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RECURRENT MIDFACIAL PLEXIFORM NEUROFIBROMA ASSOCIATED WITH NEUROFIBROMATOSIS TYPE 1: A CASE REPORT

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Abstract

Plexiform neurofibroma (PNF) is a rare benign peripheral nerve sheath tumor and a pathognomonic manifestation of Neurofibromatosis Type 1 (NF1). These tumors are characterized by diffuse infiltrative growth involving multiple nerve fascicles and are associated with significant cosmetic deformity, functional impairment, recurrence, and risk of malignant transformation. Craniofacial involvement poses considerable diagnostic and surgical challenges because of extensive soft tissue infiltration and proximity to vital anatomical structures. A review of head and neck neurofibromas reported that approximately 25% of all neurofibromas are seen in the head and neck region and 6.5% occur in the oral cavity as solitary or multiple lesions associated with NF-1. 1 This report presents a 29-year-old male with a 17-year history of progressively enlarging recurrent midfacial swelling associated with NF1. The patient had previously undergone two surgical debulking procedures, both followed by rapid recurrence. Clinical examination revealed a large lobulated left midfacial mass with classical “bag of worms” consistency, axillary freckling and an intraoral palatal swelling. MRI and ultrasonography demonstrated diffuse infiltrative soft tissue involvement with associated vascular-lymphatic malformation. Histopathological examination showed thickened nerve bundles composed of Schwann cells with wavy hyperchromatic nuclei embedded within a myxoid stroma, confirming the diagnosis of plexiform neurofibroma. This case highlights the aggressive recurrent nature of craniofacial PNF and emphasizes the importance of clinicoradiological and histopathological correlation for accurate diagnosis and long-term management.

Keywords- Plexiform neurofibroma, Neurofibromatosis Type 1, Crowe sign, 3T MR, Axillary freckling

Introduction

Neurofibromatosis Type 1 (NF1), also known as Von Recklinghausen's disease, is an autosomal dominant neurocutaneous disorder with an estimated incidence of approximately 1 in 2,500–3,000 live births. The disorder results from mutation of the NF1 tumor suppressor gene located on chromosome 17q11.2, which encodes the protein neurofibromin. Loss of neurofibromin activity leads to dysregulation of the RAS/MAPK signaling pathway and uncontrolled proliferation of neural tissue.

Neurofibromas are benign peripheral nerve sheath tumors arising from Schwann cells, perineural cells, fibroblasts and axons within a myxoid extracellular matrix. They are classified into localized, diffuse, and plexiform variants. Among these, plexiform neurofibroma (PNF) is considered pathognomonic for NF1 and occurs in approximately 25–50% of affected individuals. Clinically, PNFs are characterized by diffuse infiltrative growth involving multiple nerve fascicles, producing a characteristic "bag of worms" consistency on palpation. The head and neck region are frequently affected because of extensive neural innervation, although oral involvement remains relatively uncommon. A review of head and neck neurofibromas reported that approximately 25% of all neurofibromas are seen in the head and neck region and 6.5% occur in the oral cavity as solitary or multiple lesions associated with NF-1. Intraoral lesions most commonly involve the tongue and buccal mucosa, followed by the palate and floor of the mouth. Craniofacial PNFs may produce severe facial asymmetry, cosmetic disfigurement, speech difficulty, mastication problems and psychological distress. Surgical management is often challenging because of the infiltrative nature, vascularity, and tendency for recurrence. Additionally, PNFs possess an estimated 8–13% risk of malignant transformation into malignant peripheral nerve sheath tumors (MPNST).

This report describes a recurrent midfacial plexiform neurofibroma associated with NF1 in a 29-year-old male with extensive craniofacial and intraoral involvement.

Case Report

A 29-year-old male presented to the Government Dental College and Hospital (GDCH), Ahmedabad, with a chief complaint of disfiguring swelling on the left side of the face for 17 years. The patient reported gradual progressive enlargement of the swelling over time. He had previously undergone two surgical procedures, one in 2014 and a subsequent debulking surgery at Civil Hospital, Ahmedabad; however, both interventions were followed by rapid recurrence.

Clinical Examination

Extraoral examination revealed a large lobulated baggy mass measuring approximately 7 × 6 cm involving the left midfacial region. The lesion extended from the infraorbital region to the upper lip, resulting in significant facial asymmetry and sagging skin folds.

