

## Spontaneous haemothorax: a cause of sudden death in von Recklinghausen's disease

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### Summary

**Vasculopathy is a relatively frequent but poorly recognised manifestation of von Recklinghausen's neurofibromatosis. One of its more dramatic presentations is as spontaneous haemothorax. Clinicians and pathologists should be aware of this syndrome as a cause of sudden death in patients with neurofibromatosis.**

**Keywords:** von Recklinghausen's disease; neurofibromatosis; haemothorax; sudden death

Clinicians and pathologists are familiar with the neoplastic complications of von Recklinghausen's neurofibromatosis: neuroma, pheochromocytoma, optic nerve glioma and neurofibrosarcoma. Much less well known, however, is the vasculopathy associated with this disorder which may clinically mimic vasculitis.<sup>1</sup> Recent clinical reports have drawn attention to acute intrathoracic haemorrhage as a frequently fatal manifestation of this vasculopathy. We report a case of fatal retropleural haemorrhage occurring in an elderly woman with neurofibromatosis.

### Case report

A 63-year-old woman with cutaneous neurofibromatosis was admitted to the medical ward one hour after the acute onset of lower left-sided pleuritic chest pain. She had a previous history of angina and took diltiazem and a glyceryl trinitrate spray. Six years previously a gastrointestinal stromal tumour had been removed from the proximal jejunum. She was a non-smoker.

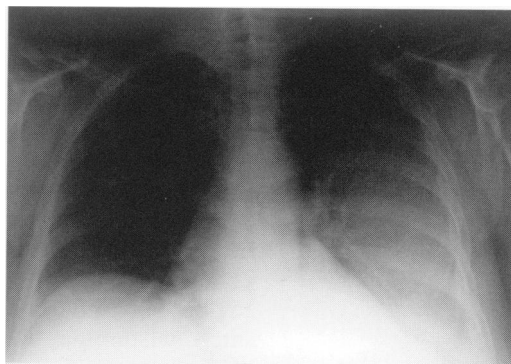
On admission, she was afebrile with a tachycardia of 100 beats/min. She had physical signs of a left-sided pleural effusion but showed no evidence of respiratory distress. A clinical differential diagnosis of pulmonary embolism or pneumonia was considered and, because of neutrophilia of  $19.3 \times 10^9/l$ , antibiotics were commenced. The chest X-ray showed dense opacification of most of the left lung field (figure 1) and ultrasound scanning confirmed that a large pleural effusion was present.

At 16.00 h on the following day, a diagnostic pleural tap was performed; 200 ml of heavily blood-stained fluid flowed readily into the syringe. Cytologically, this appeared to be frank blood. At 17.00 h the patient was shocked, perspiring profusely with tachycardia and at

19.10 h she became severely dyspnoeic, suffered a cardiorespiratory arrest and died.

Autopsy revealed a well-nourished, elderly, white woman covered with abundant soft neurofibromata and cafe-au-lait spots. On opening the chest wall, the left lung was compressed and airless, the left hemithorax almost completely filled by a large, smooth, shiny, blue mass which was shown to be an accumulation of over 1.5 l of clotted blood behind the parietal pleura. Despite careful dissection of all major intrathoracic and intercostal vessels the source of haemorrhage could not be found. Left ventricular hypertrophy was present (total cardiac weight 580 g) with no significant coronary artery atherosclerosis. A 6-cm diameter tumour was present in the jejunum and two small tumours 0.5 cm diameter were found on the serosal surface of the stomach. The remainder of the autopsy was unremarkable.

Death was attributed to haemorrhagic shock due to a total loss of over 1.5 l of blood due to therapeutic aspiration and retropleural haemorrhage. The source of haemorrhage was not established at autopsy. Review of the chest X-ray on admission (figure 1) shows an opacification presenting a convex surface to the hilum, a feature indicating either a loculated pleural effusion or a retropleural process. Since a loculated effusion was not present at autopsy, we conclude that the haemorrhage was retropleural at the time of presentation. We surmise that the haemorrhage initially stabilised due to the tamponade effect of the tense retropleural haematoma on a bleeding vessel in the chest wall, and that death may have followed a reduction in pressure due to aspiration and consequent resumption of haemorrhage.

