detect, metastasise widely and often have a poor prognosis. MPNST usually, but not invariably, arise in preexisting plexiform neurofibromas. NF1 patients should seek an urgent expert opinion from specialist neurofibromatosis clinics or soft tissue tumour units if they develop any of the following in association with a subcutaneous or plexiform neurofibroma: persistent pain lasting for longer than a month or pain that disturbs sleep; new or unexplained neurological deficit or sphincter disturbance; alteration in the texture of a neurofibroma from soft to hard; and rapid increase in the size of a neurofibroma. Clinicians should be aware that occasionally symptoms arise from a plexiform neurofibroma that is not visible or palpable.[21]

Glomus tumours: An association has been reported recently between glomus tumours and NF1. Glomus bodies are small, dermal, encapsulated arteriovenous anastomoses, commonest in the fingertips where they

regulate peripheral blood flow and hence body temperature. The glomus tumour is usually solitary but multiple lesions have been observed in NF1 individuals. The lesion is located most frequently under the fingernail and presents with pain, cold sensitivity and excruciating very localised tenderness. The symptoms should be differentiated from those caused by subcutaneous neurofibromas and the treatment is local excision of the tumour.

Neurological problems: Neurological examination should be undertaken during annual assessment. Any unexplained neurological signs and symptoms merit referral to a neurologist. Urgent advice is mandatory if individuals experience acute or progressive sensory disturbance, motor deficit and incoordination or sphincter disturbance which could be indicative of an intracranial lesion or spinal cord compression. Headaches on waking, morning vomiting and altered consciousness are suggestive of raised intracranial pressure and constitute a neurological emergency.

Cognitive problems and behavioural difficulties

Cognitive problems are the commonest neurological complication in NF1 individuals and usually present as an IQ in the low average range; severe intellectual deficit with an IQ ,70 is rare.[22]

Central nervous system tumours: Glioma is the predominant tumour type in NF1 and occurs in all

parts of the nervous system, with a predilection for the optic pathways, brainstem and cerebellum. Brainstem gliomas manifest as diffuse or focal tumours and frequently have a more indolent course in NF1 than in the general population although occasionally they can behave aggressively.[23]

Conclusion:

Since oral manifestations may be encountered in at least70% of NF-1 patients; it is imperative for oral healthcare providers to be aware of the clinical oral manifestations of NF. Despite no direct correlations between the severity of oral manifestations and oral health status, the psychological effects of a multisystem disorder like NF-1, combined with oral and dental abnormalities results in significant oral health compromise in majority of the patients. Thus, the importance of patient education toward oral hygiene maintenance and regular dental check-ups must be emphasized to improve the oral health status in patients with NF-1.

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Conflicts of interest:

There are no conflicts of interest.

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