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Sleep-disordered breathing due to parapharyngeal space plexiform neurofibroma in neurofibromatosis-1: a case report and literature review

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Abstract

Background Neurofibromatosis type 1 is an autosomal dominant disorder with an incidence of 1 in 3000 births. Neurofibromas can occur anywhere in the body. Of all the head and neck tumours parapharyngeal space tumours constitute 0.5%. Neurofibromas can constitute about 9% of all the neurogenic tumours (41%) of the parapharyngeal space. Prevalence of nasal obstruction and obstructive sleep-disordered breathing symptoms due to Plexiform neurofibroma in Neurofibromatosis type 1 is rare amounting to less than 0.5% of cases of parapharyngeal space tumours.

Case presentation

We present a case report of a 24-year-old female patient of Neurofibromatosis type 1 who presented with obstructive sleep-disordered breathing symptoms due to Plexiform neurofibroma in the parapharyngeal space. She had complaints of progressive nasal obstruction with associated snoring, disturbed sleep, and daytime somnolence without any significantly large external neck swelling. She underwent excision of the right parapharyngeal tumor by combined trans parotid and transcervical approach. After histopathological examination, a diagnosis of Plexiform neurofibroma was made. On 1-year follow-up, she is doing well without any recurrence and her presenting symptoms of obstructive sleep-disordered breathing symptoms had improved.

Conclusion The symptoms of obstructive sleep-disordered breathing symptoms need to be kept in mind while evaluating such patients and careful attention needs to be given to the patients who report disturbed sleep. Neurofibromatosis type 1 is a multi-system disease which needs holistic care and approach. Such patients should be offered symptomatic treatment and leading questions on the quality of sleep should be asked. Any treatable cause of disturbed sleep like organic sleep disorder should be treated promptly in such patients.

Keywords Case report, Neurofibroma, Plexiform, Neurofibromatosis 1, Parapharyngeal space, Sleep-disordered breathing, Sleep apnoea, Obstructive, Nasal obstruction

Background

Neurofibromatosis type 1 (NF1) is a multi-system autosomal dominant disorder with an incidence of 1 in 3000 births. It predominantly affects the skin and the nervous system. Other organs affected by NF1 are the eyes, bones, mediastinum, gastrointestinal tract etc. [1]. Neurofibromas can occur anywhere in the body. Parapharyngeal space tumours (PPT) account for 0.5%

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of all head and neck tumours. Neurofibromas can constitute about 9% of all the neurogenic tumours (41%) of the parapharyngeal space [2, 3]. Plexiform neurofibroma (PN) is a benign tumor which arises from nerve sheath. Plexiform neurofibromas are usually seen in NF1; however, solitary lesions are also encountered in clinical practice [4]. PN in NF1 causing nasal obstruction and obstructive sleep-disordered breathing symptoms (SDB) symptoms are rare amounting to less than 0.5% of cases of PPT [5]. Here we present a case report of a 24-year-old female patient of NF1 who presented with SDB symptoms due to plexiform neurofibroma in parapharyngeal space (PPS).

Case presentation

A 24-year-old female patient presented with complaints of nose block predominantly on the right side for 2 years. It was of insidious onset and gradually progressive. It was associated with hyponasal voice. She also had a history of snoring at night time with disturbed sleep and daytime somnolence. The patient had a history of multiple small swellings on the skin all over the body for 9 years. These swellings were painless and gradually increased in size. The swellings were otherwise unremarkable. She also had tingling and numbness sensations all over the body for 6 years. She did not complain of any significantly large external neck swelling.

There was no history of any other associated symptoms like nasal discharge, dysphagia, breathing difficulty or nasal regurgitation and aspiration. The patient did not have disturbances in vision, smell, taste, facial weakness, or reduced hearing. There was similar positive history in the patient's father, two brothers and one sister. The rest of the history was unremarkable.

On examination, she had stable vitals. There were multiple café au lait macules all over the body (around 15) largest measuring around 1–2 cm. There were multiple palpable small swellings on the skin all over the body which were around 1–2 cm each, non-tender, mobile and without any external skin changes. There was freckling over the axilla. There were multiple plexiform neurofibromas on the trunk. Examination of the nose revealed bilateral inferior turbinate hypertrophy. Diagnostic nasal endoscopy revealed a smooth mucosa-covered bulge on the right side of the nasopharynx completely obscuring the choana on the right side. Oral cavity examination was unremarkable. Oropharynx revealed a bulge of size 5 × 3 cm on the right side of the soft palate pushing the uvula to the opposite side. There was no palatal movement on the right side. There was a minimal bulge of the right lateral wall of the oropharynx. Indirect laryngoscopy revealed mobile bilateral vocal cords. Examination of the neck revealed freckling of skin and multiple small swellings on both sides of the neck in level II, III, and IV regions similar to the swellings described above. There was no large external swelling palpable on the right side. Otological, ophthalmic, orthopedic, and neurological examinations were within normal limits (Fig. 1).