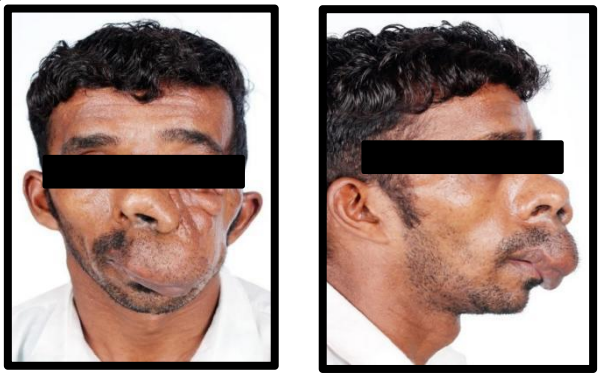

Figure 1: A large lobulated baggy mass involving the left midface.

On palpation, the lesion exhibited the classical "bag of worms" consistency characteristic of plexiform neurofibroma.

Dermatological examination revealed multiple small freckles within the skin folds of both axillae, suggestive of axillary freckling (Crowe sign). In addition, a small soft dome-shaped skin-colored subcutaneous nodule was observed in the arm region.

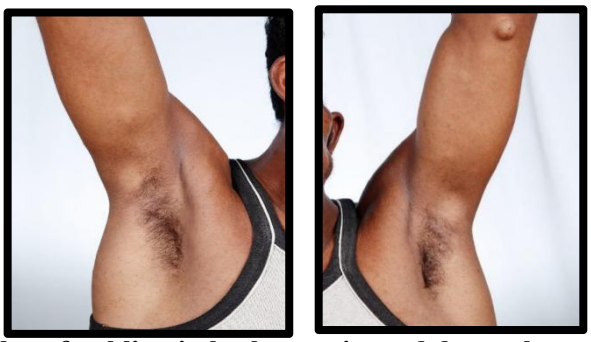

Figure 2: Axillary freckling in both armpits and dome-shaped nodule on left arm.

Intraoral examination demonstrated a diffuse firm non-tender swelling measuring approximately 4 × 1.2 cm involving the left side of the hard palate.

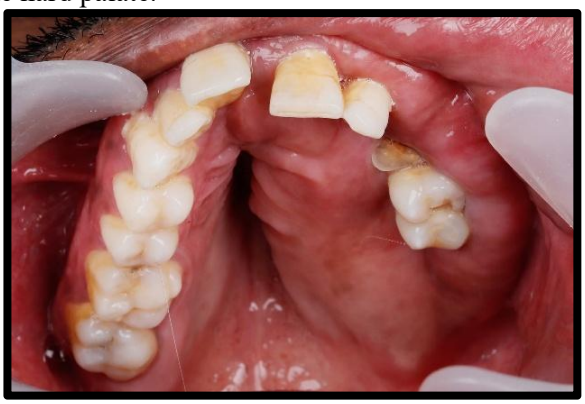

Figure 3: Diffuse swelling involving the left hard palate.

Based on the clinical findings, differential diagnoses considered included plexiform neurofibroma, vascular malformation, lymphangioma, hemangiomas, schwannoma, and malignant peripheral nerve sheath tumor.

Radiological Findings

The patient underwent magnetic resonance imaging (MRI) and ultrasonographic (USG) evaluation.

Advanced multiplanar MRI sequences of the neck demonstrated a diffuse lobulated area of altered signal intensity involving the skin and subcutaneous plane of the left side of the face. The lesion involved both eyelids, the left premolar space, the left side of the dorsum of the nose, upper and lower lips on the left side, philtrum, angle of the mouth, and left zygomatic region with associated skin thickening. The lesion appeared hypointense on T1-weighted images and heterogeneously hyperintense on T2-weighted and STIR sequences, showing mild post-contrast enhancement. Multiple serpiginous tubular structures were identified within the subcutaneous plane of the scalp, temporal and infratemporal fossa on the left side, left masseter and pterygoid muscles, parapharyngeal space, and left orbit. These structures showed no post-contrast enhancement, suggestive of an associated vascular-lymphatic malformation.

The larynx, pharynx, thyroid lobes, and major neck vessels appeared normal. No abnormal lymphadenopathy or spinal malalignment was noted. Ultrasonographic examination of the neck revealed a large ill-defined heterogeneously hypoechoic lesion involving the left side of the face with minimal internal vascularity. Color Doppler and waveform analysis demonstrated high diastolic flow.

