Chelonian Conservation And Biology

Vol. 19No.1 (2024) | https://www.acgpublishing.com/ | ISSN - 1071-8443

DOI:doi.org/10.18011/2024.01(1). 818-830

REPORT OF A RARE CASE OF TYPE I NEUROFIBROMATOSIS IN A FEMALE PATIENT IN RIYADH, SAUDI ARABIA.

Fatima Yahya ALBishry[1], Hadeel Saad[2], Nawaf Alotaibi[3], Fahad Alnafisah[4], Al Hanouf Al Assiri[5]

1. King Saud University Medical City, Consultant-Special Care clinic. Riyadh, Kingdom of Saudi Arabia.
2. SBFD ,Senior Registrar -Aseer specialist dental Center-special care clinic. Abha, kingdom of Saudi Arabia .
3. Saudi Board Family Residency Program, King Saud University Medical City, Riyadh, Kingdom of Saudi Arabia.
4. Dental intern, Prince sattam bin abdulaziz university, Al-kharj, Kingdom of Saudi Arabia.
5. General dentist, Abha, Kingdom of Saudi Arabia.

Abstract:

Neurofibromatosis type 1 (NF-1), which is sometimes called von Recklinghausen's disease, is a rare genetic trait that causes many neurofibromas to form on the skin and nerves. These are harmless lumps. Most neurofibromas in the head and neck are found in soft tissues. We talk about a case of NF-1 in a 53-year-old Saudi woman in this report. During childhood, numerous darkly pigmented macules appeared on the epidermis, indicating the onset of the disease. The patient had pervasive freckling and café au lait spots on her body, as well as a diffuse, approximately 4 cm 3 cm swelling. Notably, large masses extending from her left ear to her left orbit were observed on her visage. These aggregates were distinct, painless, and mobile. On the margins, dorsum, and central border of the tongue, there were numerous exophytic lesions.The patient's diagnosis of NF-1 was confirmed based on the fulfillment of two or more diagnostic criteria established by the National Institute of Health Consensus Development Conference. Following a thorough surgical ablation, no recurrence was detected during the 15-month follow-up period.

Key Words: Neurofibromatosis 1, Soft tissue, Neurofibromas, Case report.

Introduction:

Neurofibromatosis (NF) is a group of genetically different diseases that cause various skin lesions and tumors to grow in the brain and other nerves. The type that happens most often is NF-1, which is also called von Recklinghausen disease. About 1 in 3500 people around the world are affected by it [1, 2]. NF-1 is caused by changes in the NF1 gene, which is found on

chromosome 17q11.2 and helps stop tumors from growing [3, 4]. Nearly half of all cases of NF-1 are caused by a positive family background. The other half are caused by spontaneous changes in the NF1 gene. [5] The presence of multiple light brown macules ranging from 10 to 40 mm in diameter and exhibiting an ovoid shape is a defining clinical feature of NF-1. [5] According to diagnostic criteria for NF-1, at least six of these macules must be present. [5] NF-1 follows an autosomal dominant pattern of inheritance, impacting individuals regardless of race or gender. [6, 7] In the absence of a cure, Neurofibromatosis type 1 (NF-1) is managed by addressing the associated symptoms and complications. NF-1 treatments vary according to individual symptoms and requirements. Medication may be prescribed to treat specific NF-1 symptoms, such as oral neurofibroma-related discomfort or dental issues. Individuals with NF-1 and their families are advised to seek genetic counseling for guidance on the condition, evaluation of transmission risks, and discussion of reproductive options or prenatal testing. In addition to skin manifestations, NF-1 can manifest diverse dental and oral characteristics. [9] Neurofibromas, benign lesions originating from nerve tissue, can develop in the oral cavity of individuals with NF-1. NF-1 is characterized by a high prevalence of dental abnormalities, including neurofibromas. These neurofibromas may manifest as swellings or nodules of soft tissue, influencing the tongue, gingiva, palate, or other oral structures. Some individuals with NF-1 may have hypertrophy or enlargement of the jawbones, resulting in facial asymmetry and malocclusion. NF-1 can cause abnormalities in tooth development, including delayed eruption, missing teeth (hypodontia), extra teeth (supernumerary teeth), and irregularly shaped teeth [11], crowded or malpositioned teeth, jawbone abnormalities and overcrowding can lead to crowded or malpositioned teeth, contributing to bite problems and difficulties with oral hygiene or skeletal abnormalities affecting the face and skull. NF-1 can cause skeletal abnormalities in the face and cranium, such as macrocephaly, hypertelorism, and bony deformities. [10]

