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# VON-RECKLINGHAUSEN DISEASE: A CASE REPORT

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**ABSTRACT**

Von-Recklinghausen disease, also known as neurofibroma type 1(NF-1), is a benign peripheral nerve sheath tumor, which is one of the most frequent tumors of neural origin.. Neurofibromatosis type-1 occurs due to an alteration in the long arm of chromosome 17 and is an autosomal dominant inherited disease. There is no family history of the disease in about 50% of the NF-I patients. NF1 occurs in approximately one in 2,500-3,300 live births, regardless of the race, age, ethnic background but with slight female predilection. NF-I is characterized by the presence of skin lesions, bone malformations, and central nervous system tumors. A series of clinical criteria decide the diagnosis of NF-I. This article reports a case of in Von-Recklinghausen disease in a 45-year-old female patient with classical features of Crowe's sign, Lisch nodules, café au lait spots along with intra-oral pyogenic granuloma and radiological changes of the mandible.

**Key words:** Neurofibromatosis, Lisch nodules, Café au lait Pigmentation, Crowe's sign.

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## INTRODUCTION

Neurofibromatosis are a group of autosomal dominant genetic disorders that primarily affect the growth of neural tissues. [1] This clinical entity was first described by German pathologist von Recklinghausen in the year 1882. It is such disorder that affects the bone, nervous system, soft-tissue, and the skin, [2] caused by a multiple point mutations that affect the gene located on the 17q11.2 chromosome, known as the NF1 gene which affect the production of tumor suppressor protein 'Neurofibromin'. [3] Only 50% of NF1 patients have a positive family history of the disease, whereas the others shows spontaneous mutations. [4] There are eight different clinical phenotypes f neurofibromatosis have been identified till date. NF1 occurs in approximately one in 2,500-3,300 live births, regardless of the race, age, ethnic background but

with slight female predilection. [2]The major subtypes are: Peripheral neurofibromatosis or neurofibromatosis type 1 (NF1). Central neurofibromatosis or neurofibromatosis type 2 (NF2), Segmental neurofibromatosis, which is limited to a single body region.

The frequency of oral manifestations in neurofibromatosis seen in approximately 37% of the total NF cases.[5] Intraorally, neurofibromas of the oral soft tissue tongue is the most common site, which is usually macroglossic. The buccal mucosa, alveolar ridge, gingiva, lips, palate, floor of the mouth, and the pharyngo-maxillary space can also be involved. [6] Enlargement of the fungiform papillae, an enlarged mandibular foramina, and intrabony lesions are the other features of neurofibromatosis. Hypoplasia of the orofacial complex including a hypoplastic maxilla and zygomatic bone, ramus of mandible , notching of the inferior border of the mandible, are other hard tissue findings seen [7,8] Intraosseous involvement of a neurofibroma in NF-1 is very uncommon. Here, the case of a neurofibroma in a 45-year-old female patient reported.

**Case Report**

A 45-year-old Female patient reported to the department of oral medicine and radiology with a complaint of growth in gum regarding Left upper backside teeth region and associated Occasional bleeding from same region, when exposed to minor trauma like toothbrushing since last 2 month. The patient revealed that the growth was small in size initially and continued to grow to attain the present size without any pain. Past medical history revealed patient is hypertensive and taking medications for that since last 4 years. Habit history was non-contributory in this case. The family history of the patient revealed presence of multiple nodules all over the body in her father.

Extraoral examination showed multiple nodules of varying size all over the body, including the head and neck and Face area, which were more concentrated specially on the back of the body. The nodules were sessile or sometimes pedunculated, soft and non-tender, suggestive of a cutaneous neurofibroma and brownish macular pigmentations were seen on the body, eight to ten in number, the largest was on the left Forearm area, which were irregular in shape, measuring about 2-3 cm in size, suggestive of café-au-lait spots. This type of pigmentation was present on the neck and back also. Auxiliary freckling was seen under the arms, suggestive of a Crowe sign. No inguinal freckling present. Pigmented lesions of the iris were seen, suggestive of Lisch nodules.

Upon Intraoral Examination, a solitary nodular pedunculated soft tissue growth was present involving attached gingiva in left upper back tooth region measuring about 1.5cm x 1.5cm cm in size. The overlying mucosa appeared to be normal with no visible pulsations. On palpation, the growth was non-tender and firm in consistency. A well-defined submerged growth palpated on dorsum of tongue area, around 1x1 cm in diameter, rounded in shape and non-tender on palpation and firm in consistency. A provisional diagnosis of Pyogenic Granuloma in relation to 26, 27 and Von-Recklinghausen disease were considered based on history and clinical examination.

