

Neurofibromatosis (von Recklinghausen's disease)—an unusual cause of parenchymal lung disease

A case report

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Summary

Interstitial pulmonary fibrosis and bullae are uncommon findings in neurofibromatosis. A case of this disease with pulmonary parenchymal involvement is presented and the association between the two is discussed.

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Neurofibromatosis is a relatively common autosomal dominant trait¹ with a frequency of about 1 in 3000.² Spontaneous mutations do occur. One-third of patients are discovered accidentally, one-third seek advice about the cosmetic aspects of the disease, and the remainder have neurological syndromes.¹ The manifestations take many forms, but the defining features are multiple *café au lait* spots, often with axillary freckling, multiple neurofibromas and Lisch nodules.² Parenchymal lung involvement has been reported in 10% of patients.³ This may be due to neurofibromatous tumours within the lung or to diffuse interstitial fibrosis and bullous lung disease, either alone or in combination.^{4,5} The most prominent respiratory symptom tends to be dyspnoea on exertion.⁴

Case report

A 46-year-old man with neurofibromatosis presented with a 1-year history of progressive dyspnoea. On admission he stated that he had difficulty in climbing one flight of stairs and developed shortness of breath while dressing and shaving. This was associated with episodes of ankle oedema for which he had recently received diuretics. The patient had stopped smoking 2 years previously (having smoked 10 - 20/d for 15 years) because of shortness of breath. There was no history to suggest chronic bronchitis, allergies or asthma. The patient had been admitted to hospital in respiratory failure in October 1981. The patient's mother and aunt had both been known to suffer from neurofibromatosis, but the exact cause of their deaths was not known. There were no siblings and the patient was unmarried. Medication before admission included furosemide, spironolactone and aminophylline tablets.

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There were no further respiratory or cardiovascular complaints and no gastro-intestinal symptoms, and there was no history of seizures, transient neurological deficits, or visual or hearing loss. Kyphoscoliosis had been present since youth.

On examination the patient was short in stature with an obvious kyphoscoliosis from T8 upwards. Typical cutaneous manifestations of neurofibromatosis were present: *café au lait* spots (more than six greater than 1,5 cm in diameter), and palpable, multiple neurofibromas along the supraclavicular nerves and multiple soft-tissue tumours, some of which were sessile and pedunculated. There were no axillary freckles or Lisch nodules. The skin appeared generally hyperpigmented. Central cyanosis was present.

The blood pressure was 110/80 mmHg and the pulse rate 120/min. The jugular venous pressure was raised to 5 cm above the sternal angle, and prominent 'a' waves were noted. There was pedal and sacral oedema. A left parasternal heave was present and on auscultation a right ventricular 4th heart sound and a loud and narrowly split pulmonic component of the 2nd sound were heard. Chest expansion was asymmetrical, the right hemithorax moving more than the left. Kyphoscoliosis was present to the right but the trachea was central. There was hyperresonance to percussion over the left anterior hemithorax, with diminished breath sounds. The right lung, abdomen, and central nervous system were clinically normal. Funduscopy revealed no abnormalities.

Special investigations

The haemoglobin value was 16 g/dl, the white cell count $16 \times 10^9/l$ and the erythrocyte sedimentation rate 1 mm/h (Westergren). The urine was normal. A chest radiograph (Fig. 1) revealed the scoliosis to the right and a transverse cardiomegaly. The most impressive finding was the presence of a massive bulla in the left upper lobe with compression of surrounding lung tissue; a smaller bulla was present in the right upper lobe. An interstitial pattern was present in the middle and lower lobes. Blood gas values in room air were in keeping with respiratory failure, with P_{aO_2} 5,3 kPa, P_{aCO_2} 6,0 kPa, CO_2 30,4 mmol/l and pH 7,42. The blood urea and electrolyte values were normal. The serum α_1 -antitrypsin value was 2,5 g/l (normal 2-4 g/l). A lung scintiscan showed markedly impaired ventilation and perfusion, especially in the left apical region. An ECG was consistent with right ventricular hypertrophy with systolic overload. Pulmonary function tests revealed a combined restrictive-obstructive pattern with a moderate disturbance of intrapulmonary gas mixing (Fig. 2).

