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RESEARCH ARTICLE

NEUROFIBROMATOSIS TYPE 1: FAMILIAL CASE SERIES AND REVIEW

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ABSTRACT

The neurofibromatosis type 1 (NF1) is inherited as an autosomal dominant trait, therefore, is a hereditary condition. At least eight forms of neurofibromatosis have been recognized, but the most common is the (NF1), with a prevalence of 1:2200 to 3000 births. The signs and symptoms of this condition vary widely among affected people. The most common sign on the skin is multiple neurofibromas. Bone lesions, cardiovascular and neurological abnormalities are other manifestations of this disease. Oral manifestations may occur in this disease as high as 72% to 92% of all cases. The most commonly affected sites are the tongue and buccal mucous. Oral radiographic findings include an enlarged mandibular canal, mandibular foramen, and mental foramen. NF1 is diagnosed in an individual with two or more of the following signs: cafe au lait macules, two or more neurofibromas of any type or a single plexiform neurofibroma freckling in the axillary or inguinal region and optic glioma. Proper diagnosis and management of patients with neurofibromatosis should be carried out. A multidisciplinary approach should be carried out for the proper planning of the treatment plans. The aim of this paper was to report the clinical, radiographic orofacial characteristics observed in 4 famalies patients diagnosed with NF1.

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INTRODUCTION

Neurofibromatosis (NF) is referred to a group of genetic disorders that primarily affect the cell growth of neural tissues. This disease was first described by Friederich Daniel Von Recklinghausen, in 1882. (1) There are two types of NF - Type 1 (NF1) and Type 2 (NF2) both of them share few common features and are caused by mutations on different gene. (1,2) Neurofibromatosis type 1, also known as Von Recklinghausen's disease, is a neurodermal dysplasia. It is an autosomal dominant disease caused by spectrum of mutations that affect the NF1 gene located at the 17q11.2 chromosome. It is the most common type of NF and is estimated to occur in 90% of all cases, (3, 4) with prevalence of one in 3,000 births. (1,3) There is no gender or racial predilection.. Only 50% of patients have positive family history. The expressivity of the disease is extremely variable, with manifestations ranging from mild lesions to several complications and functional impairment. The penetration is otherwise 100%. (1, 2) The diagnostic criteria for NF1 is as follows; the patient should have two or more of the following: (1) Six or more cafe Â-au-lait spots 1.5 cm or larger in post-pubertal individuals and 0.5 cm or larger in pre-pubertal individuals (2) Two or more NF of any type or one or more plexiform NF (3) Axillary or groin freckling (4) Two or more Lisch nodules (bening melanotic iris hamartomas) (5) Optic glioma (6) A distinctive bony lesion- dysplaia of sphenoid bone, dysplasia/thinning of cortex of long bones.(7) A first degree relative with NF1.(3-6) Neurofibroma, a benign nerve sheath neoplasm that is the predominant feature of NF1, is frequently found in the head and neck and can appear as a solitary or generalized, peripheral or central lesion. Clinically, they present as slow growing masses that produce deformities of the anatomical structures and may displace the adjacent teeth (5, 6) Oral manifestations may occur in this disease as high as 72% to 92% of all cases, especially if a detailed clinical and radiographic examination is performed. (5, 6) The most common location of peripheral neurofibromas within the oral cavity is the tongue, often causing macroglossia.(1,4,5,6) Radiographical characteristics include enlargement and/or ramification of the mandibular canal, thinning and concavity of the ramus, enlarged and lower mandibular foramen, increased coronoid notch, increased bone density, decreased mandibular angle, notching of the inferior border of the mandible, and hypoplastic coronoid processes and condyles. (2,3) Finally, the most fearsome complication of NF1 is the increased risk of malignant tumors; the most common NF1-associated malignancy is the neurofibrosarcoma that has also been reported to occur in the oral cavity (3,5,6,7).