Blood investigations including complete blood counts, kidney and liver function tests, and viral markers were unremarkable. She underwent a contrast-enhanced computed tomography (CECT) scan of the neck which revealed a 6 × 3 cm well-defined hypodense ovoid lesion in the right parapharyngeal space which was extending

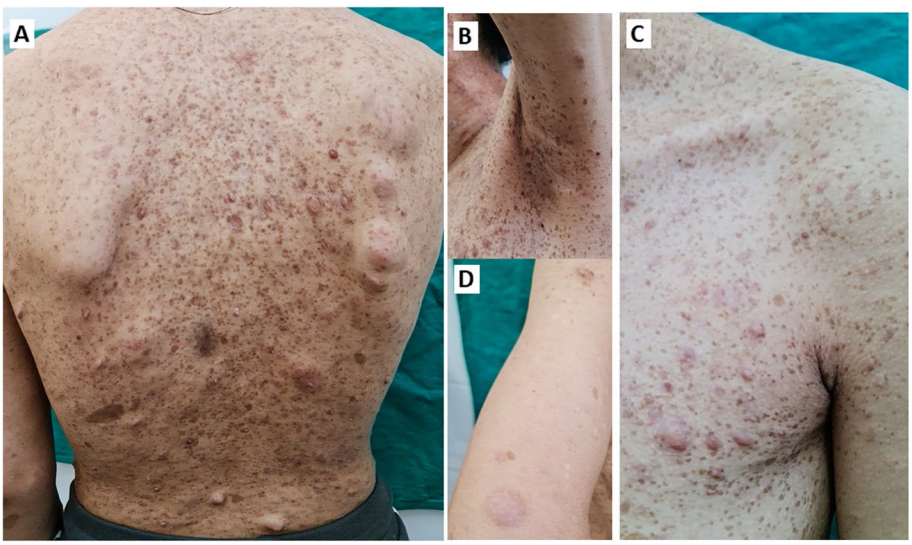

Fig. 1 **A** Demonstrates patient's dorsal surface with multiple café au lait macules and multiple neurofibromas. **B**, **C** shows axillary freckling. **D** demonstrates café au lait macules over right upper limb

superiorly to the skull base and inferiorly till level of C2 cervical vertebra. The mass was causing luminal obstruction of the nasopharynx and oropharynx. There was no intracranial extension of the tumor. The carotids and the internal jugular vein were distinct from the lesion. There was some contrast uptake by the tumor. Few enlarged lymph nodes were noted in bilateral level II cervical stations measuring up to 8 mm.

Given the above findings, she underwent a contrast-enhanced magnetic resonance imaging (CE MRI) scan of the brain, neck and whole spine which revealed a lobulated mass of size 5.8 × 4.8 × 4.6 cm in the right PPS. It revealed homogenous intermediate T2/FLAIR hyperintensities and isointense in T1-weighted sequence. There was marked heterogenous enhancement in the post contrast study. The origin of the mass in the PPS could not be made out. There were multiple enhancing ovoid paraspinal lesions along the exiting nerve roots and intercostal nerves with similar signal intensities throughout the spine. The largest mass was 4.8 × 3.3 cm seen at T5/T6 level with a hypointense central region. There were multiple enhancing intraspinal extramedullary masses showing similar intensities, the largest measuring 1 × 0.7 cm in the cervical spine indenting onto the cord at C2 level. Multiple small similar lesions were noted along the cauda equina nerve roots. Multiple subcutaneous nodules were noted in neck and chest walls measuring around 1-2 cm each. These swellings were suggestive of neurofibromas (Fig. 2).

X-ray evaluation of the limbs did not reveal any significant abnormality. Evaluation by the Neurosurgery team was done and she was planned for conservative management, i.e., to repeat CEMRI of the spine after 6 months as her gross sensory and motor functions were within normal limits. A diagnosis of NF1 with right parapharyngeal neurofibroma causing SDB was made in our patient. She underwent surgical excision of the right parapharyngeal tumor by combined transparotid and transcervical approach under general anesthesia.