Discussion

Neurofibromatosis is a well-recognized clinical entity. The principal manifestations are primarily confined to the skin (*café au lait* spots) and the nervous system (tumours of

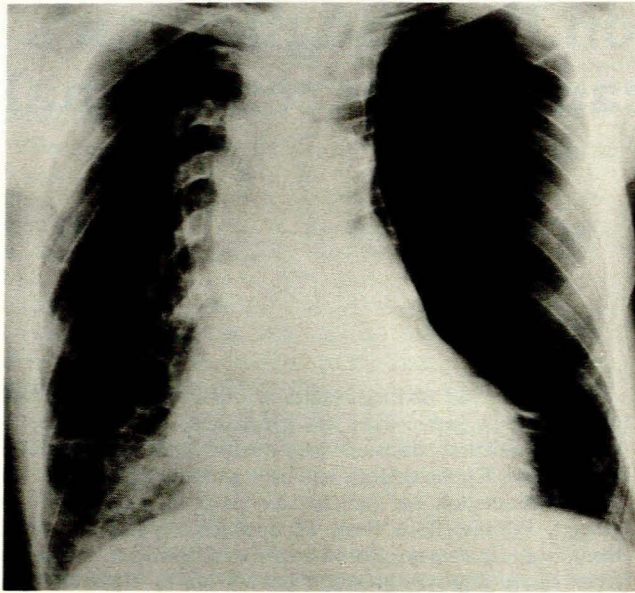


Fig. 1. Postero-anterior radiograph at time of admission showing large asymmetrical bullae in the upper lobes and an interstitial pattern in the lower lobes.

The association of neurofibromatosis with parenchymal lung disease was first recognized in 1963.⁶ The parenchymal manifestations consist of diffuse interstitial pulmonary fibrosis and bullae, which may occur alone or in combination.⁴ The interstitial fibrosis tends to be symmetrical with a basal predominance, and characteristically involves both lungs.⁴ The bullae tend predominantly to involve the upper lobes and are usually asymmetrical.⁴ Bullae may occur unassociated with evidence of interstitial fibrosis but the latter can be demonstrated in all patients with bullae on histological examination.^{3,7}

Clinically, respiratory symptoms tend to be mild and the most frequent complaint is dyspnoea.⁴ The mean age at presentation is 46 years with no sexual predominance.⁵ As with some of the other manifestations of neurofibromatosis, the pulmonary disease typically does not become manifest until the patient reaches adulthood and then is frequently progressive.^{4,5} Most patients are known to have neurofibromatosis before the development of chest symptoms and the respiratory symptoms rarely predominate. Death may occur from respiratory insufficiency and cor pulmonale.⁵ Pulmonary function tests usually reveal evidence of either a restrictive pattern, obstructive pattern or a combination.^{4,5} Diffusing capacity is often decreased.⁷ Pulmonary hypertension develops as the interstitial fibrosis progresses. The earliest finding on chest radiographs is the presence of a diffuse mottled basal interstitial infiltrate which becomes predominantly linear.⁵ Of value in the radiographic diagnosis is the presence of extrapulmonary stigmata and numerous cutaneous nodules projected over the lungs or seen in profile on the chest wall.⁴

The aetiology and pathogenesis of the parenchymal changes are uncertain. A genetic factor seems probable. Interstitial fibrosis has been reported in a mother and daughter⁸ and a mother and son⁹ with neurofibromatosis. The histological appearance of the interstitial fibrosis is indistinguishable from other causes of interstitial pulmonary fibrosis.⁵ Electron microscopy has demonstrated ultrastructural changes similar to those observed in desquamative interstitial pneumonia.⁵

Conclusion

Diffuse interstitial pulmonary fibrosis and bullae are uncommon findings in patients with neurofibromatosis. They are thought to be related to the genetic trait and occur with a familial tendency. The exact aetiology of the changes and their relation to cigarette smoking is uncertain. The diagnosis is primarily radiological and changes typically develop late in the course of the disease. Management is supportive, but bullectomy may be considered.