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CASE 1	CASE 2	CASE 3	CASE 4
A 24 year old patient reported to the Department of Oral Medicine and Radiology with the chief complaint of restricted mouth opening since 2 years.	A 21 year old female patient reported with complaint of pain in teeth since 2 months. On general examination, she was moderately built and nourished, had short stature with mild mental retardation.	A 43 year old female patient had complaint of pain in teeth since 8 days	A 50 year old male patient had complaint of missing teeth
HISTORY	**HISTORY**	**HISTORY**	**HISTORY**
Positive family history was found regarding NF His maternal uncle had similar findings of numerous nodules in entire body and plexiform pattern of growth in right chest.	Her mother also had similar nodules on entire body present since childhood.	Positive family history was elicited with her offsprings (a son and a daughter) having similar lesions	Positive family history was elicited with his mother, sister and daughter) having similar lesions
GENERAL EXAMINATION	**GENERAL EXAMINATION**	**GENERAL EXAMINATION**	**GENERAL EXAMINATION**
Well defined, irregular, scar tissue measuring about 5x3 cm in diameter at the region of right side of neck was noted. Patient had kyphotic deformity. Nodules were present all over the body which started in childhood. 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. Café au lait pigmentations were evident at neck, chest, abdomen, left upper arm, upper back and waist region.	Frontal bossing, telecanthus and square shaped face were noted. Round to oval shaped nodules with smooth surface were present in entire body which was present since birth. On palpation they were sessile, soft to firm and non-tender. (FIG 1)	she was moderately built and nourished with presence of multiple soft tissue cutaneous nodules and café au lait pigmentations (coffee with milk) on the body. Axillary freckling was evident.(FIG 2)	Nodules were present all over the body which started in childhood. 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. Café au lait pigmentations were evident at neck, chest, abdomen, left upper arm, upper back and waist region.(FIG 3)
INTRAORAL EXAMINATION	**INTRAORAL EXAMINATION**	**INTRAORAL EXAMINATION**	**INTRAORAL EXAMINATION**
multiple nodules were present on hard palate and tongue with enlargement of fungiform papillae.(FIG 4)	macroglossia with multiple nodules on right and left lateral borders of tongue and carious 36 47 teeth.(FIG 5)	Not significant	Not significant
RADIOGRAPHIC PRESENTATION	**RADIOGRAPHIC PRESENTATION**	**RADIOGRAPHIC PRESENTATION**	**RADIOGRAPHIC PRESENTATION**
enlarged mandibular canal and mandibular foramen, increased coronoid notch, increased bone density, decreased mandibular angle, notching of the inferior border of the mandible	Not significant	Not significant	Enlarged mandibular canal and mandibular foramen.(FIG-6)
DIAGNOSTIC CRITERIA	**DIAGNOSTIC CRITERIA**	**DIAGNOSTIC CRITERIA**	**DIAGNOSTIC CRITERIA**
Six or more cafe Â-au-lait spots Two or more NF of any type or one or more plexiform NF Axillary or groin freckling Two or more Lisch nodules A distinctive bony lesion- dysplaia of sphenoid bone, dysplasia/thinning of cortex of long bones. A first degree relative with NF1	Six or more cafe Â-au-lait spots Two or more NF of any type or one or more plexiform NF Axillary or groin freckling A first degree relative with NF1	Six or more cafe Â-au-lait Two or more NF of any type or one or more plexiform NF Axillary or groin freckling A first degree relative with NF1	Six or more cafe Â-au-lait Two or more NF of any type or one or more plexiform NF Axillary or groin freckling A distinctive bony lesion- dysplaia of sphenoid bone, dysplasia/thinning of cortex of long bones. A first degree relative with NF1
PROVISIONAL DIAGNOSIS	**PROVISIONAL DIAGNOSIS**	**PROVISIONAL DIAGNOSIS**	**PROVISIONAL DIAGNOSIS**
chronic generalized periodontitis and NF1were given. with recurrent facial plexiform neurofibroma were given. As the patients were not willing for any further treatment regarding NF	chronic periapical abscess and NF1 were given.	chronic generalized periodontitis and NF1were given	Completely edentulous and NF 1

The aim of this paper is to report the orofacial, clinical and radiographic characteristics observed in 4 families diagnosed with NF1.

