Original Article

Neurofibromatosis Type- I A Rare Case Report And Literature Review On Its Oral Manifestations.

Dr. Monika Bhat[1*], Dr. Basavaraj T Bhagwati[2], Dr. Preeti Dhir[3], Dr. Mandeep Kaur[4]

[1*]Junior Resident Department of Oral Medicine and Radiology Dasmesh Institute of Research and Dental Sciences Faridkot Punjab. P.no:7006597239, E-mail:monikabhat6433@gmail.com
[2]Professor and Head Department of Oral Medicine and Radiology Dasmesh Institute of Research and Dental Sciences Faridkot Punjab
[3]Professor Department of Oral Medicine and Radiology Dasmesh Institute of Research and Dental Sciences Faridkot Punjab.
[4]Associate Professor Department of Oral Medicine and Radiology Dasmesh Institute of Research and Dental Sciences Faridkot Punjab.

***Corresponding Author**:-Dr Monika Bhat

*Junior resident, Dasmesh Institute of Research and Dental Sciences Faridkot 151203 Punjab, P.no:7006597239, E-mail:monikabhat6433@gmail.com
DOI: 10.47750/pnr.2022.13.S08.447

Abstract

Neurofibromatosis (NF) refers to a group of genetic disorders that predominantly affect neural tissues. About 90% of all cases of neurofibromatosis are caused by neurofibromatosis type 1 (NF1), also called von Recklinghausen's disease. In 3,000 births, one case of this genetic disease can be found. There is an extremely wide range of expressivity of NF1, with manifestations ranging from moderate lesions to several complications and functional impairments. The condition is associated with oral manifestations in almost 72% of NF1 sufferers. The aim of this article is to report the case of NF1 with different oral and Dental orthopantomography characteristic features to review the literature.

Key Words: Café-au-lait spot, Oral cavity, Genetic diseases, neurofibromatosis type 1, Orthopantomogram, von Recklinghausen's disease

INTRODUCTION

Neurofibromatosis type I is an autosomal dominant disease caused by a mutation or a deletion of the *NF1* tumor suppressor gene localized in chromosome 17 which results in the lack of production or reduced function of the tumor suppressor protein neurofibromin.[1] This is associated with the development of multiple neurofibromas of various histologic subtypes. NF1 generally affects bones, the nervous system, soft tissues, and skin.[2,3] NF-1 is also known by another name as von Recklinghausen syndrome since it was first described by Friederich Daniel Von Recklinghausen, who was the pathologist, in 1882.[4,5]

Among genetic diseases in humans, NF has the been associated with the highest rates of spontaneous mutation, where 50% of the NF1 patients have a positive family history of the disease. The lucidity of the disease is extremely variable, with manifestations ranging from Café-au-lait spots, axillary and inguinal freckling, optic gliomas, Lisch nodules (pigmented hamartomas of the iris), spinal and peripheral nerve neurofibromas, neurological or cognitive impairment, scoliosis, abnormalities in the oral and maxillofacial region, malignant tumors of the nerve sheath, pheochromocytoma, vasculopathy, and specific bone lesions are common clinical features of NF1[7]. Oral and maxillofacial manifestations can be seen in 72 % of patients with neurofibromatosis type 1.[8]

CASE DESCRIPTION

A 22-year-old female presented to our department with, a complaint of difficulty in eating because of anterior teeth mobility. On extra oral examination, generalized nodules which were painless, brownish, soft, and measuring about 3- 4 mm in diameter were present throughout the body (fig-2), café-au-lait spots in the skin (fig 2), axillary freckles, interesting to note, oral nodes were only found in the gingiva, an unusual area of manifestation, but were seen in the rest areas of the body, altered salivary flow. Intraoral examination revealed poor oral hygiene, dental caries, tooth mobility, lower anterior teeth recession, (fig3a,3b) altered salivary flow. So, this article contains information on neurofibromatosis type 1 and its manifestation considerations are being published here to aid oral and maxillofacial physicians and radiologists in identifying the disease. We present a rare case of a 22-year-old female affected by the presence of generalized nodules throughout the body, causing aesthetic deformations, from enlarged asymmetric facial appearance. Panoramic radiograph showed a discrete enlargement of the mandibular canal, with changes in relation to the coronoid process, angle of mandible. (Fig-4)