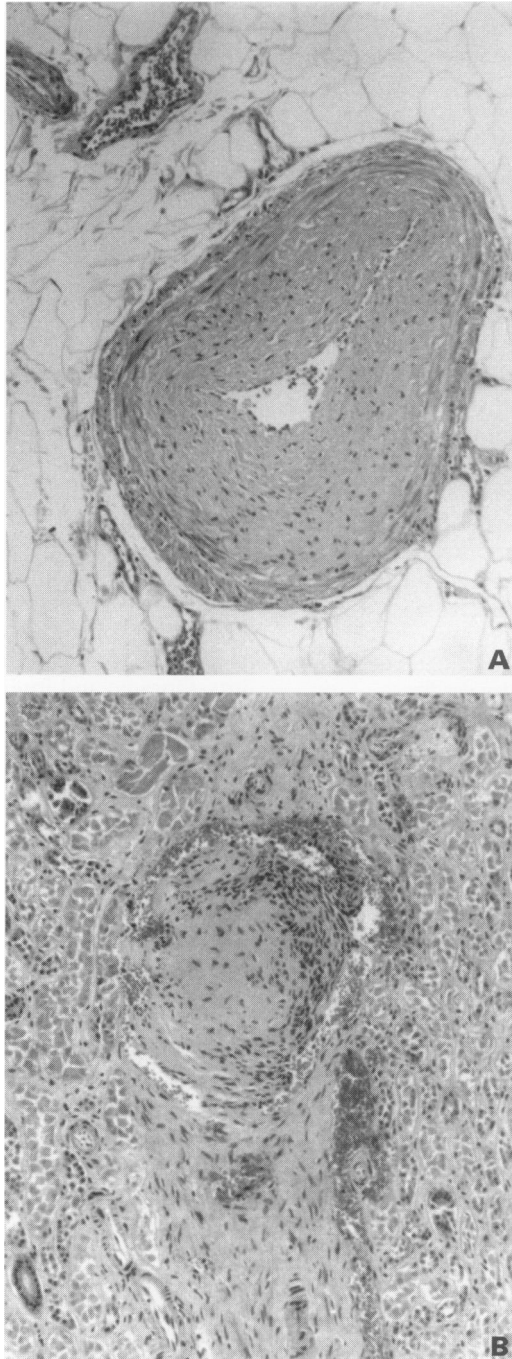


**Figure 1** A plain chest X-ray shows the large dense, left-sided opacity, convex surface towards the pulmonary hilum

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**Figure 2** (A) Submucosal vessel in the stomach shows florid fibro-intimal hyperplasia with severe luminal narrowing; (B) nodular proliferation of spindle cells within the intima is seen in this intrarenal artery

#### HISTOLOGY

Sections of stomach and kidney showed occlusive changes corresponding to the vasculopathy described in von Recklinghausen's disease (figure 2). There was pronounced fibro-intimal thickening and, in renal vessels, intimal nodules of spindle cell proliferation. These spindle cells have been shown by electron microscopy to be smooth muscle cells.<sup>2</sup> The gastrointestinal tumours were composed of spindle cells showing mild pleomorphism, no mitotic figures or necrosis, and mild immunopositivity for S100, a marker for neural differentiation.

#### Discussion

Vasculopathy in neurofibromatosis appears to consist of two different pathological processes.<sup>2,3</sup> Large vessels such as the aorta, proximal renal arteries and carotid arteries show adventitial infiltration by proliferating Schwann cells with secondary changes in intima and media leading to aneurysmal change or stenosis. Smaller vessels show a vascular dysplasia unrelated to Schwann cell proliferation and consisting of intimal proliferation, nodular proliferation of smooth muscle cells, fragmentation of elastica, thinning or loss of the media and adventitial fibrosis. Reubi originally described three categories of vasculopathy in vessels less than 1 mm in diameter:

- luminal obliteration by concentric intimal proliferation, in vessels of 50 to 400  $\mu$ m
- intimal fibrohyaline thickening, thinning of media, elastic fragmentation and aneurysmal dilation (500–1000  $\mu$ m)
- well-defined spindle cell proliferations (100–700  $\mu$ m).

This small vessel vasculopathy may be a mesenchymal abnormality unrelated to the neural malformations. Although most frequent in the renal vessels, lesions are also seen in a wide range of other sites and may simulate vasculitic syndromes.<sup>1</sup> Vascular involvement may occur in as many as 10% of cases of Type I (central) von Recklinghausen's disease. Its incidence in Type 2 is not recorded.