Regular medical and dental monitoring is essential for tracking disease progression, identifying potential complications, and treating dental abnormalities. Oral neurofibromas may necessitate surgical removal or reduction, as well as correction of abnormalities of the mandible.

Notably, NF-1 cases are rarely documented in Saudi Arabia. In this report, we describe a case of NF-1 in a Saudi Arabian woman, age 53, that is both unique and uncommon. This case illustrates the importance of recognizing and diagnosing NF-1 in populations where it is rarely reported, as early detection and treatment can substantially improve patient outcomes. Through the dissemination of this case, we hope to increase the medical and dental community's understanding and awareness of NF-1, particularly its dental and oral manifestations. This contribution is especially important in regions with few reported cases, as it seeks to close the knowledge gap and promote a better understanding of the condition.

Individuals with NF-1 must consult with healthcare professionals, including dentists and NF-1-aware specialists, to devise individualized treatment plans tailored to their specific needs and symptoms, particularly concerning dental and oral manifestations.

Case report:

Patient information:

A 53-year-old Saudi woman presented to the King Saud University Medical City Postgraduate Family Dentistry Clinic with the chief complaint of difficulty chewing after losing all her teeth. Due to mobility, the patient's teeth have been extracted for over a year. Her medical background included Type I Neurofibromatosis, epilepsy, and hypothyroidism. She was taking medications such as 200 mg Tegretol, 100 mg levothyroxine, and 200 mg phenytoin sodium. The patient underwent surgery as a toddler to remove a neurofibrous tumor on her tongue, as reported by her mother.

In terms of her social history, the patient is divorced and lives with her mother and sisters. Due to financial constraints, she cannot receive the necessary dental care. No family history of NF1 has been reported in her immediate family.

TABLE 1. DIAGNOSTIC CRITERIA FOR NF-1	
1. **Optic pathway glioma (tumor of visual pathway)**	**NO**
2. **More than two Lisch nodules or choroidal abnormalities**	**NO**
3. **Freckling in axilla (armpit) or groin**	**NO**
4. **Six or more brown spots (café-au-lait macules) that are at least 5mm in diameter in prepubescent children and at least 15mm in diameter in an adult.s**	**YES**
5. **Multiple neurofibroma tumors or a plexiform neurofibroma as the only kind of neurofibroma**	**YES**
6. **recognizable osseous defect, such as sphenoid dysplasia, tibial dysplasia, or pseudarthrosis of a long bone.**	**NO**

7. **Seventh, a direct family member diagnosed with NF 1 according to the above criteria**	**NO**

Clinical Findings & Diagnostic assessment:

On examination, facial asymmetry was identified as a result of a large mass extending from the patient's left ear to the left orbit. The mass had distinct boundaries, was painless, and was mobile. Figure 1 depicts the presence of small nodules on the face and extremities of the patient.