Histopathological Findings

Based on the clinical and radiological findings, a provisional diagnosis of plexiform neurofibroma was made, and an incisional biopsy was performed from the left lower two-thirds of the face.

Gross examination revealed a single brownish soft tissue specimen measuring approximately 3.7 × 3 × 2.3 cm with soft-to-firm consistency and an irregular external surface.

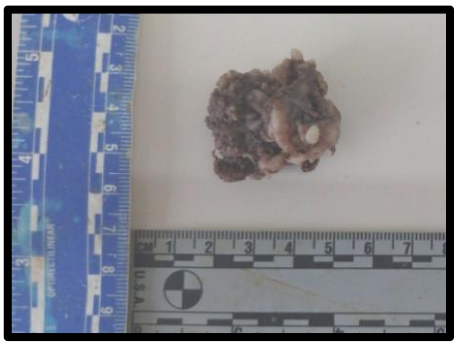

Figure 4: Gross specimen showing a single soft tissue specimen received for histopathological examination.

Microscopic examination revealed a tumor mass characterized by proliferation of abundant thickened nerve bundles sectioned in various planes. These nerve bundles were surrounded by a distinct perineural layer within a dense collagenous fibrous stroma.

At higher magnification, the lesion demonstrated intersecting fascicles of Schwann cells with wavy hyperchromatic nuclei embedded within a loose myxoid stroma. The surrounding connective tissue stroma also showed skeletal muscle fibers, adipose tissue, and multiple dilated engorged blood vessels.

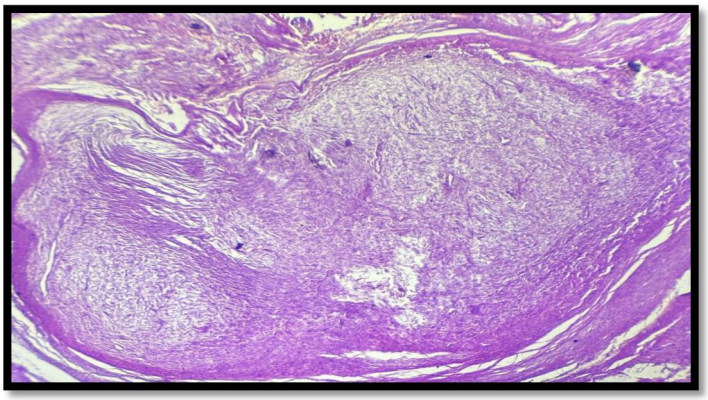

Figure 5A: H&E-stained section showing thickened nerve bundles sectioned in various planes within dense collagenous stroma.

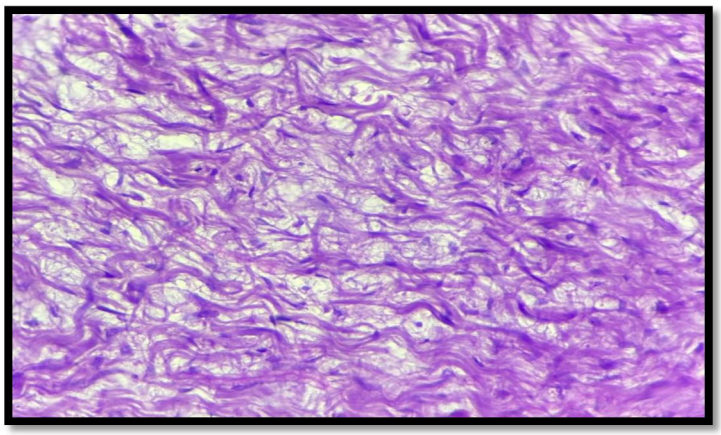

Figure 5B: H&E-stained section showing intersecting fascicles of Schwann cells with wavy hyperchromatic nuclei within loose myxoid stroma.

The histopathological findings confirmed the diagnosis of plexiform neurofibroma associated with Neurofibromatosis Type 1.

