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SPONTANEOUS PRIMARY PNEUMOTHORAX AS A COMPLICATION OF NEUROFIBROMATOSIS TYPE 1

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ABSTRACT

Neurofibromatosis type 1 (NF1) is a genetic disorder that affects the skin and the neurological, ocular and skeletal systems. Many are unaware of the extent of pulmonary involvement, including lung cysts and emphysematous bullae, which enhances the risk of secondary spontaneous pneumothorax (SSP). We report the case of an 18-year-old male with NF1 who presented with acute dyspnoea and chest pain due to a right-sided pneumothorax caused by the rupture of lung apical bullae. The patient received supplemental oxygen and a chest tube of 18F was inserted, with a complete resolution of the pneumothorax. He was discharged on the third day of hospital stay.

This case highlights the importance of considering SSP as a possible clinical manifestation and complication of NF1. Early recognition and appropriate management of this condition can prevent serious complications and improve patient outcomes.

KEYWORDS

Pneumothorax, neurofibromatosis type 1, bullous lung disease

LEARNING POINTS

- NF1 is a genetic disease that results in cutaneous conditions, including neurofibroma, axillary, inguinal lentigines and *café au lait* spots. In some cases (5–20%) it can also affect the lungs, causing neurofibroma, infiltrative and cystic lesions, emphysema or bullae, leading to chronic respiratory failure.
- SSP is a clinical presentation of NF1 caused by the rupture of lung cysts or bullae, with an unclear relationship to smoking.
- Early diagnosis of pulmonary manifestations in patients with NF1 is crucial as surgical removal of lung cysts and bullae seems to prevent recurrence of SSP.

INTRODUCTION

A pneumothorax is a medical emergency that occurs when air leaks into the pleural cavity, causing the lung to collapse. Neurofibromatosis type 1 (NF1) is a genetic illness inherited as an autosomal-dominant feature[1,2]. Apical lung bullae and cysts, and bilateral, symmetrical and basal NF-related interstitial fibrosis are pulmonary manifestations of the disease, which can occur in up to 20% of patients[3].

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In patients with NF1, the risk of secondary spontaneous pneumothorax (SSP) may be increased due to lung bullae rupture. We present a case of a non-smoking male patient with NF1 and a SSP.

CASE DESCRIPTION

An 18-year-old male, non-smoker, presented to the emergency department with sudden shortness of breath and chest pain rated at a severity of 6–7 out of 10.

The pain increased with deep breathing; there were no signs of trauma, fall or extreme physical exertion. He denied having any additional symptoms such as fever, digestive or urinary issues. The patient had a history of NF1 since he was eight years old, but he had never taken medication or had any drug or dietary allergies.

On physical examination he was alert, cooperative, apyretic and haemodynamically stable (with a blood pressure of 106/68 mmHg and a heart rate of 91 bpm). He had multiple *café au lait* lesions scattered across his torso. Pulmonary auscultation revealed a decrease in breath sounds on the right side. The arterial blood gas test showed a partial pressure of oxygen (PaO_2) of 110 mmHg. The results of the hemogram and biochemistry analyses indicated no significant alterations; the electrocardiogram was unremarkable. A moderate volume right-sided pneumothorax was identified on the chest radiograph *(Fig. 1)*.

A chest tube of 18F was inserted, resulting in near-total lung expansion within a few hours of drain placement *(Fig. 2)*. The drain was clamped the following day, with no evidence of pneumothorax recurrence, and subsequently removed without any accompanying complications *(Fig. 3)*.

A chest computed tomography (CT) scan was performed, identifying several small subpleural bullae in both pulmonary apices. The bullae measured 15 mm on the left side and 9 mm on the right side, along their longest axis. No changes were observed in the remaining examination of the lung parenchyma and no pleural or pericardial effusion was identified *(Fig. 4)*.

The patient was instructed to seek medical attention immediately if he experienced chest pain or shortness of breath in the future. He was also advised to avoid activities leading to barotrauma, such as diving or air travel. Regular follow-up appointments were emphasised to monitor for any recurrence of pneumothorax or other complications associated with his condition.