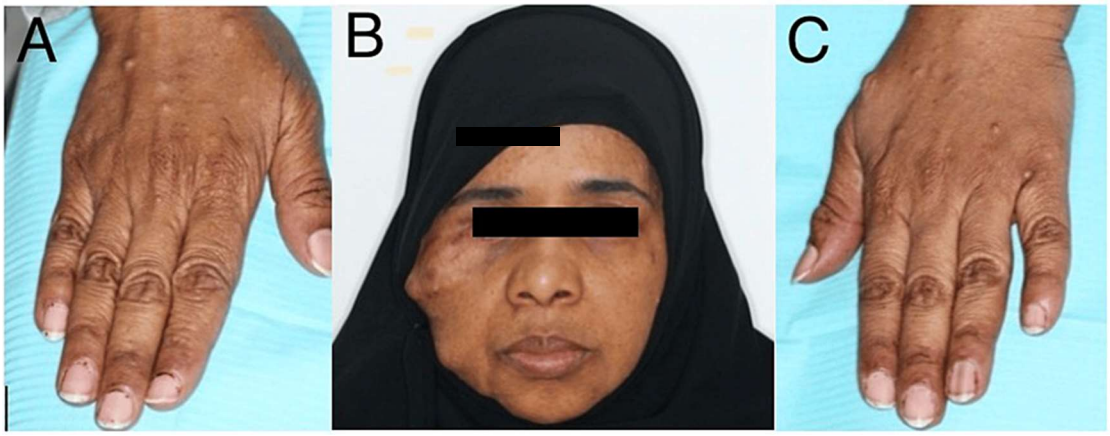

Figure (1) Extra-oral examination

The intraoral examination revealed a number of anomalies. Multiple diffuse exophytic lesions were observed on the lateral, dorsal, and middle border regions of the tongue. In addition, small nodules were found on the palate, labial mucosa, and floor of mouth (Figure 2). In infancy, the patient's mother underwent surgery for the removal of a neurofibrous tumor.

