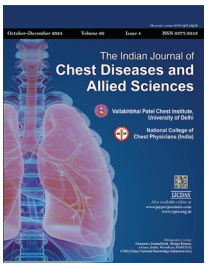
CASE REPORT

A Hidden Rarity: Incidental Posterior Mediastinal Neurofibroma with Middle Mediastinal and Lung Parenchymal Extension in a 20-year-old Male with Neurofibromatosis Type 1



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Basil Paul[1], Pratap Upadhya[2], Zeenathalam Nadaf[3], Rajesh N Ganesh[4]

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Abstract

Neurofibromatosis type 1 (NF1) is a rare genetic disorder characterized by multiple benign tumors of the nerves and skin, known as neurofibromas. Mediastinal involvement in NF1, particularly with anatomical extension to both posterior and middle mediastinum along with extension into lung parenchyma, is an uncommon occurrence. Here, we present the case of a 20-year-old male with a known history of NF1 who was incidentally found to have a mediastinal mass during a pre-surgical fitness evaluation. Histopathological analysis confirmed the mass to be a neurofibroma. This case highlights the importance of considering neurofibromas in the differential diagnoses of mediastinal masses in patients with NF1, even when they are asymptomatic. The potential risk for malignant transformation into a malignant peripheral nerve sheath tumor (MPNST) warranted surgical intervention and hence the patient was referred to a thoracic surgeon.

Keywords: Asymptomatic mediastinal mass, Case report, Lung parenchymal involvement, Mediastinal neurofibroma, Multidisciplinary management, Neurofibromatosis type 1, Plexiform neurofibroma, Rare presentation, Thoracic neurofibroma.

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Abbreviations used in this Article

CECT = Contrast-enhanced computed tomography; CT = Computed tomography; MPNSTs = Malignant peripheral nerve sheath tumors; NF1 = Neurofibromatosis type 1.

Introduction

Neurofibromatosis type 1 (NF1) is a rare genetic disorder that occurs in ~ 1 in 3,000 individuals. It is an autosomal dominant condition caused by mutations in the NF1 gene on chromosome 17. It is characterized by multiple café-au-lait spots, Lisch nodules, and neurofibromas. Patients may also develop plexiform neurofibromas, which can cause significant morbidity due to their size and potential for malignant transformation.[1] Thoracic manifestations of neurofibromas include the development of meningoceles, bullous and interstitial lung diseases, pulmonary hypertension, intrathoracic neurogenic neoplasms, and skeletal abnormalities like kyphoscoliosis.[2] While the manifestation of neurofibromas in the skin and peripheral nerves is common, their presence in the mediastinum is rare occurring in only 4.5% of all cases of NF1.[3] Mediastinal neurofibromas in NF1 usually arise from the posterior mediastinum and are typically confined to this area.[4] However, in rare instances, these tumors can extend into other compartments of the mediastinum as well as into adjacent structures, leading to more complex clinical presentations.[5]

Mediastinal neurofibromas can pose diagnostic challenges due to their asymptomatic nature and uncommon location. This case report presents a rare instance of a 20-year-old male with NF1 who was incidentally found to have a large neurofibroma involving the posterior and middle mediastinum and extending into the right upper lung parenchyma.

[1–3]Department of Pulmonary Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

[4]Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

Corresponding Author: Basil Paul, Department of Pulmonary Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India, Phone: +91 7907983452, e-mail: basilpaul119@gmail.com

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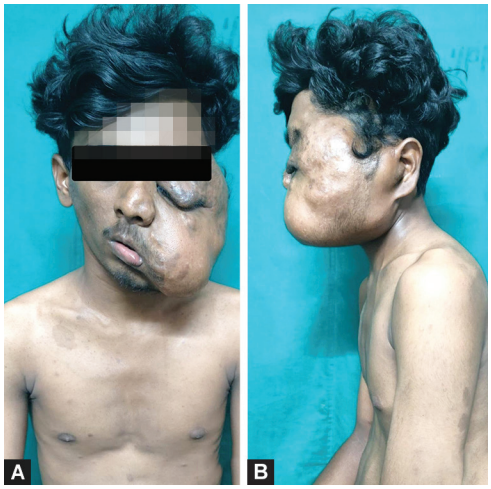
Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