The incision was given from the tragus and extended into the neck in a curvilinear fashion. The right PPS was entered and a cystic tumor of approximate size 6 × 5 cm was delivered intoto from the PPS after blunt dissection. The carotid artery and the internal jugular vein were both distinct from the tumor. The origin of the tumor could not be made out intraoperatively. The patient's postoperative period was uneventful without any cranial nerve deficits. Following the surgery, the patient's presenting symptoms of nasal obstruction and snoring improved significantly. The histopathological analysis of the tumor revealed a well-circumscribed grey-white smooth glistening surface with soft to cystic consistency. On the cut section, it revealed yellowish to grey white homogenous areas. After histopathological examination, a diagnosis of plexiform neurofibroma was made. The margins of the tumor were free and there was no evidence of malignancy. On 1-year follow-up, she is doing well without any recurrence and her presenting symptoms of SDB had improved (Fig. 3).

Discussion

Neurofibroma in parapharyngeal space

Neurofibromas are benign tumours with many cell types, i.e., Schwann cells, perineural cells and fibroblasts. NF1 is a genetic disease with both skin and other system manifestations. It can occur in three forms: localized, diffuse, and plexiform neurofibromas [6]. The National Institute of Health (NIH) has suggested that a minimum of 2 out of 7 diagnostic criteria must be met for diagnosis of NF1. Our patient had 4/7 criteria i.e., ≥ 6 café-au-lait spots, greater than 15 mm, ≥ 2 neurofibromas or ≥ 1 plexiform neurofibromas, freckling in axilla or groin, I degree relative with NF1 establishing the diagnosis of NF1 [1].

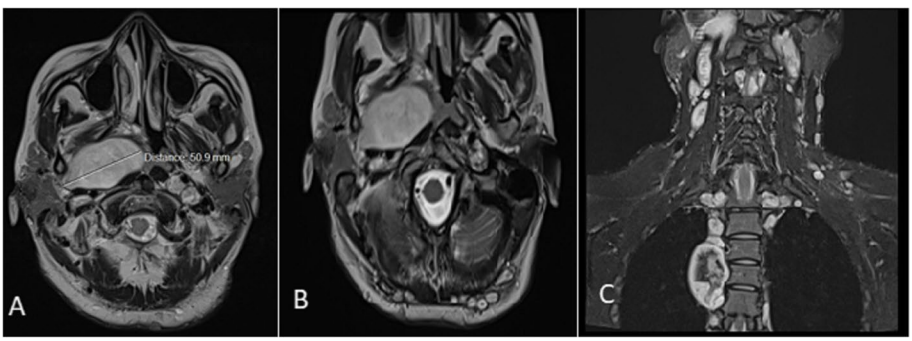

Fig. 2 **A** is T2 weighted and [B] is T1 weighted CE-MRI of neck in axial cut showing tumor of 5 × 4.8 × 4.6 cm in right parapharyngeal space causing narrowing of nasopharynx and oropharynx. **C** is a T1-weighted CE-MRI of neck and cervical spine in coronal cut showing multiple enhancing ovoid/rounded paraspinal SOLs seen throughout the spine. Also showing multiple subcutaneous nodules in neck and chest walls. All these are suggestive of neurofibromas

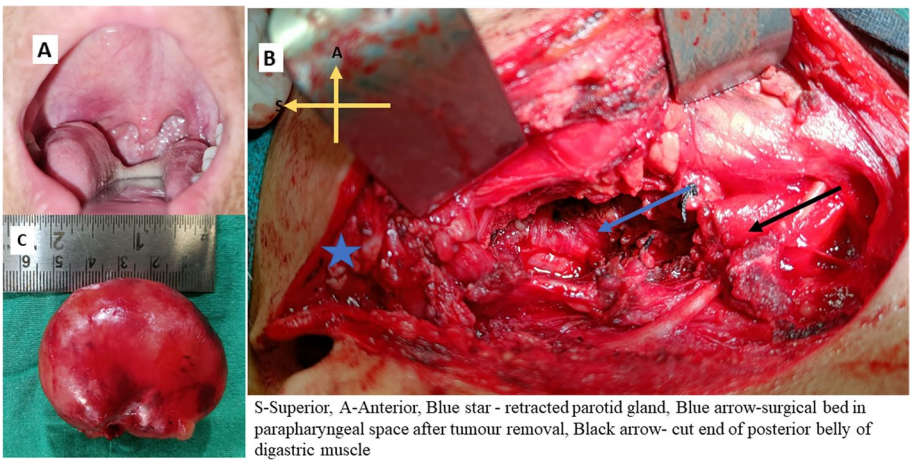

Fig. 3 **A** shows smooth bulge in right side soft palate pushing uvula to opposite side. **B** shows intraoperative picture. S—superior, A—anterior, blue star mark—retracted parotid gland, blue arrow—surgical bed in parapharyngeal space after tumor removal, black arrow—cut end of posterior belly of digastric muscle. **C** shows tumor mass removed in toto

PNs are benign neurofibromas which arise from the nerve sheath of muscle nerve fascicles with the potential to infiltrate the surrounding structures. They are seen in 25–50% of people with NF1 and can undergo malignant transformation in 8–13% of cases [1].