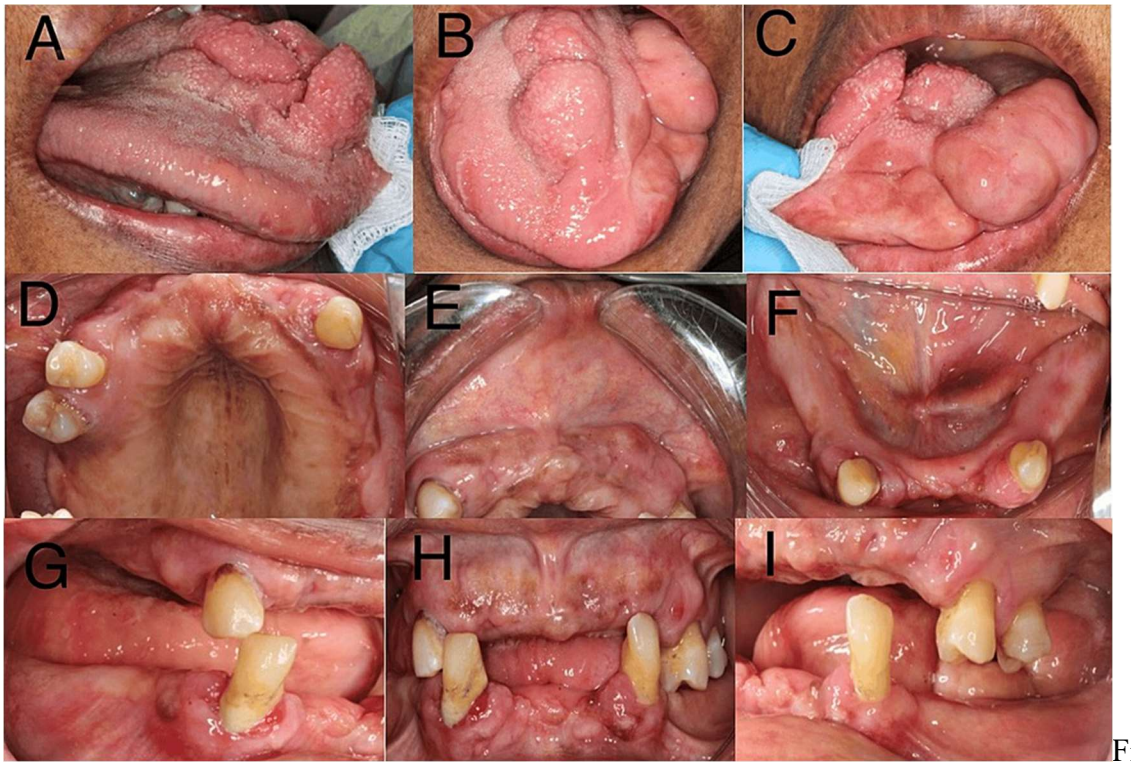

Figure (2) Intra-oral examination

The radiographs revealed multiple missing teeth, which were primarily caused by periodontal disease. Figure 3 depicts that only molars #13, #24, #25, #43, and #33 were present. The patient was diagnosed with generalized periodontitis, stage IV, grade c, according to the new classification of Periodontal and Peri-Implant Diseases.

It is essential to emphasize that the patient's overall medical prognosis is favorable and will not interfere with dental treatment. However, from a dental standpoint, it is important to observe that poor oral hygiene maintenance can have negative consequences. In addition, the patient suffers from seizures, which can be effectively controlled by identifying and avoiding specific triggers.

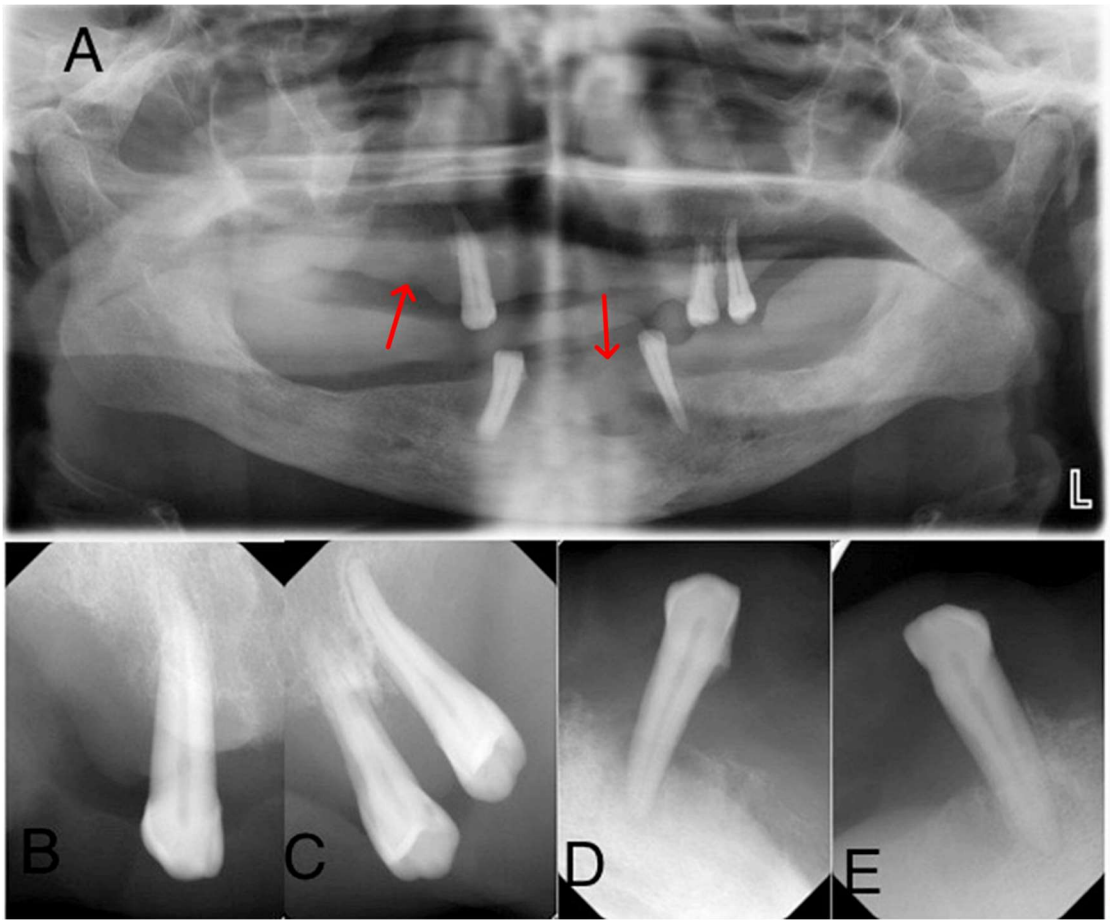

Figure (3) Radiographic examination shows severe bone loss (periodontitis stage IV grade C)

