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Neurofibromatosis-Associated Diffuse Lung Disease: A Case Report and Literature Review

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Abstract

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder with multisystem involvement, affecting the skin, nervous system, bones, and cardiovascular system. Pulmonary manifestations, particularly neurofibromatosis-associated diffuse lung disease (NF-DLD), remain underdiagnosed due to overlapping clinical and radiological features with smoking-related emphysema. This report describes a 61-year-old male with NF1 and a history of chronic smoking who presented with exertional dyspnoea and chronic dry cough. High-resolution computed tomography (HRCT) of the chest revealed bilateral upper lobe cysts and bullae with well-defined borders, findings consistent with NF-DLD, alongside coexistent emphysema. Given the challenges in distinguishing NF-DLD from smoking-related lung disease, this case highlights the importance of recognizing distinct imaging characteristics, implementing smoking cessation strategies, and conducting long-term pulmonary surveillance.

Keywords: Neurofibromatosis; Chest

Introduction

Neurofibromatosis type 1 (NF1) is a common autosomal dominant neurocutaneous disorder that affects approximately 1 in 2,500 to 3,000 individuals worldwide. It results from mutations in the NF1 gene, located on chromosome 17q11.2, which encodes neurofibromin, a tumor suppressor involved in the regulation of RAS signalling. Loss of neurofibromin function leads to uncontrolled cell proliferation, contributing to the development of neurofibromas and other systemic manifestations. NF1 primarily presents with cutaneous, skeletal, and neurological abnormalities, including café-au-lait macules, neurofibromas, Lisch nodules, and scoliosis. However, pulmonary involvement in NF1, particularly NF-DLD, is rare and often underrecognized. NF-DLD is characterized by bilateral, upper lobe-predominant cysts and bullae with well-defined borders, which are frequently misdiagnosed as smoking-related emphysema. The relationship between NF-DLD and cigarette smoking remains controversial. Some studies suggest that NF1 increases lung susceptibility to tobacco-related injury, leading to early-onset emphysema. Given the diagnostic complexity and potential for significant morbidity, recognizing NF-DLD as a distinct entity from emphysema is crucial. This case report highlights the radiological features of NF-DLD in a patient with NF1 and a history of chronic smoking, emphasizing the need for early diagnosis, smoking cessation, and clinical surveillance.

Case Presentation

Clinical history

A 61-year-old male with a known diagnosis of NF1 presented to a private respiratory clinic with complaints of chronic dry cough and exertional dyspnoea over several years. His symptoms had an insidious onset, with no clear exacerbating factors. He denied experiencing wheezing, orthopnoea, paroxysmal nocturnal dyspnoea, fever, weight loss, or systemic symptoms.

Medical and occupational history

The patient had a history of anxiety but was not on any regular medications. He was a current smoker with a 42 pack-year history. His occupational history revealed significant exposure to

environmental and industrial pollutants. He had worked as a diesel mechanic for six years, during which he was exposed to diesel fumes and industrial chemicals. Following this, he worked as a railway labourer for 20 years, where he encountered coal dust and industrial chemicals. Later, he worked as a traffic controller for nine years, near a mining site, where he was regularly exposed to dust and airborne particulates. There was no known family history of NF1 or lung disease. On examination, the patient had multiple cutaneous neurofibromas and café-au-lait macules scattered across his body. Lung auscultation revealed global expiratory rhonchi, which suggested airflow limitation. Cardiac auscultation identified a pansystolic murmur, which was loudest over the mitral area, necessitating further evaluation [1-5].

Imaging and diagnostic workup

Pulmonary Function Tests (PFTs)

Pulmonary function tests demonstrated a restrictive pattern on spirometry. However, lung volumes and diffusing capacity for carbon monoxide (DLCO) were within normal limits. The flow-volume loop exhibited a scooping pattern, which is suggestive of airflow limitation.