Case Description

A 20-year-old male with a known history of NF1 presented to the Department of Pulmonary Medicine at our institute in the year 2024, for a pre-surgical fitness evaluation prior to a planned debulking surgery for a plexiform neurofibroma on the left side of his face. On physical examination, the plexiform neurofibroma on the left side of the face involved the eyelids, the left cheek, forehead and mandible. He was unable to open his left eye due to the drooping folds affecting the eyelids (Fig. 1). He also had multiple cutaneous neurofibromas on his body, including one in the right forearm

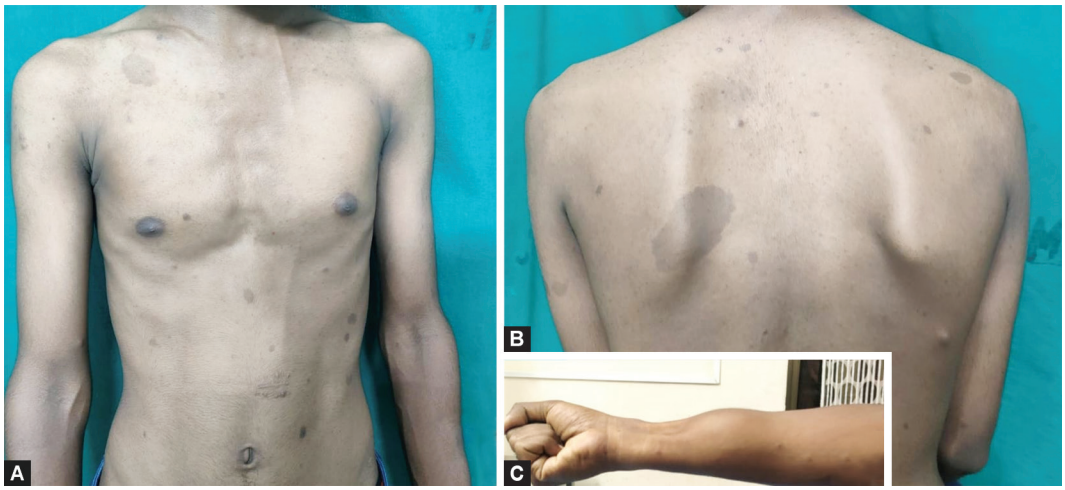
and another in the right posterior thoracic region below the scapula (Fig. 2). Additionally, he had ventriculomegaly for which a ventriculoperitoneal shunt had been placed in July 2023 and was in situ at the time of presentation. He exhibited multiple café-au-lait macules distributed across his body and had Lisch nodules in both the eyes. The patient had previously undergone a debulking surgery for the facial plexiform neurofibroma, but the tumor recurred, necessitating a second procedure planned by the plastic surgery team. A routine chest X-ray done for the pre-surgical fitness evaluation revealed a homogenous opacity in the right upper zone with tracheal shift to the left (Fig. 3A), prompting referral to the Pulmonary Medicine Department for further evaluation.



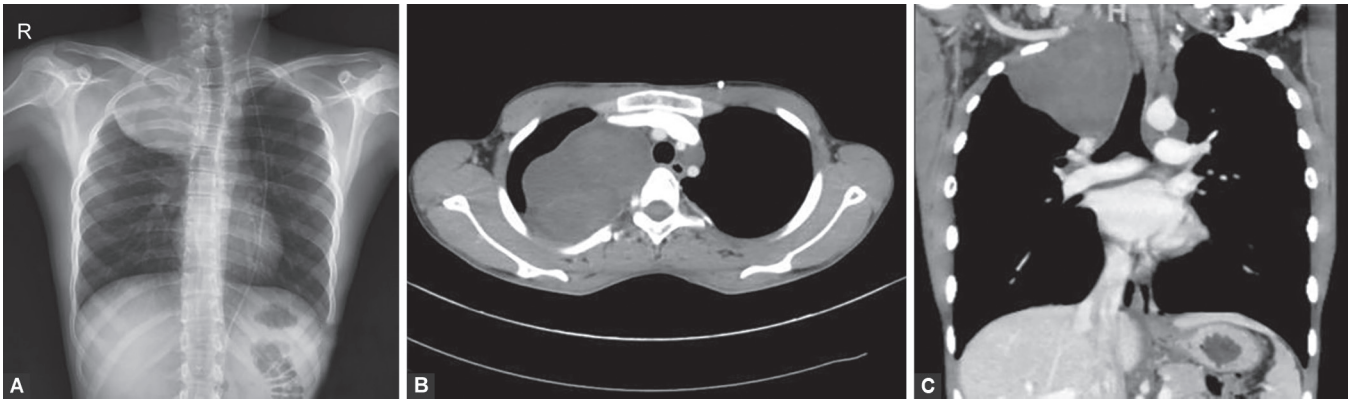
Figs 1A and B: Plexiform neurofibroma involving the whole of the left side of face