The patient's treatment options included removable transitional partial dentures for both the upper and lower mandible, an implant-supported overdenture, and a conventional complete denture. The patient was given a comprehensive explanation of the treatment procedure prior to the procedure. In addition, the first stage involved scaling and prophylaxis, and the second step involves completing the necessary restorations on teeth #24 and #25. Thirdly, transitional removable partial dentures were fabricated based on the socioeconomic status and unstable systemic condition of the patient. The final step involved evaluating sore areas, occlusion, and reinforcing care and wear instructions. Oral health examination was done with a 3-month recall period for pathogenic saliva testing.

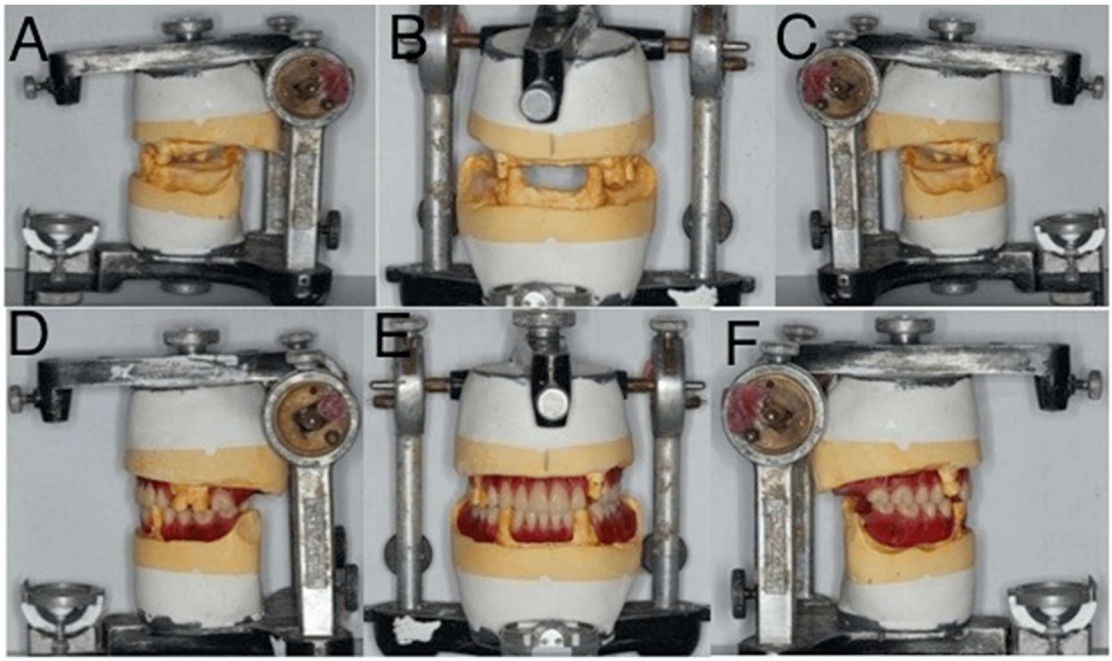

Figure (4) Mounted diagnostic casts

Discussion:

Numerous skeletal manifestations have been associated with NF-1, including dysplasia of the orbital and sphenoid bones as well as mandibular skeletal alterations. Some of these changes are abnormalities in the mandibular ramus and glenoid fossa, the condylar cranium, bigger coronoid notch measurements, and a smaller jaw angle.. In addition, hypoplastic and hyperplastic osseous alterations have been observed in the maxilla, mandible, zygoma, and temporomandibular joint. Multiple studies have documented these alterations. [12-17] These conditions can cause facial asymmetry [18], erosion of the cortical bone in the mandible due to soft tissue tumor growth [19], and alterations in the alveolar process and temporomandibular joint [15, 20-22].