SDB in our case

Parapharyngeal space tumours are known for their non-specific presentation. They usually present with external or intraoral swelling (49%), otalgia (26%), dysphagia (15%), pain (10%), dysphonia (9%), and foreign body sensation (5%). The incidence of PPTs presenting with nasal obstruction and SDB symptoms is rare ranging from 0 to 5% of PPTs with one systematic review giving an incidence of 0.29% [5, 7–9]. SDB is a broader term and is defined as obstructive sleep apnea (OSA) in a patient in whom the objective measures such as polysomnography is not done [10].

Our patient, a young adult, visited a physician for her complaints of SDB. Her presenting complaints were progressive nasal obstruction with associated snoring at night time, disturbed sleep and daytime somnolence. She obtained a score of 3 in STOP BANG questionnaire which was administered preoperatively. A score of 3 or more is indicative of OSA [11]. In a few case series from India, SDB or OSA was neither a presenting symptom nor an associated symptom demonstrating the rarity or possibly underreporting of the symptom [3, 7]. Hence the symptoms of SDB need to be kept in mind while evaluating such patients and careful attention needs to be given to the patients who report disturbed sleep.

Evaluation and origin of the tumor

Fine needle aspiration cytology (FNAC) was not done in our case as we were suspecting neurofibroma and there was no gross external swelling but only oropharyngeal swelling. FNAC has the risk of hemorrhage or being non-diagnostic in the evaluation of PPT [12]. The surgical approach for PPT is decided based on the location, size and extent of the tumor. Intraoperatively the origin of the tumor could not be identified. However, the tumor was removed into without any significant cranial nerve deficits. In a case series by Bulut OC et al., the origin of the neurogenic tumor in parapharyngeal space was from vagus, glossopharyngeal, hypoglossal, and facial nerves. In 2 out of 48 patients (4%) the origin of the tumour in neurogenic cases could not be identified [13]. In our case, after histopathological examination, the diagnosis of plexiform neurofibroma was made. This can explain the reason for the above as the tumour may have originated from nerves of the muscle fascicles thereby making it difficult to locate the origin of the nerve [1].

Therapy

Surgical excision is the mainstay of treatment for PPT [12]. Treatment in our case was divided into two segments. The first was on the presenting symptom and the second was on the syndrome. Surgery was done in our case considering the patient's presenting symptoms and the risk of malignancy. The second part of the treatment was holistic care for the patient. She received neurology, neurosurgery, dermatology, ophthalmology, orthopedic consultations, and counseling with a complete evaluation. The patient was counseled about her condition and that the risk of NF1 in her offspring was 50% in each pregnancy owing to the autosomal dominant disease trait. Genetic testing was not done in our case as the diagnosis was made based on clinical features. It should be considered in the following: Patients who do

not satisfy the NIH criteria but are suspected to be having NF1, young patients with tumors in critical sites and suspicious of NF1 to decide on further treatment, Prenatal or preimplantation genetic testing in pregnancy and high-risk individuals in families with spinal NF1 [14, 15].

In an ideal setting of adequate resources, educated and affluent patients the option of prenatal diagnosis by fetal DNA sequencing using chorionic villi sampling or amniocentesis should be offered in high-risk individuals [16].

NF1 can be associated with many tumours of the nervous and non-nervous systems. The currently recommended therapy for tumors associated with NF1 is surgical resection depending on the type and location of the tumor. Novel drugs targeting the signaling pathways like Sunitinib, Sorafenib, Imatinib and Selumetinib have been studied in clinical trials in PN in NF1 with promising results [6].

Conclusion

NF1 is a multi-system disease which needs holistic care and approach. The article highlights the importance of a rare symptom in neurofibromatosis type 1 (NF1). Patients of NF1 should be offered symptomatic treatment and leading questions on the quality of sleep should be asked. Any treatable cause of disturbed sleep like organic sleep disorder should be treated promptly in such patients. To conclude, the decision for surgical excision of plexiform neurofibroma in parapharyngeal space should be based on the patient's symptoms and the approach should be based on the location and extent of the tumor. The aim of the surgery will be complete excision of the tumour with the least morbidity.

