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Spontaneous Pneumothorax: A Rare Complication of Neurofibromatosis Type 1 Associated Diffuse Lung Disease

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ABSTRACT

The visually striking neurocutaneous manifestations of neurofibromatosis type 1 (NF1) are well recognized and extensively documented throughout the scientific literature. While not uncommon, the pulmonary manifestations of NF1 are largely unknown to many physicians. NF1-associated diffuse lung disease (NF-DLD) complications include pulmonary hypertension, pulmonary artery stenosis, subpleural cysts, and spontaneous pneumothorax. We present a rare case of a 34-year-old non-smoking male with NF-DLD found incidentally in adolescence with previous apical bleb repair, presenting nearly 20 years later with spontaneous pneumothorax. In NF1 patients with pulmonary complaints, NF-DLD should be assessed with computed tomography (CT), and physicians should be familiar with associated complications. Our case adds to the evidence that NF-DLD is a clinical entity distinct from the effects of smoking.

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KEYWORDS
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INTRODUCTION

Neurofibromatosis type 1 (NF1), formerly referred to as von Recklinghausen disease, is the most common neurocutaneous disorder worldwide.[1] In the United Kingdom, the incidence of NF1 is estimated to affect 1 in 3,000 births.[2] While the neurocutaneous findings, such as café-au-lait macules and neurofibromas, are widely studied, the thoracic manifestations of the disease are commonly overlooked. Thoracic neurocutaneous lesions and abnormalities of the ribs and spine are the most common thoracic manifestations of the disease.[3] Rib and spine abnormalities seen in NF1 include erosion of the ribs, separation of adjacent ribs, kyphoscoliosis, posterior scalloping of the vertebral bodies, and enlargement of neural foramina.[4]

Much less studied are the pulmonary manifestations of NF1. 10%-20% of adult patients with the disease have pulmonary findings on imaging, including bullae, cysts, nodules, and interstitial parenchymal lesions.[5–7] Interstitial lung disease is typically basilar, bilateral, and symmetrical with associated thin-walled bullae of the apices.[8] NF1-associated diffuse lung disease (NF-DLD) represents the spectrum of apical bullae and basilar interstitial lung disease most commonly seen on radiographic imaging, although it is not pathognomonic of the disease.[7] Complications of NF-DLD include pulmonary hypertension,[9–11] pulmonary artery stenosis,[12] subpleural cysts,[13] and spontaneous pneumothorax.[14,15] Here, we present a rare complication of NF-DLD: a case report of a 34-year-old male non-smoker with NF1 with spontaneous pneumothorax (SP).

CLINICAL CASE

A 34-year-old male never-smoker with NF1 presented to an outpatient clinic with complaints of pleuritic chest pain, rib pain, and constant non-productive

cough for the past few days. He denied any injury to the chest wall. Spontaneous right-sided apical pneumothorax was confirmed with a chest X-ray (CXR), and the patient was prompted to go to the emergency department (ED). The patient has a history of sporadic NF1 diagnosed clinically with cutaneous neurofibromas of the thorax, neck, groin, and tongue, café-au-lait macules, kyphoscoliosis, and pectus excavatum. He has no history of prior spontaneous pneumothorax.

In 2003, while he was being worked up for surgical correction of pectus excavatum, apical and paraseptal bullae were found incidentally on non-contrast chest CT. Thoracoscopic resection of bilateral apical blebs with endoscopic repair of pectus excavatum was completed in 2003 at an outside facility. On follow-up with pulmonology in 2010, the patient was found to have worsening bullous disease, as demonstrated by chest CT (Figure 1, Ai). Pulmonary function testing and spirometry were performed, which showed no abnormalities.

In the ED, SpO2 was 95% on room air, and he was afebrile, normotensive, and in no acute distress. The patient complained of right-sided rib and back pain exacerbated by a non-productive cough. Physical exam revealed neurofibromas of the face, neck, and torso, clear lungs to auscultation, non-labored respirations, and a normal cardiovascular exam. Chest CT with contrast showed right pneumothorax, bullous disease of the bilateral upper lobes with apical scarring and staple lines, small right pleural effusion, and evidence of scoliosis (Figure 1, Aiii and Biii). A chest tube was placed under CT guidance by interventional radiology. Repeat CXR showed an interval decrease in the size of pneumothorax with the chest tube in place.

