

A case report of neurofibromatosis Type 1 – plexiform variant

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ABSTRACT

Neurofibromatosis type 1 is a neurocutaneous disorder which is autosomal dominant. The incidence is 1 in 2500 births. It was earlier termed Von Recklinghausen's disease. The clinical features range from café-au lait spots, multiple neurofibromas of the skin along with plexiform variants, axillary freckling, optic glioma and Lisch nodules. This paper reports a case of Neurofibromatosis type 1 with review of literature.

KEY WORDS: Neurofibromatosis; Neurofibromas; Café-au lait spots; Plexiform.

INTRODUCTION

Neurofibromatosis 1 is an autosomal dominant neurocutaneous disorder with an incidence of 1 in 2500 births. The disease was earlier termed as von Recklinghausen's disease with a prevalence of one in 4-5000 births [1]. In 1956 Crowe, Schull, & Neel called this syndrome as sectorial neurofibromatosis. They proposed that it may result due to a later development of a somatic mutation of the neurofibromatosis type I gene, thus resulting in a localized form of the disease [2].

The Nf1 gene is situated on chromosome 17q11.2 whereas the protein product coined neurofibromin functions as a tumour suppressor [3-5]. It is an autosomal dominant disorder, with an almost balanced split among spontaneous and inherited mutations. 8 different clinical phenotypes of neurofibromatosis are identified and have been linked to at least two genetic disorders. Neurofibromatosis type I (NF-1) is the most common type of the disease accounting 90% of the cases, and is characterized by multiple café-au-lait spots along with the occurrence of neurofibromas along peripheral nerves [6,7]. Certain diagnostic criteria are not sensitive in young children, as they may manifest later in life. Cutaneous neurofibromas maybe sessile or dome shaped, flesh coloured, occasionally pedunculated and are most numerous on the trunk and limbs. Axillary freckling is also a prominent clinical

finding. Lisch's nodules may also be seen in the eyes, which are melanocytic pigmented iris hamartomas. The childhood complications may manifest as an optic glioma, disturbances in endocrine function and involvement of lower urinary tract. Learning disabilities may also be present in children. Primarily, the clinical features are neurocutaneous in nature. But any organ system may be involved. [7]

CASE REPORT

A 40-year-old male patient reported to the department of oral medicine and radiology with a complaint of pain in the upper right back tooth since 4 days. The pain was of pricking type, localized and intermittent in nature, aggravated while having sweets and relieved on its own. The medical, dental and drug allergy history was non-contributory. There was no history of consanguineous marriage between the parents. The patient was moderately built and nourished. The extra oral examination revealed multiple cutaneous nodules ranging from 2mm to 10mm on the face, neck, chest, abdomen, back and limbs (Figure 1, 2, 3). The nodules were soft, flesh coloured, non-tender with no signs of inflammation. Coffee brown patches with irregular margins were seen in multiple areas of the body suggestive of cafe au lait spots (Figure 4). Axillary freckling was present (Figure 5). 2 nodules measuring approximately 3cm and 7 cm were present on the midline of the neck and right chest area (Figure 2).



Figure 1. Clinical photograph showing cutaneous nodules on the face.



Figure 2. Clinical photograph showing cutaneous nodules on the trunk, abdomen



Figure 3. Clinical photograph showing cutaneous nodules on the back

On intraoral examination, grade 3 mobility was seen with respect to 17 and 26. Grade 2 mobility was seen with respect to 14, 25, 34, 35, 44, 45, 46. On the right ventral surface of the tongue, a pinkish leaf shaped growth was seen measuring about 2cm in diameter. On palpation, inspeitory findings were confirmed. The lesion was firm in consistency, sessile and non tender, which was suggestive of fibroma (Figure 6).

Based on the history and clinical findings a provisional diagnosis of chronic generalized periodontitis was made. A diagnosis of Neurofibromatosis Type1 was given for the multiple cutaneous nodules.

As part of radiographic investigation an intraoral periapical radiograph was made which revealed a radiolucency in the

proximal area involving enamel and dentin with respect to 17 and radiolucency extended below the cemento enamel junction suggestive of root caries. Vertical bone loss was also associated with the same tooth, involving upto the apex which was suggestive of localized periodontitis (Figure7).

A panoramic radiograph revealed missing teeth with respect to 18, 27, 28, 36, and 37. Generalised horizontal bone loss was also present suggestive of generalised periodontitis. 38 and 48 were found to be impacted.

The patient was advised to extract 17, 26, 38 and 48 along with periodontal evaluation of the remaining teeth along with removal of the fibroma of the tongue. However the patient refused removal of the fibroma (Figure 8).



Figure 4. Clinical photograph showing Café-au lait spots



Figure 5. Clinical photograph showing axillary freckling

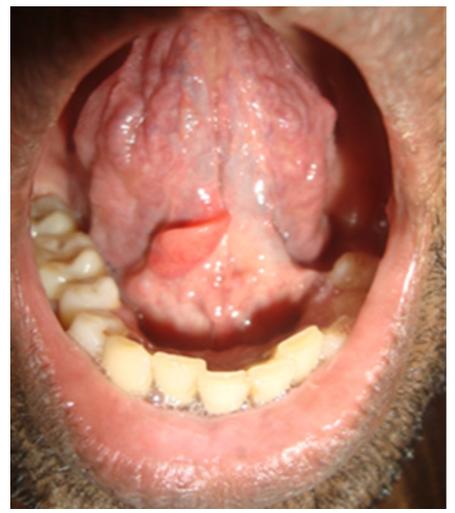


Figure 6. Clinical photograph showing a leaf shaped growth (fibroma) on the right ventral surface of the tongue