Computed tomography (CT) chest findings

A CT scan of the chest revealed several significant findings. There was evidence of bilateral upper lobe-predominant emphysema, displaying a combination of centrilobular, panlobular, and paraseptal emphysema patterns. Additionally, the scan identified well-defined cysts and bullae in the upper lobes, which are characteristic features of NF-DLD. Minor atelectasis was present in the right lower lobe. Furthermore, a 7 mm subpleural nodule was observed in the right lower lobe, requiring follow-up evaluation. The imaging also revealed a left apical paraspinal mass measuring 56 mm × 39 mm, which extended into the spinal canal. This finding was highly suggestive of either a meningocele or a neurofibroma. Additionally, multiple cutaneous neurofibromas were documented throughout the scan [6-11].

Discussion

Neurofibromatosis-associated diffuse lung disease (NF-DLD) is a distinct pulmonary complication of NF1, characterized by bilateral, well-defined cysts and bullae in the upper lobes. Differentiating NF-DLD from smoking-related emphysema is crucial since NF-DLD cysts have well-defined margins, whereas emphysematous cysts tend to have ill-defined borders. Patients with NF1 have an increased susceptibility to smoking-induced lung injury, which may accelerate the progression of early-onset emphysema. While smoking is a known risk factor for NF-DLD progression, the disease can also develop in non-smokers, reinforcing its classification as a primary pulmonary manifestation of NF1.

Complications of NF-DLD

Neurofibromatosis-associated diffuse lung disease is associated with several severe complications. Patients may experience spontaneous pneumothorax due to the rupture of cysts. Pulmonary hypertension is another recognized complication that can significantly impact morbidity. In advanced cases, chronic respiratory failure may develop. Although there is inconclusive evidence linking NF1 to lung cancer, some reports have suggested an association with adenocarcinoma.

Management and Follow-Up

Current interventions

The patient was prescribed a long-acting muscarinic antagonist (LAMA), long-acting beta-agonist (LABA), and inhaled corticosteroid (ICS) combination inhaler to relieve respiratory symptoms. Given his ongoing tobacco use, he received smoking cessation counseling, which is critical for stabilizing his lung disease. To reduce further exposure to environmental pollutants, he was advised to wear dust masks when exposed to industrial particles. Given the presence of a pansystolic murmur, an echocardiogram was scheduled to assess potential underlying cardiac pathology. Additionally, an MRI of the chest was planned to further evaluate the left apical paraspinal mass, which was suspected to be either a meningocele or neurofibroma. The patient was advised to undergo high-resolution computed tomography (HRCT) and repeat pulmonary function tests (PFTs) in six months to monitor disease progression.

Long-term considerations

The patient was advised to undergo periodic lung imaging and pulmonary function tests for long-term surveillance. If his respiratory function declined, pulmonary rehabilitation would be considered. Currently, there is no curative treatment for NF-DLD; however, smoking cessation remains the most important intervention to slow disease progression.

Conclusion

This case highlights the diagnostic challenges of NF-DLD, particularly in smokers with emphysema. The presence of well-defined upper lobe cysts and bullae is a key radiological clue for distinguishing NF-DLD from other smoking-related lung diseases. Given the absence of disease-specific treatment, early smoking cessation and long-term pulmonary monitoring are essential for optimizing patient outcomes.