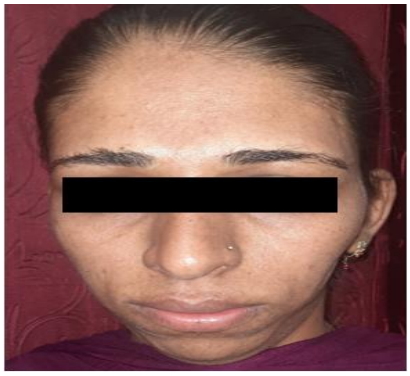

Fig 1 front profile showing asymmetric enlarged face

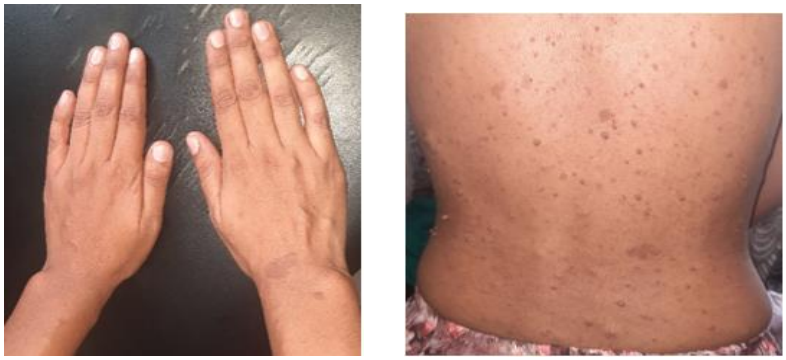

Fig 2 showing café-lait spot on left hand and back of the patient with multiple nodules

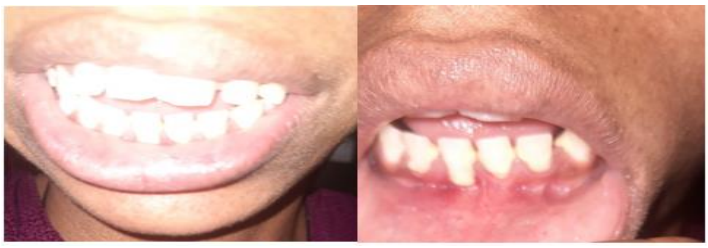

Fig 3. (a) showing anterior open bite with protruded maxilla,
(b) mandibular anterior teeth recession

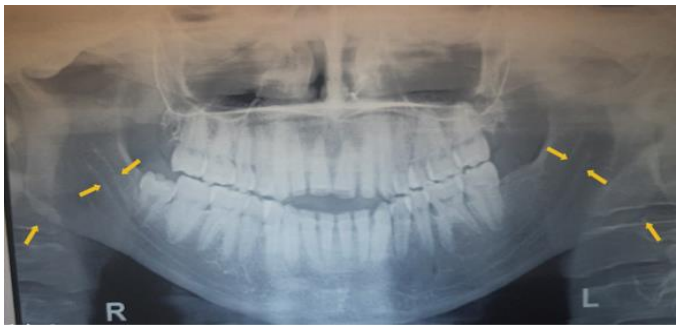

Fig.4 Panoramic radiograph showing discrete enlargement of the mandibular canal with normal anatomy of the mandible's border and coronoid notch, Anterior alveolar bone loss.

≥6 cafe au-lait macules of >5 mm (greatest diameter) in prepubertal individuals, and >15 mm (greatest diameter) in postpubertal individuals
≥2 neurofibromas or one plexiform neurofibroma
Axillary or inguinal freckling
Optic glioma
≥2 iris hamartomas (Lisch nodules)
Distinctive bony lesion, such as sphenoid dysplasia, or medullary narrowing and cortical thickening of the long bone cortex with or without pseudarthrosis
A first-degree relative with neurofibromatosis type 1 diagnosed based on the above criteria

Table-1 Diagnostic criteria for neurofibromatosis type- 1
(Reference: Hong, C. and Haberland, C.M., 2021. Pediatric Oral Medicine. *Burket's Oral Medicine*, pp.943-989.)