Orthopantomogram (OPG) was advised that showed pressure erosion in relation to 26,27 teeth region. OPG also revealed the classic sign of deepening of sigmoid notch and bilateral widening of inferior alveolar canal.

Pre-operative hemogram was within normal limit. Serology tests were non-reactive for HIV-I & II, HBV. Excisional biopsy was done under local anesthesia (LA) which histopathologically revealed discontinuous parakeratinized stratified squamous epithelium with underlying connective tissue stroma that was fibrous and numerous endothelial cell lined capillaries with perivascular inflammatory infiltration and thick bundles of collagen fibers throughout the stroma, suggestive of pyogenic granuloma regarding 27 and 28 teeth region.

In the biopsied lesion from tongue, H/E stained section showed non-encapsulated lesion along with proliferation of neural tissue component. There was area of stromal mucin deposition along with numerous mast cells, which histopathologically confirm it as neurofibroma**.**
Considering all clinical finding, Diagnostic Criteria – Total 5 criteria were matched, Radiological and histological findings confirm the case as Von Recklinghausen's disease with pyogenic granuloma.

As patient was not interested for the cosmetic correction of the nodular growth treatment of oral prophylaxis was done and oral hygiene instructions were given along with a prescription of 0.2% chlorhexidine mouthwash and periodic check-up was advised.

**Discussion.**

Von-Recklinghausen disease is benign peripheral nerve sheath tumor, transmitted as an autosomal dominant disease, with an incidence of approximately 1:2500 to 3000 individuals with a slight predilection toward females.[1] Neurofibromatosis type 1 was first described by Frederich von Recklinghausen in 1882. Oral manifestations seen in approx. 37 % of total NF Patients .It basically affects middle aged individual with mean age of occurrence is 27.5 years.[2,3] It is shown to be related to a mutation in the pericentric proximal gene locus on chromosome 17q11.2. The pathogenesis is thought to be due to hampering the production of neurofibroma, which acts as potent tumor suppressor and by stopping activity of RAS proto-oncogenes for tumor genesis.[4]

Von-Recklinghausen disease is clinically characterized by multiple nodular growth, café-au-lait spots that are brownish irregular skin pigmentation with 1-2mm in diameter to several centimeters. Specifically 'Coast of California'- smooth edge and iris Lisch nodules that are translucent brown pigmented spots on iris. [5] The other features that can be associated with von Recklinghausen's neurofibromatosis are macrocephaly, coarctation of aorta, adrenal medullary tumor, renal artery stenosis, short stature, seizures, hypertension, deafness, constipation, kypho-scoliosis, developmental and learning disorders, cosmetic disfigurement, and neurofibrosarcomas etc. [6] In this patient, Patient was hypertensive and multiple neurofibromas, café-au-lait spots, Axillary Freckling (Crowe's sign) and Lisch nodules were present.

Cutaneous neurofibromas, which involves dermis and epidermis in neurofibromatosis type I patients, are sessile, but become pedunculated at a later stage. They are reddish to bluish, soft, and usually not painful. In later stages of NF-I, these cutaneous neurofibromas may cover all areas of the body, including the hands and soles of the feet, which was noted in our case, with a positive family history.[7]

In NF1, bone malformations such as kyphoscoliosis or pseudoarthrosis, Sphenoid dysplasia may appear, and the temporomandibular joint may also be involved. [8] Skeletal involvement is present in almost 40% of the patients with NF1, scoliosis being the most common skeletal pathology, which was not observed in our case. Intracranial nerves also can be involved in NF-I. Involvement of cranial nerves VII and IX results in decreased taste and gag reflexes. If cranial nerves V or VII are affected, the tongue can deviate to one side and the patient may experience altered sensation. [9]
Intra-oral finding generally present as multiple or solitary fibromatous macule in any area of Oral Cavity and enlargement of the fungiform papillae.

Orthopantomogram radiograph patient shows enlargement of the mandibular foramen, enlargement or branching of the mandibular canal, increased bone density , concavity of the medial surface of the ramus, increase in dimension of the coronoid notch.[10] Cephalometric analysis often shows a hypoplasia of mandible, maxilla, and cranial base. Patients with NF-1 should be reviewed regularly for early detection and appropriate management of any

disease complications, such as, optic gliomas, which may cause visual loss or field defects.