Appendix 1 – Chest CT

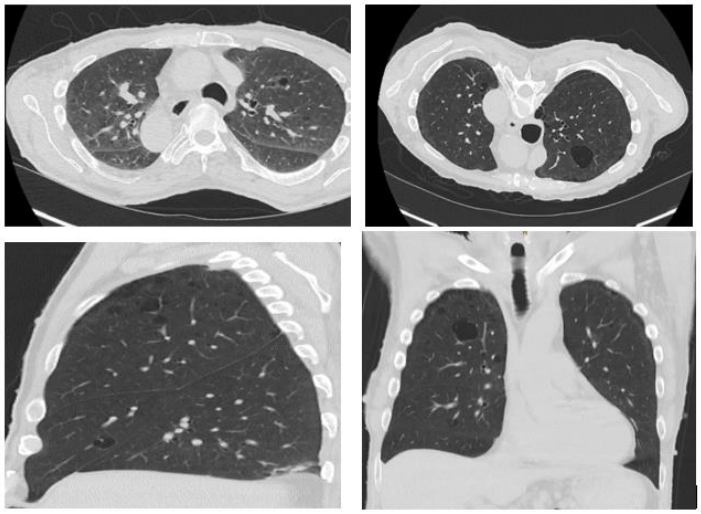
Bilateral marked emphysematous changes

Large emphysematous bullae seen at lung apices and right upper lobe

Large soft tissue mass extending through the left T2/T3 neural foramen, encroaching on left lung apex

Subpleural nodule at the right lower lobe

Multiple cystic changes across bilateral lung fields (Figure 1).

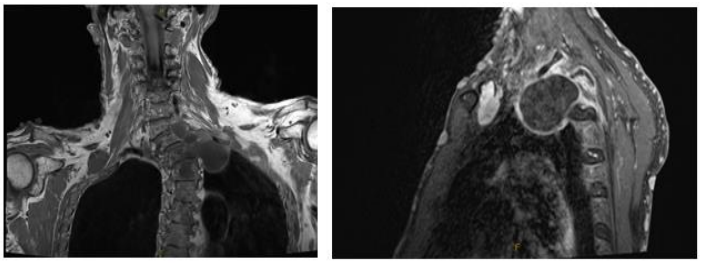


Appendix 2 – MRI CERVICOTHORACIC SPINE

At C7-T1 and T2-3 on the left side large meningocele secondary to dural ectasia through widened neural foramina with the largest at T2-3 corresponding to the lesion noted on the CT

Thoracic scoliosis, convex to the left

Flattening and minimal volume loss of the cervical cord in the upper thoracic spine (Figure 2).



References

1. Ferner RE, Gutmann DH. Neurofibromatosis type 1 (NF1): diagnosis and management. Handb Clin Neurol. 2013; 115: 939-955.
2. Hirbe AC, Gutmann DH. Neurofibromatosis type 1: a multidisciplinary approach to care. Lancet Neurol. 2014; 13: 834-843.
3. Dehal N, Gastelum AA, Millner PG. Neurofibromatosis-Associated Diffuse Lung Disease: A Case Report and Review of the Literature. Cureus. 2020; 12: 8916.
4. Gutmann DH, Parada LF, Silva AJ, Ratner N. Neurofibromatosis type 1: modelling CNS dysfunction. J Neurosci. 2012; 32: 14087-14093.
5. Zamora AC, Collard HR, Wolters PJ, Webb WR, King TE. Neurofibromatosis-associated lung disease: a case series and literature review. European Respiratory Journal. 2006 Dec 29; 29: 210-214.
6. Cantin L, Bankier AA, Eisenberg RL. Multiple cystlike lung lesions in the adult. AJR Am J Roentgenol. 2010; 194: 1-11.
7. Jutant EM, Girerd B, Jaïs X, Savale L, O'Connell C, Perros F, et al. Pulmonary hypertension associated with neurofibromatosis type 1. Eur Respir Rev. 2018; 27: 180053.
8. Oikonomou A, Vadikolias K, Birbilis T, Bouros D, et al. HRCT findings in the lungs of non-smokers with neurofibromatosis. Eur J Radiol. 2011; 80: 520-523.
9. Spinnato P, Facchini G, Bazzocchi A, Albisinni U. Diffuse lung disease associated with neurofibromatosis type-1 can also affect children. World J Pediatr. 2018; 14: 207.
10. Melo AS, Alves Jr SF, Antunes PD, Zanetti G, Marchiori E. Lung cancer and parenchymal lung disease in a patient with neurofibromatosis type 1. J Bras Pneumol. 2019; 45: 20180285.
11. Nguyen KA, Elnaggar M, Gallant NM, Tanios M. Neurofibromatosis type 1: a case highlighting pulmonary and other rare clinical manifestations. BMJ Case Rep. 2018; 2017222614.