Abbreviations

NF1	Neurofibromatosis type 1
PPT	Parapharyngeal space tumours
PN	Plexiform neurofibroma
SDB	Sleep-disordered breathing
OSA	Obstructive Sleep Apnoea
PPS	Parapharyngeal space
CECT	Contrast enhanced computed tomography
CE MRI	Contrast enhanced magnetic resonance imaging
NIH	National Institute of Health
FNAC	Fine needle aspiration cytology

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Authors' contributions

MCB collected clinical materials, drafted the article after literature search. AB helped in drafting the article and proof read the article. AD helped with collection of clinical materials and patient follow up. BN helped in article drafting and proof reading the article. PP helped with the radiological images and helped in article drafting. All the authors have read and agreed to the contents.

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Availability of data and materials

This is a case report and all the data pertaining to the case report have been included in this published article without revealing the identity of the patient.

Declarations

Ethics approval and consent to participate

This is a case report and it does not require approval from the Institute Ethics Committee, NEIGRIHMS, Shillong. Written Informed Consent was obtained prior to publication of the case report from the patient.

Consent for publication

Written informed consent for publication of the patient's clinical details and clinical images was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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References

1. Le C, Bedocs PM. Neurofibromatosis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2021. Cited 2021 Dec 31. Available from: http://www.ncbi.nlm.nih.gov/books/NBK459329/. Accessed 20 Dec 2022
2. Watkinson JC, Clarke RW (eds) (2018) Scott-Brown's otorhinolaryngology and head and neck surgery. CRC Press, Boca Raton
3. Bharathi MB, Rakesh BS, Rudrappa BA, Aggarwal N (2021) Neurogenic tumors of parapharyngeal space–clinical evaluation and management: Our experience. J Head Neck Phys Surg 9(1):28
4. Ahmedou AB, Mohamed Amine M, Youssef O, Sami R, Abada R, Mohamed R et al (2021) A rare cause of cervical swelling: Solitary plexiform neurofibroma. Ann Med Surg 64:102225
5. Kuet M-L, Kasbekar AV, Masterson L, Jani P (2015) Management of tumors arising from the parapharyngeal space: a systematic review of 1,293 cases reported over 25 years: Parapharyngeal Space Tumors. Laryngoscope 125(6):1372–81
6. Foiadelli T, Naso M, Licari A, Orsini A, Magistrali M, Trabatti C et al (2020) Advanced pharmacological therapies for neurofibromatosis type 1-related tumors. Acta Bio Medica Atenei Parm 91(7-s):101–14. https://doi.org/10.23750/abm.v91i7-S.9961
7. Joshi P, Joshi KD, Nair S, Bhati M, Nair D, Bal M et al (2021) Surgical management of parapharyngeal tumors: our experience. South Asian J Cancer 10(3):167–71
8. van Hees T, van Weert S, Witte B, René Leemans C (2018) Tumors of the parapharyngeal space: the VU University Medical Center experience over a 20-year period. Eur Arch Otorhinolaryngol 275(4):967–72
9. Gopinath M, Ramachandran V, Jose R (2011) Cervical sympathetic neurofibroma masquerading as obstructive sleep apnea syndrome. Int J Phonosurgery Laryngol 1(2):84–7
10. Memon J, Manganaro SN. Obstructive sleep-disordered breathing. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. Cited 2023 May 29. Available from: http://www.ncbi.nlm.nih.gov/books/NBK441909/. Accessed 29 May 2023
11. Foroughi M, Razavi H, Malekmohammad M, Adimi Naghan P, Jamaati H (2016) Diagnosis of obstructive sleep apnea syndrome in adults: a brief review of existing data for practice in Iran. Tanaffos 15(2):70–4
12. Strohl MP, El-Sayed IH (2019) Contemporary management of parapharyngeal tumors. Curr Oncol Rep 21(11):103
13. Bulut OC, Giger R, Alwagdani A, Aldabal N, Stenzinger A, Heimgartner S et al (2021) Primary neoplasms of the parapharyngeal space: diagnostic and therapeutic pearls and pitfalls. Eur Arch Otorhinolaryngol 278(12):4933–41
14. Khajavi M, Khoshsirat S, Ahangarnazari L, Majdinasab N (2018) A brief report of plexiform neurofibroma. Curr Probl Cancer 42(2):256–60

15. Legius E, Messiaen L, Wolkenstein P, Pancza P, Avery RA, Berman Y et al (2021) Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. Genet Med 23(8):1506–13
16. Stewart DR, Korf BR, Nathanson KL, Stevenson DA, Yohay K (2018) Care of adults with neurofibromatosis type 1: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med 20(7):671–82

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