Case Report

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Dentistry Section

An Unusual Case of Multiple Intraoral Manifestations of Neurofibromatosis Type 1: Case Report with Literature Review

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ABSTRACT

The various oral manifestations of neurofibromatosis in dentulous patients have been documented in literature. Although most of the previous documents have discussed on common findings like a prominent lingual papillae, or solitary overgrowth of gingival soft tissue, this article focuses on a relatively rare occurrence of multiple nodular manifestations of Neurofibromatosis–1 on an edentulous alveolar ridge, tongue, palate and lips of an elderly female patient.

Keywords: Edentulous ridge, Intraoral neurofibroma

CASE REPORT

A 50-year-old female was referred to the Department of Prosthodontics, KMCT Dental College, Manassery, Kozhikode, Kerala, India for prosthetic rehabilitation of oral cavity. She had short stature, and was moderately built and nourishment for her age. The general clinical examination revealed multiple cutaneous nodules of different sizes ranging from 2mm to 6 cm unevenly distributed over the head and neck, trunk and upper arms [Table/Fig-1a-c]. The nodules were soft, flesh coloured, non tender, with no signs of inflammation. A large number of both cutaneous and subcutaneous neurofibromas were scattered over the entire patient's skin. Lymph nodes were not enlarged. More than 10 café-au-lait spots were noted on the trunk and upper arms which were flat and brown pigmented. Freckles could be seen diffusely over the back and axillary region. The patient reported that some pigmented lesions were present at birth and the other ones appeared when she was a child, nodules began to develop in puberty and increased during the pregnancy. There was no family history of neurofibromatosis. Hers was a non consanguineous marriage, and her parents were also unrelated. Written consent was obtained from the patient to avoid ethical conflicts in documenting and publishing her case.

Extraorally, she had mild prognathism of the mandible. Isolated nodules of few millimeter sizes were seen on the upper and the lower lip. Intraorally isolated nodule on the dorsum of tongue was noted [Table/Fig-1a,2]. There were multiple bilaterally distributed nodules on edentulous alveolar ridges of maxilla and mandible which were non-ulcerated, non painful with normal color and firm on palpation [Table/Fig-3a]. The nodules were also present on the palate [Table/Fig-3b]. There were no symptoms associated with the nodules other than creating discomfort for the patient in mastication. The patient reported that the nodules were noted to appear on the ridges after the teeth were lost due to extraction. All the teeth were extracted previously due to caries or periodontitis and there was no history of accidental traumatism.

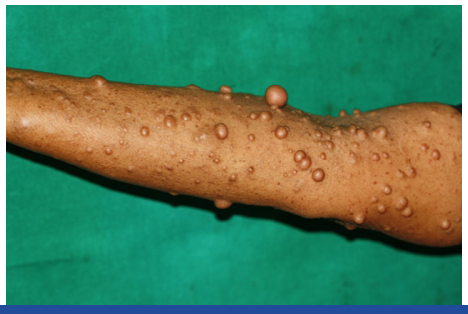
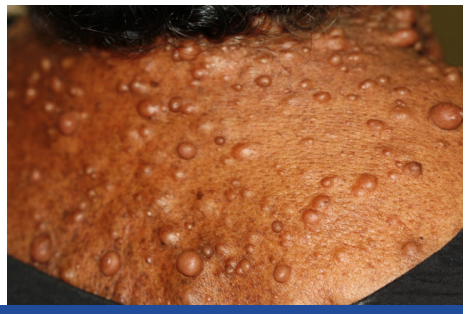
The OPG radiograph revealed widening of mandibular canal, decreased mandibular angle and alteration in coronoid notch morphology [Table/Fig-4]. A clinical diagnosis of neurofibromatosis – 1 (NF-1) was made based on diagnostic criteria formulated by the National Institutes of Health Consensus Development Conference for neurofibromatosis- 1(NF1) [1].

An excisional biopsy of the oral lesion was performed [Table/Fig-5]. Histopathologically, there were atrophic startifed squamous epithelium, underlying connective tissue was fibrous moderately cellular with capillaries. There were numerous delicate proliferating spindle cells with wavy nuclei. Neurovascular bundles were seen. Under high power mast cells, melanophages and melonocytes were seen suggestive of neurofibroma. Immunohistochemical analysis for S-100 protein was positive for some spindle cells.