On evaluation in Pulmonary Medicine Department, the patient had no obvious respiratory complaints and on auscultation, there was only reduced breath sound intensity in the right supraclavicular region. Based on clinical history and chest X-ray, the initial differentials included germ cell tumors, lymphoma, and metastases from a non-lung primary cancer.[6,7]

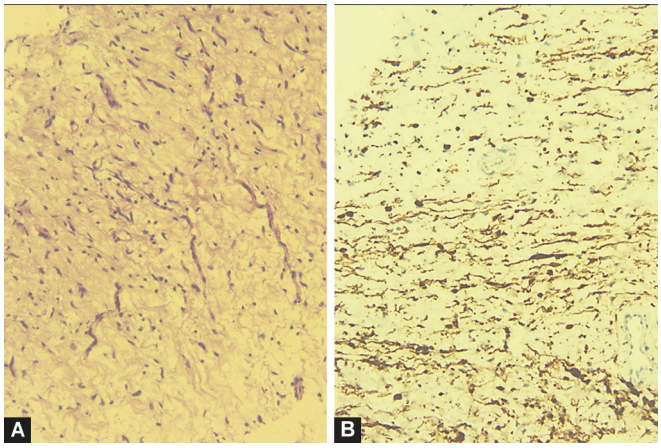
A contrast-enhanced computed tomography (CECT) scan of the chest was done subsequently which showed a large, well-defined, heterogeneously enhancing solid cystic lesion measuring ~ 9.6 × 7 × 9 cm. The mass was arising from the posterior mediastinum, extending into the middle mediastinum and involving the right upper hemithorax into the lung parenchyma with a broad base toward the mediastinum and it was closely abutting the trachea



Figs 2A to C: (A and B) Multiple café-au-lait macules distributed across the body both anteriorly and posteriorly; (C) Neurofibroma in the right forearm



Figs 3A to C: (A) Posteroanterior view of the chest X-ray demonstrates the right upper zone homogenous opacity suggestive of a mass; (B and C) Sagittal and coronal view of the contrast-enhanced CT of thorax showing the mediastinal mass with right upper hemithorax involvement



Figs 4A and B: (A) Sections from the posterior mediastinal mass highlight a sparsely cellular spindle cell neoplasm with wavy nuclei, inconspicuous nuclear atypia, pleomorphism, or mitosis arranged in a loose edematous stroma with delicate plexiform thin-walled blood vessels. Hematoxylin and eosin stain, ×200; (B) Section highlights strong nuclear positivity for S-100 stain in the spindle cell nuclei. Immunoperoxidase stain with DAKO primary antibodies, USA. Diaminobenzidine stain with Hematoxylin counterstain, ×200

(Figs 3B and C). Additionally, the computed tomography (CT) scan revealed multiple well-defined hypodense fusiform lesions along the bilateral lower cervical, thoracic, and lumbosacral nerves with mild neuraminal widening, suggestive of multiple nerve sheath tumors. The imaging characteristics suggested a neurogenic tumor arising from the posterior mediastinum thus narrowing down the differentials and prompting a biopsy for exact diagnosis. Histopathological examination of the CT-guided transthoracic biopsy showed tissue comprising benign spindle cells with bland nuclear morphology and loose edematous stroma (Fig. 4). These features were consistent with neurofibroma. Most mediastinal neurofibromas arise from the posterior mediastinum and are usually confined to this area. However, in this case, the neurofibroma extended into the middle mediastinum and the right upper hemithorax into the lung parenchyma, making it a rare presentation. Despite the presence of the mediastinal mass, the patient was completely asymptomatic. However, it carries a risk of progression into malignancy. Hence, the patient was planned for surgery as it remains the main treatment approach. And he was referred to a thoracic surgeon for the same. The patient gave his written permission to use his data to publish this case report and any accompanying images.