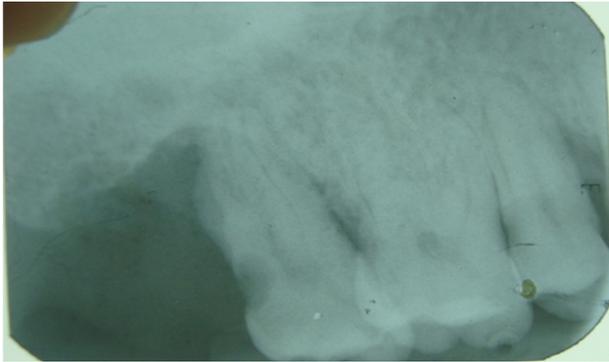


Figure 7. Intraoral periapical radiograph showing vertical bone loss and root caries



Figure 8. Panoramic radiograph showing generalized bone loss and impacted lower third molars

DISCUSSION

The clinical expression and severity in NF-1 is diverse, even within families [8]. Café au lait patches are present on the skin in 95% of NF1 individuals and usually appear by the age of 3 years [9]. These spots are zones of focal epidermal melanosis due to proliferation of cutaneous nerve endings [10,11]. Six or more café au lait patches >15mm in adults and >5mm in children are pathognomonic of Neurofibromatosis type 1, which was also observed in our case [1].

Neurofibromas present as cutaneous, subcutaneous or plexiform nodules. The cutaneous neurofibromas cause itching and stinging sensation. The subcutaneous lesions often cause pain and neurological deficit due to pressure on peripheral nerves. Neurofibromas rarely appear before the age of 7 years, commonly emerging in late adolescence and their frequency increases during pregnancy [9]. Two or more neurofibromas or one plexiform neurofibroma are characteristic of NF1 [1]. In our case, it was associated with multiple neurofibromas and 2 plexiform neurofibromas.

The complications affect many of the body systems ranging from disfigurement, scoliosis and vasculopathy to cognitive impairment and malignancy including peripheral nerve sheath tumours, and central nervous system gliomas. Macrocephaly, short stature along with cutaneous angiomas comprise the minor features of the disease [9,11,12,13].

Table 1. Diagnostic criteria for Neurofibromatosis type 1 [1]

Two or more criteria are needed for diagnosis:
1. Six or more café au lait patches 4-15mm in adults and 4-5mm in children
2. Two or more neurofibromas or one plexiform neurofibroma
3. Axillary or groin freckling
4. Lisch nodules (iris hamartomas).
5. Optic pathway glioma.
6. A first degree relative with Nf1.
7. A distinctive osseous lesion such as sphenoid wing dysplasia or thinning of the long bone cortex with or without pseudoarthrosis.

According to the above criterion, café au lait spots, multiple neurofibromas along with a plexiform neurofibroma, axillary freckling have been present in our case. Hence, the diagnosis of neurofibromatosis type 1 can be considered.

About 50% of patients have NF-1 as a new mutation, while an affected parent has a 50% chance of having an offspring with the disease [9]. The risk of an individual with mosaic NF-1 passing on generalised disease to an offspring is small but not cannot be quantified. This is due to its dependency on the percentage of body that is affected. In case of apparently normal parents of an affected child, they should be carefully examined for the presence of mosaic NF-1. Mosaic (segmental) neurofibromatosis type 1 is the one which presents characteristic features of NF1 which are limited to one or more regions of the body [14].

If the parents are normal, the risk of recurrence is probably only above the background risk of 1/6000. Due to the variability of the phenotype, it is difficult to predict the risks of complications in any one individual. A patient who is mildly affected may have an offspring with severe disease, and vice versa. An individual with NF-1 may have an 8% chance of having a severely affected offspring [15].

ORAL MANIFESTATIONS

The oral physician should be aware of the oral manifestations associated with the condition. Due to an increase in the number of cells, gingival enlargement is a common manifestation in patients, especially among children. They manifest as diffuse unilateral enlargement of the attached gingiva. The enlargements are usually fibrous without any signs of inflammation [16]. Supernumerary teeth, impacted teeth, missing or displaced teeth along with overgrowth of the alveolar process have been commonly reported [17]. Periapical cemental dysplasia was reported in vital mandibular teeth of female patients with NF1 [18]. Neurofibromas of the oral cavity mostly involve the tongue, palate, vestibule, buccal mucosa, lip, gingiva and floor of the mouth. They are usually nodular [19].

MANAGEMENT

The patient should be referred to a geneticist, paediatrician, neurologist or dermatologist. Due to increased learning and behavioral problems in children, monitoring is required. The chief purpose of management is age specific monitoring of manifestations of disease, along with patient education. Counselling regarding inheritance of disease and psychological support are advised as neurofibromas often develop in late adolescence. All children with uncomplicated disease should be assessed once in a year. Older adults should have the opportunity to be assessed annually. Monitoring after mid-twenties depends on preference of the patient and severity of the disease. Adults with severe disease are usually detected by this stage and require life long monitoring. Psychological problems result from disfigurement due to neurofibromas and also from the complex and unpredictable nature of the disease. Anxiety and depression related issues often occur in this condition. The patients usually respond to a combination of antidepressants and counselling. NF1 specialist advisors, psychiatrists and counsellors play a role in managing the disease [20].

CONCLUSION

Neurofibromatosis 1 is a complex disease which requires periodic supervision and management by a multidisciplinary team to prevent further complications. Since there is no cure for neurofibromatosis 1, genetic counseling should also be provided for those with the disease. The clinical diagnosis is clear-cut in most individuals.

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