DISCUSSION

A multi-system disorder, NF1 affects multiple organ systems and has a highly variable clinical course. It is believed that NF1 is caused by an alteration in the NF-1 gene, which can affect various tissues of the mouth, including bones, mucosa, and salivary glands. The associated gene comes under tumor suppressor which is located on the long arm of chromosome 17 (17q11.2).[10] Alteration in its function due to a mutation leads to an intensification in cell proliferation and progress of tumors. NF1 is an inherited autosomal dominant gene, with a penetrance of 100% by age of 20 years[10] In our case the family history was not significant but the age of patient was found to be 22 years which was relevant in context. Also it known that the mutated genes expressing rapidly in females, In this presented case report also the patient was of female gender.[10] The disease is also known for its multisystem involvement with specific diagnostic criteria as their manifestations, (table 1). Though because of the disease rarity the studies are very less representing the maxillofacial complications which are presented as enlarged face with multiple cutaneous/disseminated and plexiform neurofibromas, various bony changes causing the deformity of mandibular ramus , glenoid fossa, condylar head , increased dimensions of the coronoid notch, decreased jaw angle, and enlarged mandibular canals [11,12,13]. In our case report also the mandibular bony changes were also appreciated in the panoramic radiograph.(fig 7). Oral manifestations include pigmentation of oral mucosa, enlarged tongue and fungiform papillae, malposed teeth with an increased incidence of dental caries, periapical cemental dysplasia, perineural fibrous thickening of pulpal tissue and malocclusion[11,12,13]. In our case report, enlarged tongue, malocclusion as open bite was seen plus poor periodontal status was present. In a study performed by Shapiro *et al* Oral manifestations were found in 72% of the patients[14], with NF1. Another survey performed by D'Ambrosio et al., concluded 66% of his NF1 patients had at least one intraoral manifestation of the disease and 58% presented with manifestations in the maxilla and the mandible, which were distinguished on panoramic radiographs[8], as we appreciated in our case report also.

CONCLUSION

So, by concluding this case report, periodontal destruction, functional salivary changes correlating with carious lesions with alteration in mandibular canal width in NF1 patients, can be found in these cases, when there occurs variations in manifestation, an incisional biopsy, CT scan, and MRI scan, apart from a conventional orthopantomogram should be performed for further evaluation, so as oral physicians and maxillofacial radiologists, we have an obligation to rule out all possible details, to ensure patients have a excellent outcome.

REFERENCES

1. Shah KN. The diagnostic and clinical significance of cafe-au-lait macules. *Pediatr Clin North Am.* 2010;57(5): 1131–1153.
2. Ghalayani P, Saberi Z, Sardari F. Neurofibromatosis type I (von Recklinghausen's disease): A family case report and literature review. Dent Res J. (Isfahan). 2012; 9(4): 483-8.
3. Gutmann DH, Ferner RE, Listernick RH, Korf BR, Wolters PL, Johnson KJ. Neurofibromatosis type 1. Nat Rev Dis Prim. 2017; 3.
4. Bekisz O, Darimont F, Rompen EH. Diffuse but unilateral gingival enlargement associated with von Recklinghausen neurofibromatosis: A case report. J Clin Periodontol 2000;27:361- 5.
5. Hillier JC, Moskovic E. The soft tissue manifestations of neurofibromatosis type 1. Clin Radiol 2005;60:960-7.
6. Friedman JM, Gutmann DH, MacCollin M, Riccardi Y. Neurofibromatosis. Phenotype, natural history and pathogenesis. Baltimore: The Johns Hopkins University Press; 1999
7. García-de Marcos JA, Dean-Ferrer A, Alamillos-Granados F, Ruiz- Masera JJ, García-de Marcos MJ, Vidal-Jiménez A, *et al*.Gingival neurofibroma in a neurofibromatosis type 1 patient. Med Oral Patol Oral Cir Bucal 2007;12:E287-91.
8. D'Ambrosio JA, Langlais RP, Young RS. Jaw and skull changes in neurofibromatosis. Oral Surg Oral Med Oral Pathol 1988;66:391-6.
9. Hong, C. and Haberland, C.M., 2021. Pediatric Oral Medicine. *Burket's Oral Medicine*, pp.943-989..
10. Jouhilahti EM, Peltonen S, Heape AM, Peltonen J. The pathoetiology of neurofibromatosis 1. Am J Pathol. 2011;178:1932–9.
11. Curtin JP, McCarthy SW. Perineural fibrous thickening within the dental pulp in type 1 neurofibromatosis: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997;84:400–3.
12. Visnapuu V, Peltonen S, Ellila T, Kerosuo E, Vaananen K, Happonen RP, Peltonen J. Periapical cemental dysplasia is common in women with NF1. Eur J Med Genet. 2007;50:274–80.
13. Visnapuu V, Peltonen S, Alivuotila L, Happonen RP, Peltonen J. Craniofacial and oral alterations in patients with Neurofibromatosis 1. Orphanet J Rare Dis. 2018;13:131.
14. Gucev Z, Krstevska-Konstantinova M, Tasic V, Jancevska A, Kirovski I, Pop-Jordanova N. Four generations in a family with neurofibromatosis 1: Precocious puberty and optic nerve tumor (OPT). Prilozi 2010;31;253-9.