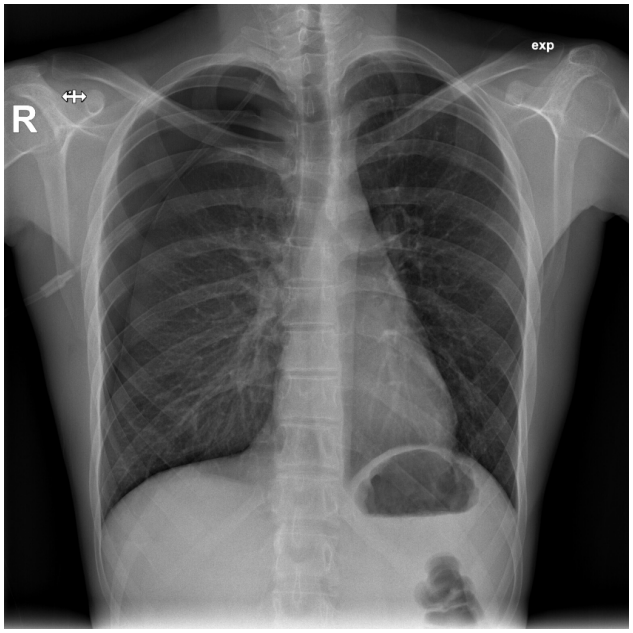

Figure 1. Posteroanterior chest radiograph on admission showing a moderate right-sided pneumothorax.

DISCUSSION

There are three types of NF: type 1, NF2-related schwannomatosis (formerly known as NF type 2) and others,

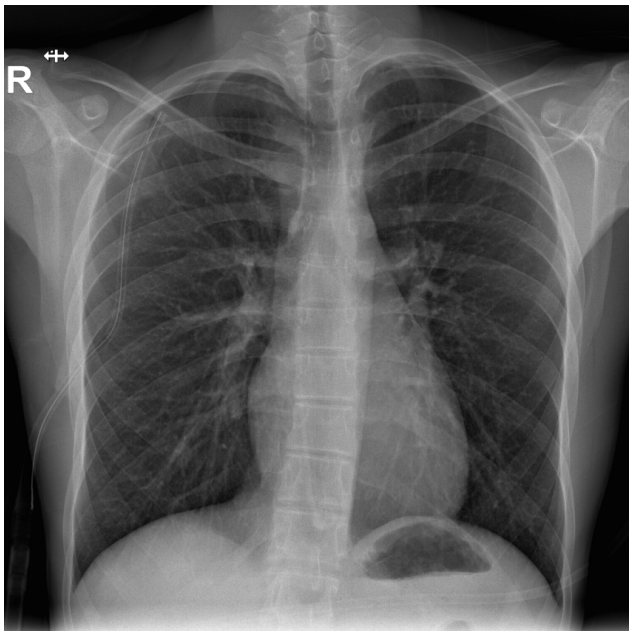

Figure 2. Posteroanterior chest radiograph after a thoracic drain with an almost complete lung expansion.

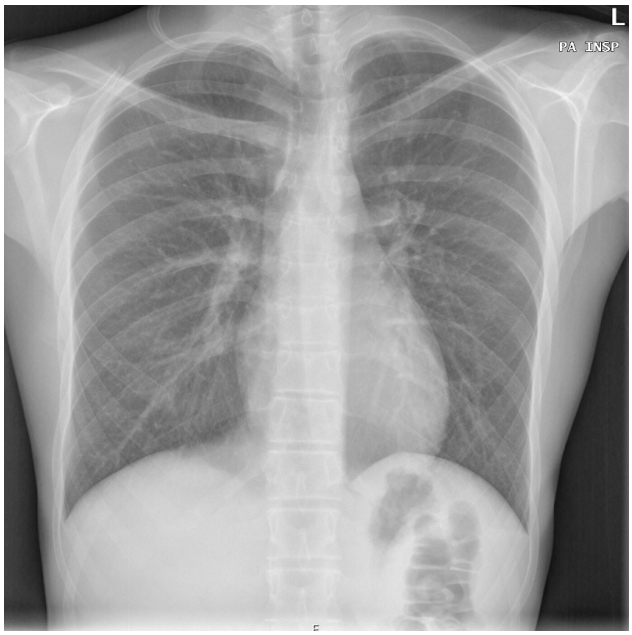

Figure 3. Posteroanterior chest radiograph after chest tube removal with no evidence of pneumothorax recurrence.