Discussion

Plexiform neurofibroma is a rare benign peripheral nerve sheath tumor characterized by diffuse proliferation of neural tissue involving multiple nerve fascicles in a tortuous infiltrative pattern. According to the World Health Organization classification, neurofibroma consists of Schwann cells, fibroblasts, perineurial-like cells,

mast cells, and residual axons embedded within a myxoid collagenous matrix.4 Al-Ali et al. described PNF as a diffuse elongated lesion with a plexiform arrangement involving multiple nerve bundles.7

PNF is strongly associated with Neurofibromatosis Type 1, an autosomal dominant disorder caused by mutation of the NF1 gene on chromosome 17q11.2.1,3 Anand et al. reported that NF1 accounts for approximately 90% of neurofibromatosis cases11 and affects nearly 1 in 3000 individuals.2 The present case demonstrated characteristic clinical manifestations of NF1, including axillary freckling and subcutaneous neurofibroma-like nodules, supporting the diagnosis of syndromic plexiform neurofibroma.

Clinically, PNFs are slow-growing painless lesions; however, progressive enlargement may result in severe cosmetic deformity and functional impairment6,8. Similar to the findings reported by Tchernev et al. and Bang et al., the present patient demonstrated extensive unilateral craniofacial involvement with marked facial asymmetry and sagging soft tissue folds.6,8 The characteristic “bag of worms” consistency observed on palpation is attributed to proliferation and intertwining of enlarged nerve fascicles.

Head and neck involvement is common in PNF because of rich neural innervation in this region. Anand et al. noted that cranial and upper cervical nerves, particularly the trigeminal, glossopharyngeal, and vagus nerves, are frequently involved. In the present case, MRI demonstrated extensive infiltration involving the facial soft tissues, eyelids, infratemporal fossa, orbit, parapharyngeal space, and masticatory muscles, emphasizing the aggressive infiltrative nature of the lesion.6

Radiological evaluation is essential for determining lesion extent and surgical planning. MRI is considered the imaging modality of choice because it accurately delineates soft tissue infiltration and neurovascular involvement. Grover et al. described the characteristic “target sign” on MRI and ultrasonography, representing central nerve fibers surrounded by peripheral myxoid tissue. In the present case, MRI demonstrated hypointense T1-weighted and heterogeneously hyperintense T2-weighted and STIR signals with mild post-contrast enhancement. Multiple serpiginous tubular structures without contrast enhancement suggested an associated vascular-lymphatic malformation. Ultrasonography further revealed an ill-defined heterogeneously hypoechoic lesion with minimal vascularity and high diastolic Doppler flow.8

Histopathological examination remains the gold standard for definitive diagnosis. The present case showed abundant thickened nerve bundles arranged in multiple planes within a collagenous fibrous stroma. Higher magnification demonstrated intersecting fascicles of Schwann cells with wavy hyperchromatic nuclei embedded within loose myxoid stroma, findings consistent with plexiform neurofibroma. Similar microscopic findings have been reported by Begum et al. and Al-Ali et al., who described multinodular neural proliferation with Schwann cells arranged in a haphazard plexiform pattern.2,4

One of the most significant clinical concerns associated with PNF is recurrence and malignant transformation into malignant peripheral nerve sheath tumor (MPNST). Tchernev et al. reported malignant transformation rates ranging from 2% to 16%5, whereas Bakshi reported an estimated 8–12% risk.3 Rapid enlargement, pain, ulceration, neurological deficits, or hardening of the lesion may suggest malignant transformation and require immediate evaluation. The present case is particularly significant because of repeated recurrence following surgical intervention. Surgical excision remains the treatment of choice for symptomatic and disfiguring lesions; however, complete excision is often difficult because of diffuse infiltration into adjacent tissues and close proximity to vital structures. Incomplete excision contributes significantly to recurrence. Begum et al. emphasized recurrence as a major challenge in management of oral and craniofacial PNFs.4 Long-term follow-up is therefore mandatory in such patients.

Recently, targeted molecular therapies such as selumetinib have demonstrated promising outcomes in symptomatic unresectable PNFs. Aneja et al. highlighted the growing importance of targeted therapy in managing extensive disfiguring lesions associated with NF1.7

Conclusion

Plexiform neurofibroma is a rare but clinically significant peripheral nerve sheath tumor associated with substantial cosmetic, functional and psychological morbidity. Craniofacial lesions demonstrate aggressive infiltrative behavior and a high tendency for recurrence following surgical intervention. The present case highlights the importance of detailed clinicoradiological and histopathological evaluation for accurate diagnosis of recurrent craniofacial plexiform neurofibroma associated with NF1. Long-term follow-up is essential because of the risk of recurrence and malignant transformation. Surgical excision remains the cornerstone of treatment, although management remains challenging because of diffuse tissue infiltration and proximity to vital anatomical structures.

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