DISCUSSION

This disease is a slowly evolving neurodermic dysplasia. Troubles begin at the embryonic stage before differentiation of the neural crests. After birth, the disease evolves in bursts, especially during growth, puberty, and pregnancy. (1) This finding was duplicated in our study, in case 2, the mother reported an increase of her lesions during pregnancy and other patients experiencing increase in number of lesions during pubertal growth spurt. There are basically 4 types of neurofibromas found in NF1: (1) Cutaneous: superficial, soft button-like tumors with no malignant potential. (2) Subcutaneous: tumors in the dermis that may cause localised pain or tenderness. (3) Nodular plexiform: large network of tumors involving the dorsal nerve roots. (4) Diffuse plexiform: invasive tumors that may involve all layers of skin, muscle, bone and blood vessels.(1) Both cutaneous lesions and subcutaneous lesions are circumscribed; neither is specific for type1 NF. These nodules may be brown, pink, or skin colored. They may be soft or firm to the touch, and they may have the pathognomonic buttonhole invagination when pressed with a finger. The plexiform subtype is hallmark for type 1 NF. (1-5) Plexiform neurofibromas are noncircumscribed, thick, and irregular, and they can cause disfigurement by entwining important supportive structures. The tumor is soft and feels like a “bag of worms”. In case 1, patient had plexiform neurofibroma on right side of nape of neck and his maternal uncle had similar large sized lesion on chest.

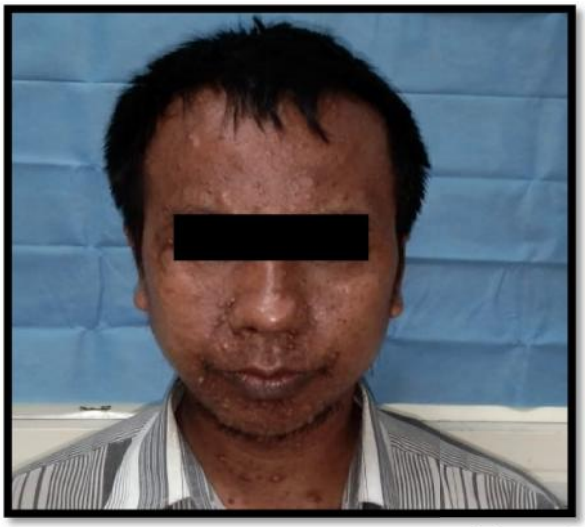

Fig. 1.Multiple skin neurofibromas on the patient´s face and neck

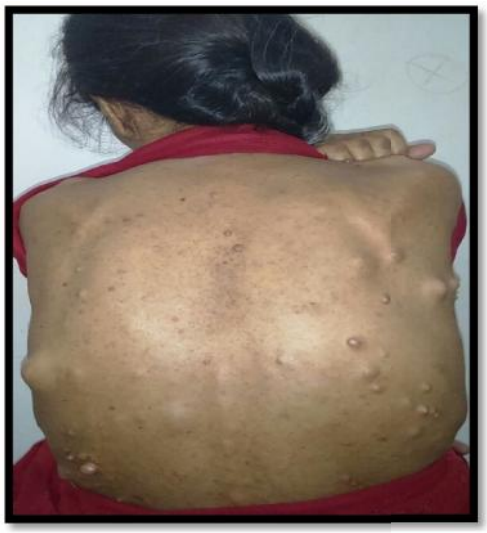

Fig. 2. Café au lait spots and small neurofibromas on the back

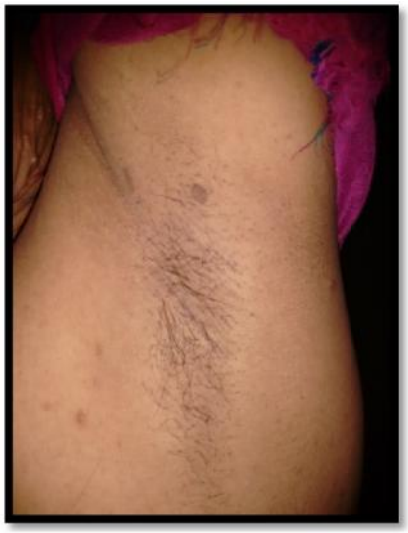

Fig. 3. Axillary freckling evident on patient´s arm pit

The lesion usually spreads along the peripheral nerve and may affect some nervous rami. The cranial nerves most involved are the fifth, ninth and tenth. A third variant is known as segmental neurofibromatosis; i.e disease limited to a single body region. Segmental neurofibromatosis may be related to mosaicism or segmental hyperexpression of the condition. Loss of heterozygosity may create the clinical impression of segmental lesions (8).