NF1 is often accompanied by numerous oral manifestations, including teeth misalignment and a higher prevalence of dental caries. Perineural fibrous pulpal tissue thickening, periapical cemental dysplasia, and class III malocclusion are some of the other effects. [27, 28]. Moreover, fused teeth, impaired amelogenesis resulting in enamel hypoplasia, and microdontia are observed

[29]. Researchers have found that people with NF1 have lower levels of 25-hydroxyvitamin D3 in their blood and higher levels of osteoclastic activity. The decreased vitamin D3 levels in NF1 patients may be caused by enhanced pigmentation, impaired synthesis due to cutaneous neurofibromas, or accelerated catabolism [30]. This weakness gets worse with age, which makes NF1 people more likely to get periodontitis that comes with getting older. [31]. It is essential to note that this condition can worsen if the patient does not adhere to a strict recall schedule and oral hygiene at home.

In addition, histological examinations of neurofibromas have revealed the presence of mast cells, which contribute to an inflammatory microenvironment by activating STAT1 via stem cell factor (SCF). This activation is regarded a clinically and pathologically characteristic feature [32-34]. In contrast, an excessive increase in mast cells, also known as mastocytosis, contributes significantly to the development of periodontitis by unleashing inflammatory cytokines and destroying periodontal tissues [35,36]. Consequently, mast cells may constitute a crucial link between neurofibromatosis and periodontitis [14]. Notably, this association, in conjunction with inadequate oral hygiene, may contribute to the progression of periodontal disease.

This study's extensive follow-up period allows for a comprehensive assessment of the patients over time, which is a notable strength. The inability to provide comprehensive information on specific NF1-mutated subtypes that could potentially explain the intra-oral complications observed in this study is hampered by the lack of genetic testing for NF-1. Integration of clinical, radiographic, and genetic data is required to establish a definitive correlation.

CONCLUSION

In conclusion, neurofibromatosis is a group of conditions of varying severity, and it is crucial to comprehend the clinical oral manifestations. While neurofibromatosis symptoms are typically mild, it is crucial to recognize the potential associated pathologies that can have a direct impact on patient management.Additionally, poor oral hygiene and delays in receiving definitive dental treatment can significantly impact a patient's dental health. Maintaining optimal oral hygiene can be difficult for individuals with motor and cognitive impairments, sensory deficits, and restricted access to dental care. These difficulties increase the likelihood of developing dental caries, periodontal disease, and other oral complications. Along with oral health education, timely and specialized dental care is essential for addressing these issues and enhancing oral health and quality of life of NF1 patients.

Informed Consent: written informed consent were granted and approved by Saudi board in family dentistry at king Saud university.

References:

1] Javed F, Utreja A, Bello Correa FO, et al.: Oral health status in children with acute lymphoblastic

leukemia. Crit Rev Oncol Hematol. 2012, 83:303-9. 10.1016/j.critrevonc.2011.11.003

2. Sham ME, Ghorpade, Shetty A, Hari S, Vinay: Malignant peripheral nerve cell tumour. J Maxillofac Oral

Surg. 2010, 9:68-71. 10.1007/s12663-010-0019-6

3. Azher U, Shiggaon N: Oral health status of children with acute lymphoblastic leukemia undergoing

chemotherapy. Indian J Dent Res. 2013, 24:523. 10.4103/0970-9290.118371

4. Nascimento GG, Seerig LM, Vargas-Ferreira F, Correa FO, Leite FR, Demarco FF: Are obesity and

overweight associated with gingivitis occurrence in Brazilian schoolchildren. J Clin Periodontol. 2013,