Spontaneous haemothorax in the general population may be caused by a ruptured aortic aneurysm, rupture of pericardial adhesions, arterio-venous fistula, neoplasia and endometriosis. Pulmonary infarction would be expected to cause intrapleural rather than retropleural haemorrhage. Recently reported cases of massive haemothorax in von Recklinghausen's disease include a 55-year-old man with mediastinal haemorrhage due to neurofibromatous infiltration of the right subclavian artery,<sup>4</sup> spontaneous rupture of an intercostal artery in a 41-year-old man (no histology performed),<sup>5</sup> rupture of an intercostal artery in a 44-year-old woman at the site of penetration of gelatinous Schwannoma,<sup>6</sup> and two cases of haemothorax in pregnant von Recklinghausen patients,<sup>7</sup> a 37-year-old gravida 7 with involvement of the right subclavian artery by a plexiform neurofibroma, and a 26-year-old gravida 3 with bleeding from a paravertebral pleural defect, presumably from an intercostal artery (no vascular histology). The latter two cases occurred at 34 and 36 weeks of pregnancy. Fuyuno *et al*<sup>8</sup> described a 17-year-old man who developed a haemothorax due to bleeding from a massive malignant Schwannoma, presumed to be from abnormal tumour vessels. More recently, Miura *et al*<sup>9</sup> have reviewed the Japanese literature and discuss 12 cases of spontaneous haemothorax, nine of whom were female, with ages ranging from 31 to 67 years. Of these, four involved an intercostal artery, four a subclavian artery, two an internal thoracic artery, one an innominate artery and in one the source was unknown. The left side was involved in eight of these patients. Overall mortality was 50%. The

pathological lesion was described in seven cases; five showed neurofibromatous infiltration or compression. In Miura's case,<sup>9</sup> neurofibromatous infiltration of the subclavian wall was not found, but there was evidence of vascular dysplasia, consisting of decreased elastic fibres and deranged smooth muscle. In the absence of a demonstrable intrathoracic tumour, we believe that a similar vascular dysplasia was responsible for haemorrhage in our case.

Out of 18 patients reported in the literature,<sup>4-9</sup> plus our own case, the four patients who had no surgical intervention died. Of the remaining 15 who underwent thoracotomy, nine survived.

Von Recklinghausen's disease is a relatively common disorder and this syndrome of spontaneous haemothorax deserves wider rec-

ognition in view of its high mortality. To the pathologist, it is another addition to the ever-lengthening list of causes of sudden death, but knowledge of the syndrome will help to explain an otherwise puzzling accumulation of blood behind the pleura or within the mediastinum and guide the search for the cause. For clinicians, recognition of the syndrome should lead to urgent referral to the nearest cardiothoracic centre. The configuration of the radiological opacity and the ease with which frank blood is withdrawn on paracentesis should suggest the diagnosis in a patient with cutaneous manifestations of neurofibromatosis.

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## The best management for 'crescendo biliary colic' is urgent laparoscopic cholecystectomy

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### Summary

Gallbladder disease due to stones is well recognised as falling into two categories, presenting with either chronic symptoms or developing acute cholecystitis or other complications. We describe an intermediate group of 14 patients (11 women, three men, median age 31 years) presenting with 4-14 days of at least daily attacks of resolving biliary colic, who underwent early laparoscopic cholecystectomy within 24 hours of presentation. None had any evidence of acute inflammation, either at laparoscopy or on histology. Their surgery was straightforward with operating times ranging from 35-80 minutes and no complications. Patients with 'crescendo biliary colic' are often young women who can rarely afford invalidity. Rather than the current practice of analgesia for each attack and elective surgery weeks later, they are optimally managed by urgent laparoscopic cholecystectomy, preventing the development of complications and

minimising the need for further medical involvement.

**Keywords:** gallstones; biliary colic; laparoscopic cholecystectomy

Patients with gallstones are usually regarded as having either intermittent biliary colic resulting in 'chronic' inflammatory changes or 'acute' complications such as cholecystitis.<sup>1</sup> Most surgeons and general practitioners will, however, be familiar with a group of patients developing acute cholecystitis or other complications of gallstones, who give a history of dramatically worsening biliary colic over the preceding couple of weeks. Such patients have frequently seen the emergency services with episodes of pain but in the UK are rarely admitted until their pain fails to resolve and acute cholecystitis or other complications supervene. Even when admitted, they are usually pain-free the following day and are discharged pending elective surgery or further emergency admission.

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