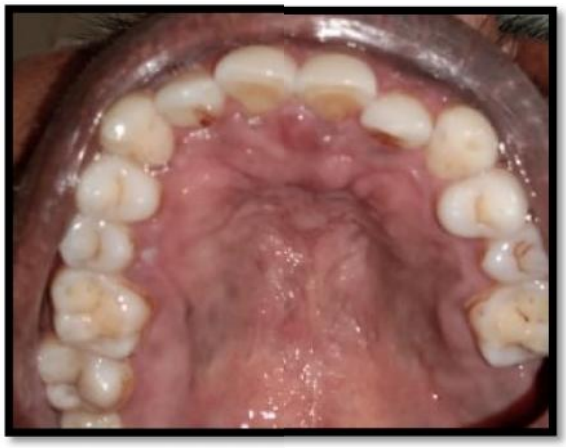

Fig. 4. Multiple nodules present on the hard palate

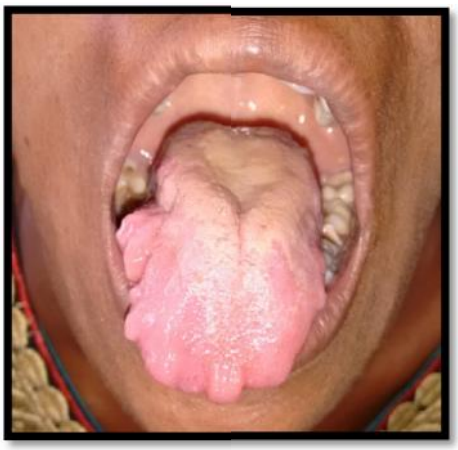

Fig. 5. Enlarged tongue with teeth indendation on lateral border of tongue

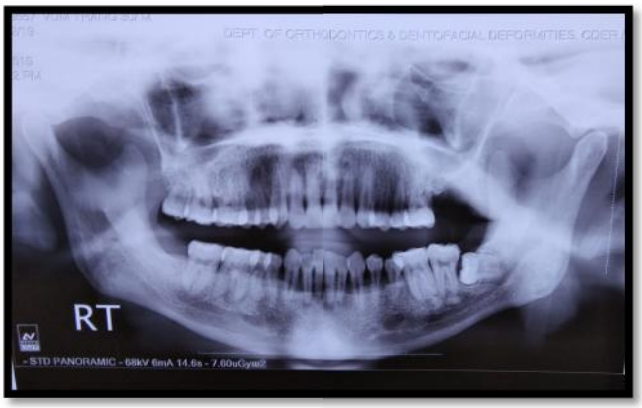

Fig. 6. Panoramic radiograph showing mandibular canal enlargement

These findings were duplicated in case 3. Pigmented lesions are common manifestation in NF1 but not pathognomonic. These lesions usually appear during the first years of life or are present at birth, either as Café au lait spots or freckles. Caféaulait spots are hyperpigmented maculae that may vary in color from light to dark brown. Their borders may be smooth or irregular. (1-10) These are composed of epidermal melanocytes with giant pigment granules (macromelanosomes) within the cytoplasm and are of neural crest origin. (9) Inguinal and axillary freckles (Crowe's sign)