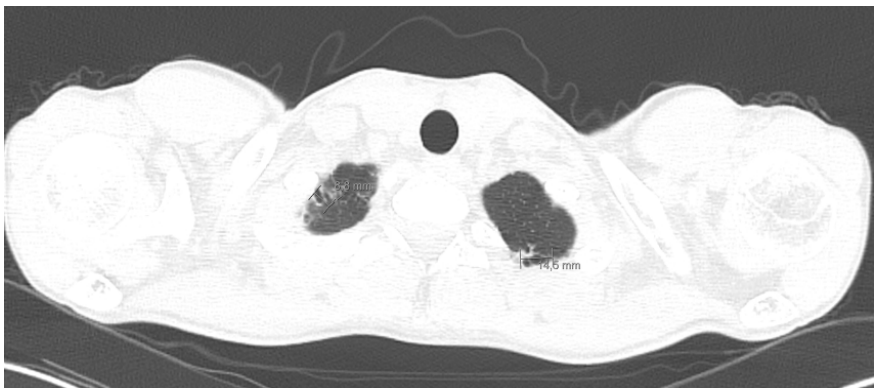

Figure 4. High-resolution CT scan (lung window) showing small subpleural bullae and emphysema.

caused by genetic variants. NF1 is a genetic condition caused by mutations in the NF1 gene, located at chromosome 17q11.2. This chromosome encodes for a tumour suppressor protein, neurofibromin, that functions as a negative regulator of Ras/MAPK and PI3K/mTOR signalling pathways[1,2]. It affects approximately one in every 3,000 people and can lead to a broad spectrum of clinical findings. The mutation is not a diagnostic criterion[2]. The presence of two or more of the following clinical features establishes the diagnosis: six or more *café au lait* macules; two or more neurofibromas, one or more plexiform neurofibroma; skinfold freckling of axilla or groin; optic pathway glioma; two or more Lisch nodules; characteristic bone dysplasia (sphenoid wing dysplasia, thinned long bone cortex); and a first-degree relative with NF1[3].

NF1 diagnosis was confirmed at the age of eight in our patient, as he met the necessary criteria by displaying multiple *café au lait* spots on his body, Lisch nodules, and having a first-degree relative (his father) also diagnosed with NF1. Genetic testing identified the mutation in the NF1 gene.

Clinical manifestation of NF1 can vary widely, including various neoplasms, cutaneous, vascular, bone and cognitive characteristics. These symptoms overlap with other hereditary diseases[4]. The presence of interstitial disease, emphysematous bullae, or pulmonary hypertension (PH) defines the pulmonary involvement[5]. These modifications are typically more prevalent in adults but can also be observed radiographically in children[2].

Centrilobular nodules and parenchymal cysts are apical, with some subpleural cysts imitating paraseptal emphysema. In advanced NF1 lesions cluster, potentially misdiagnosing centrilobular emphysema[5-7]. Diffuse cystic disease can cause chronic respiratory failure and more catastrophic complications such as SSP or PH due to hypoxaemia, like the case presented. Imaging studies have revealed the presence of nodular, bullous, cystic and interstitial lesions in the lungs of 10–20% of people with NF1[5].

The fact that this changes occurred in a young individual without any known lung disease makes the case even more unusual. This suggests that emphysematous alterations seem to occur from the moment the disease is diagnosed, which may lead to the development of SSP earlier.

SSP can be lethal in 4.6% of cases. For most clinically stable patients with a first episode of SSP whose pneumothorax is large (>3 cm from the chest wall at the apex or >2 cm from the chest wall at the hilum), similar to the case presented, drainage is recommended[6].

CONCLUSION

The patient is asymptomatic and is still seen for follow-up considering the risk of recurrence of a new pneumothorax or other pulmonary alterations.

Clinician awareness to the pulmonary manifestations of NF1 is important to identify patients at increased risk of developing SSP as preventive surgery seems to decrease the risk of new events.

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