On hospital day 3, CXR was negative for pneumothorax. Plans for robotic-assisted bleb resection with talc pleurodesis to prevent recurrent pneumothorax were discussed with the patient. Posterior pleurectomy and talc

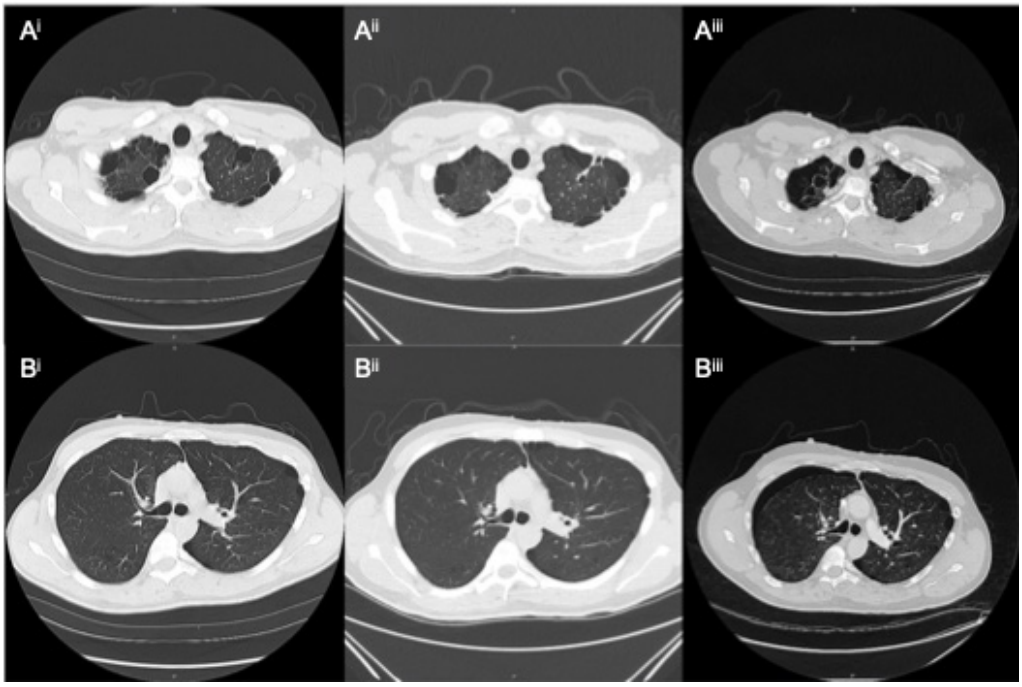

FIGURE 1. Progression of Apical Bullous Disease. CT images (lung window) at the levels of the lung apices (Ai, Aii, and Aiii) and tracheal bifurcation (Bi, Bii, and Biii) are shown. Numerous cutaneous neurofibromas of the anterior thoracic wall are visualized. Thin walled, bullae can be visualized most prominently at the lung apices and paraseptally. Ai and Bi: Non-contrast CT images from 2010. Aii and Bii: Non-contrast CT images from 2016. Aiii and Biii: Contrast images from 2021 with right-sided pneumothorax easily visualized.

pleurodesis was performed with no complications. The patient was extubated in the recovery area in stable condition. Pleural tissue sent to pathology contained fibrosis, mild chronic inflammation, and focal acute inflammation. On post-op day 5, the patient was discharged home under stable condition. The patient was amendable to follow-up in the thoracic surgery clinic, and serial CXRs showed no recurrence of pneumothorax.

DISCUSSION

Here, we present a case of spontaneous pneumothorax in a patient with NF-DLD. Our patient, with a history of bilateral apical bullous lung disease present on chest CT in adolescence, with interval worsening of bullous disease confirmed by CT, presented nearly 20 years later with right-sided spontaneous pneumothorax. Few cases of spontaneous pneumothorax associated with NF1 lung disease have been reported. Of these cases, few reports have been identified in young non-smokers and instead represent cases in smokers in the fourth and fifth decades of life.[16]

While smoking is not an independent risk factor for the development of pneumothorax, smoking does increase the risk of interstitial lung disease, potentially representing lung architecture prone to spontaneous pneumothorax.[17] It has been long disputed that NF-DLD is secondary to smoking and not a distinct phenotype of NF1. A study by Ueda et al. showed no significant difference in the presence of cysts among smokers and non-smokers when comparing chest CT findings in patients with NF1.[18] Similarly, a study by Oikonomou et al. found radiographic evidence of NF-DLD in 6 asymptomatic non-smoking patients with NF1.[5] Our case further adds to evidence that NF-DLD is a clinical entity distinct from the effects of smoking.

The current pathogenesis underlying NF-DLD is unclear, and there are no known treatments or recommendations for prevention. The pathogenesis of the effects of NF1 on the pulmonary system is not well understood. Few studies have hypothesized that NF-DLD is a result of increased collagen deposition and myofibroblast activation in the lung parenchyma.[19,20] Complications of NF-DLD, such as spontaneous pneumothorax, as seen in our patient, are often painful and can be deadly.[21] Thus, it is important for clinicians to be aware of the potential pulmonary complications of NF1.

CONCLUSION

Much is still unknown about NF-DLD, including the pathogenesis of the disease process, associated risk factors, and the role of treatment in the management of NF-DLD. We hope that this case contributes to further investigation that aids in narrowing this knowledge gap. However, it is becoming more apparent that NF-DLD is a clinical entity unique to those with NF1. Spontaneous pneumothorax is a complication of NF-DLD that has been seldomly described in the literature, especially in young non-smokers. Individuals with NF1 with pulmonary complaints should undergo chest CT to identify NF-DLD. Clinicians should be aware of the complications of NF-DLD, including spontaneous pneumothorax.

AUTHOR AFFILIATIONS

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