Histopathological Features of von-Recklinghausen disease includes presence of well-circumscribed spindle cell proliferation, but rarely encapsulated. There are presence of mucinous background along with numerous number of mast cells. Spindle cells generally shows a wavy appearance. As neurofibromas result from a proliferation of all supporting elements of neural fibers, so they may have Schwann cells, perineural cells, and blood vessels as well. Axons stains show the random distribution of individual axons in neurofibroma.[11]

Diagnosis of neurofibromatosis is done when two or three features are present based on the criteria described by

**National Institute of Health Consensus Development Conference in 1988. And Modified Revised Criteria (2018)**, which include: [11]

1.Six or more café-au-lait macules:

a. Diameter ≥1.5 cm in post-pubertal individuals

b. .≥0.5 cm in pre-pubertal individuals.

2. Two or more neurofibromas of any type or one plexiform neurofibroma.

3. Multiple freckles in the axillary area or groin.

4. Optic glioma.

5. Two or more Lisch nodules (hamartomas of the iris).

6. A distinct osseous lesion, such as:

- Sphenoid dysplasia.
- Thinning of the long bone cortex, with or without pseudoarthrosis.

7. A first-degree relative (parent, sibling or offspring) who meets the above criteria for NF1.

Treatment of NF-1 deals No specific therapy for this. Mainly directed toward prevention or management of complications. For Facial neurofibromas cosmetic surgery is indicated along with Carbon dioxide (CO2) laser and dermabrasion. For prominent hemi facial enlargement, cosmetic remodeling surgery is generally advised. For intra-oral involvement which causing functional difficulty requires excision of lesion. [12]

**Figure 1A: Profile view Of the Patient**
**Figure 1B: Multiple Fibromatous nodules on Backside of Patient.**
**Figure 1C: Axillary Freckling ; Crowe's sign**

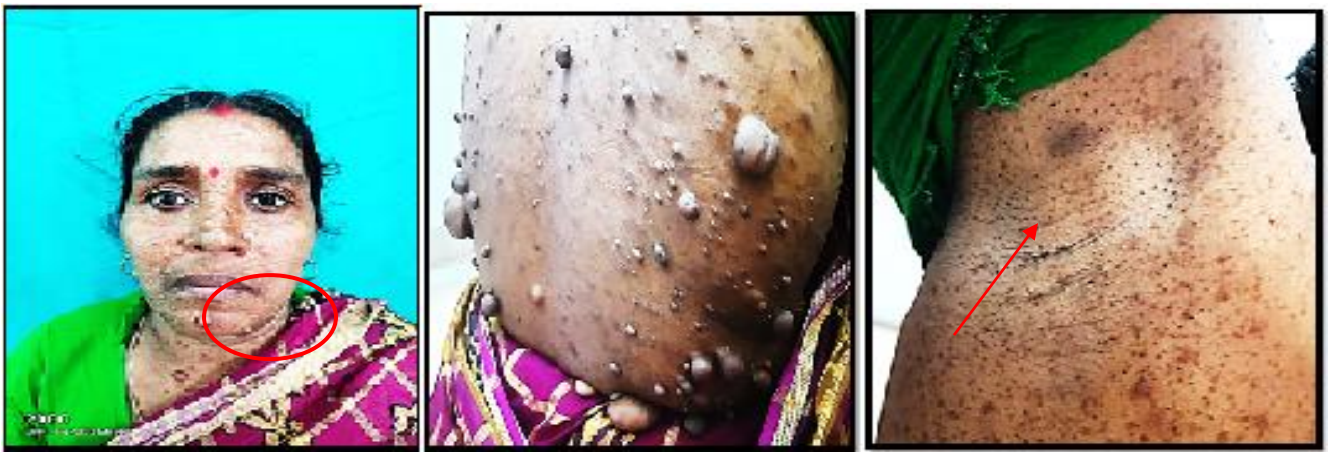


**Figure 2A: Café au lait skin Pigmentation on Forearm •**
**Figure 2B & 2C: Multiple Fibromatous nodules on Pre-pubertal area ( Forearm and Dorsal surface of Hand ) and Post-pubertal area ( Leg)**