REFERENCES

- Adams RD, DeLong GR. Developmental and other congenital abnormalities of the nervous system. In: Thorn GW, Adams RD, Braunwald E, Isselbacher KJ, Petersdorf RG, eds. *Harrison's Principles of Internal Medicine*. 8th ed. New York: McGraw-Hill, 1977: 1936-1937.
- Riccardi VM. Von Recklinghausen: neurofibromatosis. *N Engl J Med* 1981; 305: 1617-1627.
- Massaro D, Katz S. Fibrosing alveolitis: its occurrence, roentgenographic and pathologic features in Von Recklinghausen's neurofibromatosis. *Am Rev Resp Dis* 1966; 93: 934-942.
- Fraser RG, Paré JAP. *Diagnosis of Diseases of the Chest*. 2nd ed. Philadelphia: WB Saunders, 1979: 1707-1712.
- Fishman AP. *Pulmonary Diseases and Disorders*. New York: McGraw-Hill, 1980: 984-986.
- Davies PDB. Diffuse pulmonary involvement in von Recklinghausen's disease: a new syndrome. *Thorax* 1963; 18: 198.
- Webb WR, Goodman PC. Fibrosing alveolitis in patients with neurofibromatosis. *Radiology* 1977; 122: 189.
- Patchefsky AS, Atkinson WG, Hoch WS. Interstitial pulmonary fibrosis and von Recklinghausen's disease: an ultrastructural and immunofluorescent study. *Chest* 1973; 64: 459.
- Israël-Asselein R, Chebat J, Sors CH, Basset F, Le Rolland A. Diffuse interstitial pulmonary fibrosis in a mother and son with von Recklinghausen's disease. *Thorax* 1965; 20: 153.

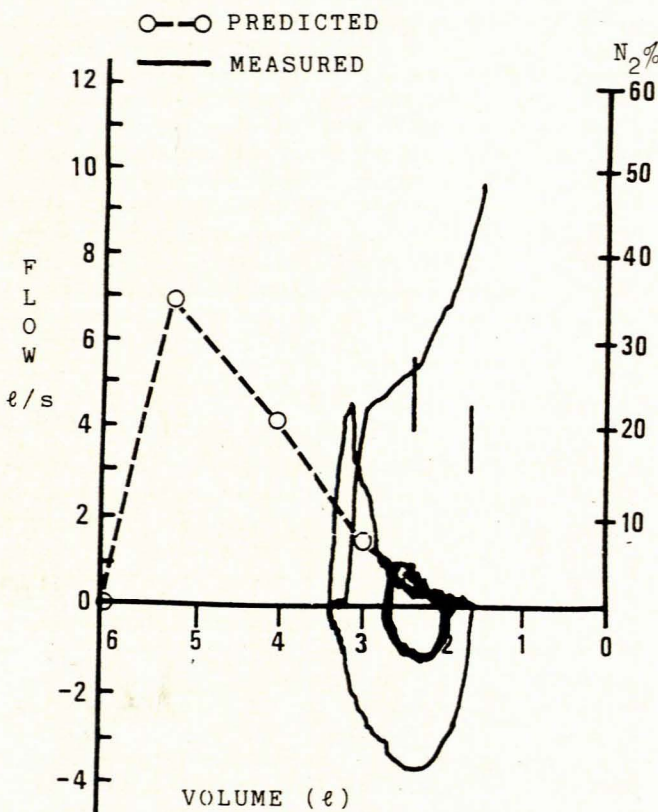


Fig. 2.

neurilemmal sheaths). Tumours of the spinal nerve roots may extend through the intervertebral foramina to form large dumb-bell tumours in the posterior mediastinum. Fibrous dysplasia, congenital vertebral abnormalities and subperiosteal bone cysts may lead to scoliosis, which occurs in up to 15% of patients with this disease.¹