are frequently present. In some patients freckling may occur diffusely over the trunk, extremities, upper eyelids, and base of the neck. (1,6,8,9) In the presented series all cases exhibited more than six Caféaulait spots more than 1.5 cm and bilateral axillary freckles in accordance to literature. Oral manifestations are prevalent in 72% of NF1 and may appear in any tissue, soft or hard, in the oral cavity. The most commonly affected site is the tongue. Enlargement of the fungiform papillae of tongue occurs in about 50% of cases. The tongue may be involved by a localized neurofibroma, but macroglossia caused by plexiform neurofibroma. (1,2) This findings were similar in case 1 and case 2 patients. Oral radiological changes are widening of the mandibular channel, mandibular foramen, and mental foramen. (1) We found these characteristics in case 1. Neurofibroma can also develop intraosseously, resulting in well demarcated unilocular, but occasionally multilocular, radiolucent lesions. In our case, however, these radiographic changes were not observed. (2) Involvement of other body parts causes: Malformation of the long bones (below the knee and elbow) and curvature of the spine (scoliosis), short stature and growth hormone deficiency, learning difficulties (speech problems), tumors on the optic nerve which can cause visual loss, high blood pressure, tumors on the spine and brain causing increase risk of epilepsy, lesions on the gastrointestinal tract that may cause bleeding or obstruction and hearing defects (8) Skeletal involvement is present in almost 40% of the patients with NF1. (2) Thoracic spinal curvatures are common in NF1 and affect approximately 10% of NF1 patients. 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. (4,6) Our patient in case 1 exhibited scoliosis and other cases did not showed such changes. Short stature has long been known to be a feature of NF1 and the average height of individuals with NF1 is less than expected for age, but reduction in height is usually mild. (2) Learning disabilities occur in 50% of patients. (6) and also behavioural problems.(8,9) This was noted in case 2 patient. The most common malignancy seen in individuals affected with NF1 is the malignant peripheral nerve sheath tumour (MPNST) in 2±16% of patients. Preexisting plexiform neurofibroma appear to be the most common precursor to MPNSTs in people with NF1. Biopsy should be done for confirmation. (2, 6) case 1 had plexiform neurofibroma but no evidence of malignancy was found.

Conclusion

Neurofibromatosis type 1 is an autosomal dominant disease caused by spectrum of mutations that affect the NF1 gene. The patients described in this case report are vary typical case of NF-1, which presents a considerable interest because of the high generalization of the skin lesion as well as oral involvemnt. In such cases, a detailed patient investigation is required, because of the possibility for generalized. 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 treatment of such kind of patient is surgical, seeking to achieve cosmetic improvement, and may be only palliative.

REFERENCES

Cunha KS, Barboza EP, Dias EP, Oliveira FM. Neurofibromatosis type I with periodontal manifestation. A case report and literature review. British dental journal. 2004 Apr;196(8):457-60.

Cunha KS, Barboza EP, Dias EP, Oliveira FM. Neurofibromatosis type I with periodontal manifestation. A case report and literature review. British dental journal. 2004 Apr;196(8):457-60.

Dimitrova V, Yordanova I. A case of neurofibromatosis type 1. Journal of IMAB–Annual Proceeding Scientific Papers. 2008 Oct 7;14(1):63-7.

Ghalayani P, Saberi Z, Sardari F. Neurofibromatosis type I (von Recklinghausen's disease): A family case report and literature review. *Dental research journal*. 2012 Jul; 9(4):483.

Hirsch NP, Murphy A, Radcliffe JJ. Neurofibromatosis: clinical presentations and anaesthetic implications. British journal of anaesthesia. 2001 Apr 1;86(4):555-64.

Munhoz ED, Cardoso CL, Tolentino ED, Centurion BS, Gonçales ES, Sant'Ana E, Rubira-Bulen IR. Von Recklinghausen's disease-Diagnosis from oral lesion: Neurofibromatosis I. Int. j. odontostomatol.(Print). 2010:179-83.

Puri N. A Study of Clinical Profile of Neurofibromatosis. JIMSA. 2013;26(2):103-5.

Sigillo R, Rivera H, Nikitakis NG, Sauk JJ. Neurofibromatosis type 1: a clinicopathological study of the orofacial manifestations in 6 pediatric patients. Pediatric dentistry. 2002 Dec;24(6):575-.

Thornton JB, Tomaselli CE, Rodu B, Creath CJ. Neurofibroma of the mandible in an adolescent with von Recklinghausen's disease. Pediatric dentistry. 1992 Sep; 14(5):347.

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