Discussion

Neurofibromas make up 4% of all mediastinal tumors, and neurofibromas associated with NF1 occur in less than 1% of all cases.[8] However, it is estimated that 4.5% of patients with NF1 develop mediastinal tumors, with simultaneous posterior and middle mediastinal involvement extending into lung parenchyma being particularly rare.[4] Intrathoracic neurofibromas usually arise from the ganglia or nerves of the sympathetic trunk and rarely from the intrathoracic vagus nerve, trachea or esophagus In NF1, mediastinal neurofibromas typically originate in the posterior mediastinum and remain confined to this region.[9] However, in rare cases, these tumors may extend into other parts of the mediastinum and adjacent structures, resulting in more complicated clinical presentations. These tumors are generally asymptomatic and are often discovered incidentally in chest radiology, as in our case. Imaging modalities such as CT and magnetic resonance imaging (MRI) play a crucial role in the identification and characterization of these masses. On MRI, a mediastinal neurofibroma typically appears as a well-defined mass with hypointensity on T1-weighted images, hyperintensity on T2-weighted images, and heterogeneous enhancement after contrast administration.[10] Biopsy and histopathological analysis remain the gold standard for definitive diagnosis. Molecular testing is also available for the diagnosis of NF1, but it is not routinely indicated for clinical care because of less genotype-phenotype correlations.[11] Neurofibromas in the mediastinum can potentially transform into malignant peripheral nerve sheath tumors (MPNSTs), thus warranting careful monitoring and follow-up.[12] Surgical resection is considered especially in symptomatic cases or when malignant transformation is suspected.

Similar cases have been reported in the literature. Hosseni Karami et al. described a rare case of a giant mediastinal neurofibroma in a 3-year-old boy with NF1, highlighting the unusual presentation and the challenges in managing large mediastinal masses in pediatric patients.[13] Zubair Ahmad et al. documented an anterior mediastinal neurofibrosarcoma, emphasizing the risk of malignant transformation of mediastinal neurofibromas into MPNSTs, which requires careful monitoring.[14] Additionally, Ryu Kanzaki et al. reported bilateral mediastinal neurofibromas arising from the vagus nerves in a patient with NF1, illustrating the diverse presentations and locations of neurofibromas in the mediastinum.[6]

Conclusion

This case underscores the importance of considering mediastinal neurofibromas in the differential diagnosis of mediastinal masses in NF1 patients, even when asymptomatic. Neurofibromas can arise in uncommon locations, such as the mediastinum, with potential extension into surrounding structures, thus complicating the diagnosis. Clinicians should maintain a high index of suspicion for neurogenic tumors in NF1 patients, particularly when evaluating mediastinal masses.

Though asymptomatic in this case, the neurofibromas carry a notable risk of progressing to MPNSTs, emphasizing the need for early detection and proactive management in NF1 patient.[15] This case also highlights the importance of a multidisciplinary approach-encompassing pulmonary medicine, radiodiagnosis, thoracic surgery, and pathology to ensure accurate diagnosis and optimal care. The risk of malignancy, coupled with the complexity of mediastinal involvement, highlights the need for early detection, multidisciplinary management, and long-term follow-up to monitor for recurrence or malignancy, as these tumors may evolve over time. In such cases, a low-dose CT scan or chest X-ray may be employed in patients with NF1 to detect thoracic manifestations and mediastinal involvement early, aiding in timely intervention.

Orcid

Basil Paul https://orcid.org/0009-0005-7708-2336
Pratap Upadhya https://orcid.org/0000-0001-9303-9008

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