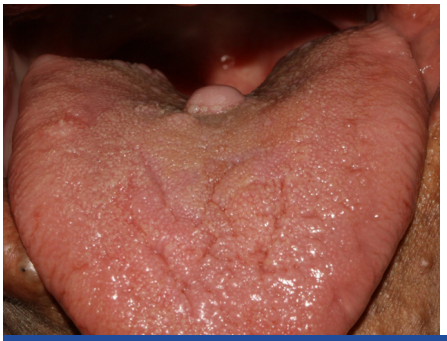
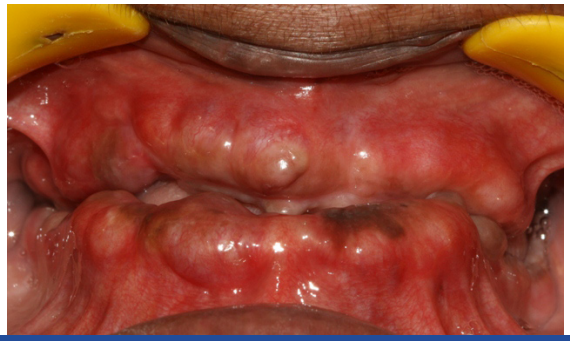
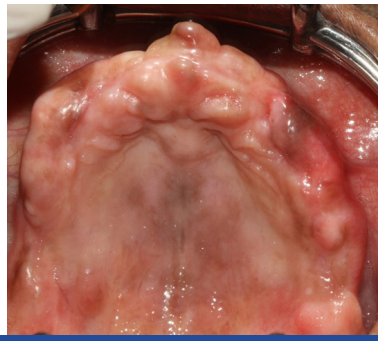
DISCUSSION

Neurofibromatosis are a set of autosomally dominant inherited disorders that result in the development of benign tumors of the nerve sheath. Currently, there are 3 different entities designated as neurofibromatosis type 1 (NF-1), neurofibromatosis type 2 (NF-2), and schwannomatosis that are distinguished by specific clinical features.

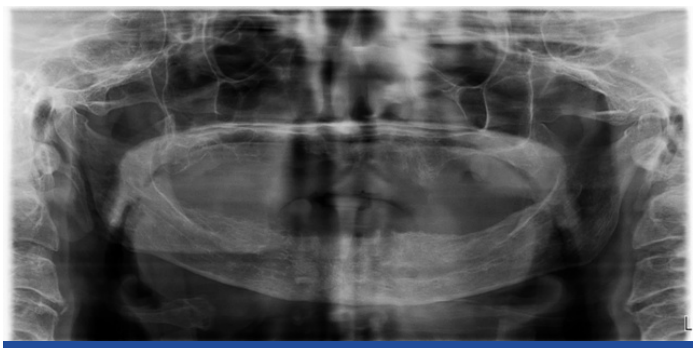
NF-1 is the most common of the disorders affecting 1 in 3000 individuals worldwide [2-4]. Deletions, insertions or mutations affecting

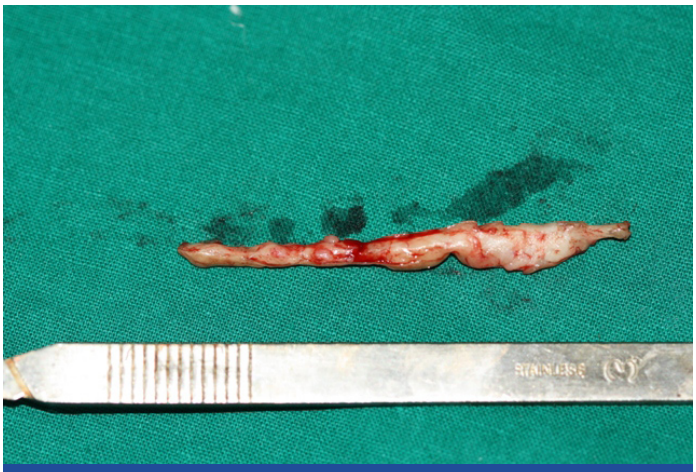
[Table/Fig-1a]: Cutaneous nodules of different sizes unevenly distributed over the head and neck **[Table/Fig-1b]:** Cutaneous nodules on arm **[Table/Fig-1c]:** Cutaneous nodules on back