40:1072-8. 10.1111/jcpe.12163

5. Neville BW, Hann J, Narang R, Garen P: Oral neurofibrosarcoma associated with neurofibromatosis type I.

Oral Surg Oral Med Oral Pathol. 1991, 72:456-61. 10.1016/0030-4220(91)90560-y

6. Javed F, Correa FO, Nooh N, Almas K, Romanos GE, Al-Hezaimi K: Orofacial manifestations in patients

with sickle cell disease. Am J Med Sci. 2013, 345:234-7. 10.1097/maj.0b013e318265b146

7. Angst PD, Dutra DA, Moreira CH, Kantorski KZ: Periodontal status and its correlation with

haematological parameters in patients with leukaemia. J Clin Periodontol. 2012, 39:1003-10.

10.1111/j.1600-051x.2012.01936.x

8. Messiaen L. M., Callens T., Mortier G., et al.: Exhaustive mutation analysis of the NF1 gene allows

identification of 95% of mutations and reveals a high frequency of unusual splicing defects. Human

Mutation. 2000, 15:541-555. 10.1002/1098-1004(200006)15:6%3C541::aid-humu6%3E3.0.co;2-n

9. Javed F, Ramalingam S, Ahmed HB, et al.: Oral manifestations in patients with neurofibromatosis type- 1:

a comprehensive literature review. Crit Rev Oncol Hematol. 2014, 91:123-9.

10.1016/j.critrevonc.2014.02.007

10. Bardellini, E.; Amadori, F.; Flocchini, P.; Conti, G.; Piana, G.; Majorana, A: Oral findings in 50 children

with neurofibromatosis type 1. A case control study. Eur. J. Paediatr. Dent. 2011, 12:256-260.

11. Friedrich, R.E.; Giese, M.; Schmelzle, R.; Mautner, V.F.; Scheuer, H.A: Jaw malformations plus

displacement and numerical aberrations of teeth in neurofibromatosis type 1: A descriptive analysis of 48

patients based on panoramic radiographs and oral findings. J. Craniomaxillofac. Surg. 2003, 31:1-9.

10.1016/s1010-5182(02)00160-9

12. Thota, E., Veeravalli, et al.: Age-dependent oral manifestations of neurofibromatosis type 1: a casecontrol

study. Orphanet J Rare Dis. 2022, 10.1186/s13023-022-02223-x

13. Jouhilahti EM, Peltonen S, Heape AM, Peltonen J: The pathoetiology of neurofibromatosis 1 . Am J

Pathol. 2011, 178:1932-9. 10.1016/j.ajpath.2010.12.056

14. Friedrich RE: Reul A. A combination of skeletal deformations of the dorsal mandible and

temporomandibular region detected in ortho-pantomograms of patients with neurofibromatosis type 1

indicates an associated ipsilateral plexiform neurofibroma. J Craniomaxillofac Surg. 2018, 46:1091-104.

10.1016/j.jcms.2018.04.018

15. Koblin 1. Riel B: Changes in the facial skeleton in cases of neurofibromatosis . J Maxillofac Surg. 3:23-27.

10.1016/s0301-0503(75)80009-9

16. James PL: Neurofibromatosis affecting the jaws; report of a case . J Oral Surg 21. 262:264.

17. Goetsch E: Schadelveranderungen bei neurolibromatosis Recklinghausen . Fortschr Rontgenstr 83.

225:1955.

18. Lorson EL, DeLong PE, Osbon B, Dolan KB: Neurolibromatosis with central neurofibromas of the

mandible: review of the literature and report of a case. J Oral Surg 35~733-738,1977.

https://pubmed.ncbi.nlm.nih.gov/407340/.

19. Freedus MS, Doyle PK: Multiple neurofibromatosis with oral manifestations . J Oral Sure. 33:360-363.

20. 20] Varghese P, Abdul Jalal MJ: A rare case of neurofibromatosis - type 1 . Asian J Neurosurg. 2015, 10:344-7.