**Figure 3A: Intra-oral view showing Pyogenic granuloma regarding 27 teeth region.**
**Figure 3B: Dorsum of the tongue**

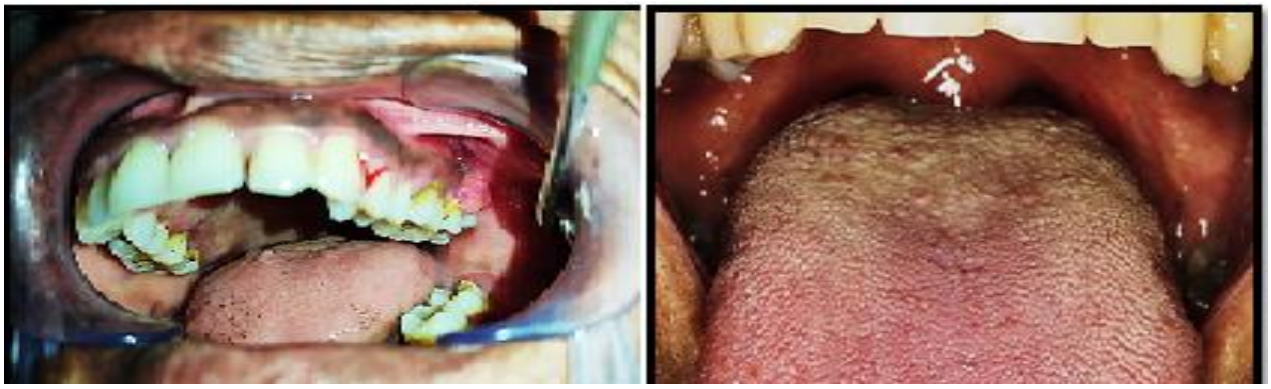
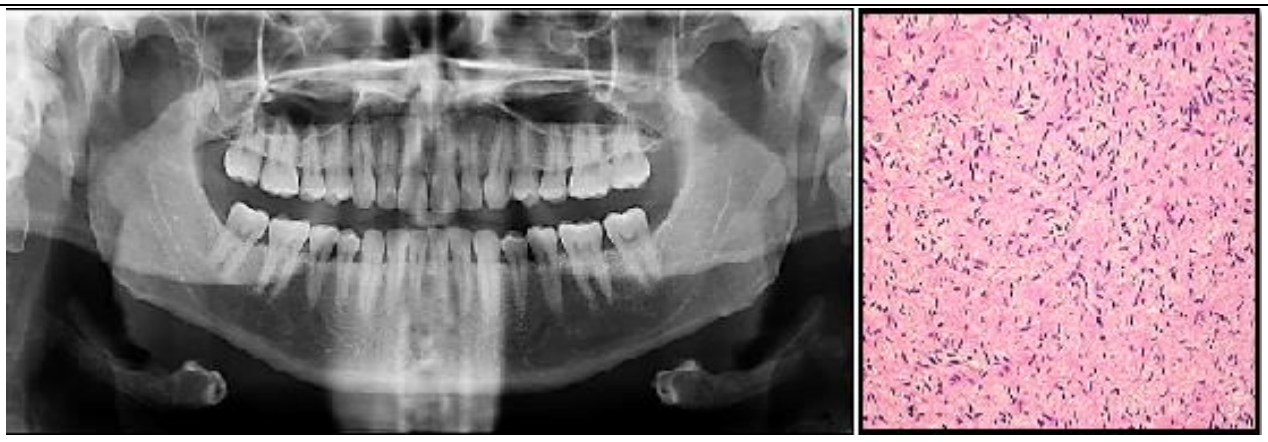


**Figure 4A: Orthopantomogram (OPG) shows pressure erosion and widening of Inferior alveolar canal, with deepened sigmoid notch.**
**Figure 4B: Histopathological view of multiple spindle cell and mucinous background along with numerous number of mast cells**



**Conclusion:**

A periodic checkup is needed to check any serious complication of neurofibromas, that may show malignant transformation, which known as malignant peripheral nerve sheath or neurofibrosarcomas. Hence, rapid growth or pain associated with the lesions must be biopsied immediately, to rule out a possible malignant transformation. Oral physicians must be aware of the characteristics of this disease and multidisciplinary monitoring is necessary for assessing the neurological complications or sarcomatous evolution at the earliest possible stage.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate consent forms from patient. In the form the patient(s) has given his consent for images and other clinical information to be reported in the journal. The patient had understood that his personal information will not be published regardingly.

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**Conflicts of interest**
There are no conflicts of interest.

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