[Table/Fig-2]: Neurofibroma on tongue **[Table/Fig-3a]:** Multiple neurofibroma on edentulous maxilla and mandible **[Table/Fig-3b]:** Solitary nodules on palate



[Table/Fig-4]: OPG of the patient



[Table/Fig-5]: Excision done

the NF1 gene that is located at 17q11.2 chromosome is responsible for the disease [3]. NF-1 expresses a characteristical cutaneous phenotype including benign neurofibromas, hyperpigmented macules, termed café-au-lait macules, the axillary/inguinal freckling, as well as pigmented hamartomas of the iris, called Lisch nodules. The hallmark lesion in NF1 is the neurofibroma. Till date the diagnosis of NF-1 are based predominantly on the clinical criteria of cutaneous manifestations and familial history.

Neurofibromas are benign and usually painless, slow growing peripheral nerve sheath tumours, which get accelerated during puberty or pregnancy [2-4]. Cafe au lait spots are zones of focal epidermal melanosis due to cutaneous nerve endings proliferation [4,5]. Our patient had findings consistent with the features documented for NF-1.

Oral neurofibromas usually present as non-tender, uninflammed, submucosal discrete masses that range from few millimeters to several centimeters. Tumors tend to grow slowly and patients are usually asymptomatic, but depending on the locality (e.g., tongue, palate), they may be traumatized and give rise to symptoms. There is no predilection towards race or sex [6].

Oral soft tissues manifestations varies in adults (3.4-92%) and children (40%) [2,4,6]. Common sites of the oral neurofibromas include tongue (26%), buccal mucosa (8%), alveolar ridge (2%), labial mucosa (8%), palate (8%), gingiva (2%), nasopharynx, paranasalsinuses, larynx, floor of the mouth and salivary gland [1]. The most commonly reported finding is enlargement of the fungiform papillae of tongue [2,6].

Although single nodular overgrowth in dentulous patients with neurofibromatosis has been documented in literature [1,6,7], this article focuses on a relatively rare occurrence of multiple nodular growths at multiple intraoral sites of an edentulous neurofibromatosis patient. The uniqueness of this case report is in the multiplicity of the intra oral nodules, their simultaneous presence in multiple locations, and most characteristically the presence of nodules on the edentulous ridges.

The introsseous expressions of NF-1 are enlargement of inferior alveolar canal, widened mandibular foramen and mental foramen, absence of sphenoid bone, coronoid notch morphology alteration and decreased mandibular angle, hypoplasia of the mandibular ramus with radiolucency in the sigmoid notch and hypoplasia of the temporal and mandibular components of the temporomandibular joint [4]. The OPG of our patient showed widening of mandibular canal, decreased mandibular angle and alteration in coronoid notch morphology.

Individuals with NF1 demonstrate increased incidence of both benign tumors, with the risk of malignant transformation being 3 to 5 % [2,4]. Total resection with 1 cm margins whenever feasible is the treatment of choice for accessible and small tumors. Radiotherapy or chemotherapy is not recommended [4]. Long term review of patients and genetic counselling is recommended owing to the likelihood (50%) of vertical transmission [8].

Although numerous neurofibroma can be seen distributed around the head and neck and solitary nodules intraorally in most of the patients, our patient had multiple presentations of NF-1 both extraorally and intraorally. The multiple intraoral presentations of the nodules at various sites in this patient seems to be a rarity compromising the quality of her life. The peculiarity being the appearance of these multiple neurofibroma after extraction of all teeth.

CONCLUSION

Since NF1 is not curable, multidisciplinary management is recommended. Oral lesions may sometimes become large enough to interfere with functions of mastication and speech causing significant disturbance to the patient. Dentists should be aware of the possible oral manifestations of neurofibromatosis and be competent to differentiate it from other common inflammatory swellings. Long term review of patients and genetic counselling is recommended owing to the likelihood of vertical transmission. It is also imperative to put these patients on a long-term follow up for early detection of any possible signs of malignant transformation.

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