10.4103/1793-5482.162728

21. 21] James PL. Treggiden R: Multiple neurofibromatosis associated with facial asymmetry . J &al Surg. 33:429-

442.

22. Van Gemert RJ, Yamashita DDR, Goodsell JF: Multiple neurofibromatosis (Von Recklinghausen's

disease) with concurrent micrognathia; review of the literature and report of a case. ORAL SURG. 43:165-

173. 10.1016/0030-4220(77)90152-9

23. Jouhilahti EM, Visnapuu V, Soukka T, Aho H, Peltonen S, Happonen RP, Peltonen J: Oral soft tissue

alterations in patients with neurofibromatosis. Clin Oral Investig. 2012, 16:551-8. 10.1007/s00784-011-

0519-x

24. Engebretson SP, Hyman LG, Michalowicz BS, et al.: The effect of nonsurgical periodontal therapy on

hemoglobin A1c levels in persons with type 2 diabetes and chronic periodontitis: a randomized clinical trial.

JAMA. 2013, 310:2523-32. 10.1001/jama.2013.282431

25. 25] Wu MC, Ma KS, Wang YH, Wei JC: Impact of tonsillectomy on irritable bowel syndrome: a nationwide

population-based cohort study. PLoS One. 2020, 15:0238242. 10.1371/journal.pone.0238242

26. 26] Lasater EA, Li F, Bessler WK, et al.: Genetic and cellular evidence of vascular inflammation in

neurofibromin-deficient mice and humans. J Clin Investig. 2010, 120:859-70. 10.1172/jci41443

27. 27] Smith RW: A treatise on the pathology, diagnosis, and treatment of neuroma . Dublin. 1849:

28. 28] Davis WB, Edgarton MT, Hoffmeister SF: Neurofibromatosis of the head and neck . Plast Reconstr. Surg.

14:186-199.

6 of 7

29. Gilbert JC, Hershman DC, Schow CE Jr: Neurofibromatosis with oral manifestations; report of a case .

Texas Dent J. 90:24-28.

30. Hsueh YJ, Huang SF, Lai JY, et al.: Preservation of epithelial progenitor cells from collagenase-digested

oral mucosa during ex vivo cultivation. Sci Rep. 2016, 6:36266. 10.1038/srep36266

31. Ma DH, Hsueh YJ, Ma KS, et al.: Long- term survival of cultivated oral mucosal epithelial cells in human

cornea: generating cell sheets using an animal product-free culture protocol. Stem Cell Res Ther. 2021,

12:524. 10.1186/s13287-021-02564-7

32. Schnabel C, Dahm S, Streichert T, Thierfelder W, Kluwe L, Mautner VF: Differences of 25-

hydroxyvitamin D3 concentrations in children and adults with neurofibromatosis type 1. Clin Biochem.

2014, 47:560-3. 10.1016/j.clinbiochem.2014.02.020

33. Machado V, Lobo S, Proença L, Mendes JJ, Botelho J: Vitamin D and Perio- dontitis: A Systematic Review

and Meta-Analysis. Nutrients. 2020, 12:2177. 10.3390/nu12082177

34. Kobayashi R, Matsune K, Ohashi H: Fused teeth, macrodontia and increased caries are characteristic

features of neurofibromatosis type 1 patients with NF1 gene microdeletion. J Pediatr Genet. 2012, 1:25-31.

10.3233/pge-2012-006

35. Liao CP, Booker RC, Brosseau JP, et al.: Contributions of inflammation and tumor microenvironment to

neurofibroma tumorigenesis. J Clin Invest. 2018, 128:2848-61. 10.1172/jci99424

36. Jackson CW, Pratt CM, Rupprecht CP, Pattanaik D, Krishnaswamy G: Masto- cytosis and mast cell

activation disorders: clearing the Air. Int J Mol Sci. 2021, 22: 10.3390/ijms2220112707