

# Cor pulmonale in an adult secondary to Niemann-Pick disease

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Niemann-Pick disease occurs most commonly in children of Ashkenazi Jewish origin. A more benign adult form of the disease with survival up to and beyond the age of 50 is now well recognised.<sup>1</sup> Further division into five separate subclasses designated A-E, each with different clinical features, has been proposed.<sup>2</sup>

In the adult form of the disease pulmonary infiltrates are a recognised radiological finding. Those cases which have been examined pathologically have shown pulmonary fibrosis, and foam cells have been seen in distended alveoli.<sup>3</sup> No case has to our knowledge been reported in which the severity of lung disease has led to right ventricular failure. We report such a case.

## Case report

The patient was a girl born on 21 December 1956 of Caucasian parents and first came to medical attention at a school medical examination at the age of 7, when massive hepatosplenomegaly was discovered. She was noted to be below the third centile for both height and weight. The only biochemical and haematological abnormalities at this time were a slightly raised transaminase level at 83 units/litre (normal range 10-40), a slight leucopenia ( $3.8 \times 10^9/l$ ), and a mild thrombocytopenia ( $119 \times 10^9/l$ ). Liver biopsy was performed and said to show a histological picture suggestive of von Gierke's disease. The slides, however, were subsequently re-examined and the diagnosis was changed to that of an unspecified lipoidosis. A chest radiograph in 1963 was reported as normal but a further film in 1964 was said to show some coarse reticular shadowing at the bases.

The patient remained quite well until 1981. In January of that year she was admitted to hospital as an emergency with an acute febrile illness which responded to erythromycin. From the previous descriptions the hepatosplenomegaly was unchanged but the chest radiograph showed increased basal reticular shadowing. During the course of this illness there was evidence of increasing haemolysis and she was treated with prednisolone. By February she was well again and having no medication. From May until December 1981 she became progressively more breathless

and developed ankle swelling for the first time in late December. This was treated with diuretics, with good symptomatic improvement.

In 1982 she was admitted to hospital in an attempt to make a definitive diagnosis. By this time she was breathless walking up hills but was otherwise well and employed full time as a hairdresser. Physical examination showed a slightly built young woman with central cyanosis; there was a right ventricular lift, a third heart sound and a loud pulmonary component to the second heart sound, and sparse crackles at the lung bases. There was no peripheral oedema, however, and the jugular venous pressure was not raised. Abdominal examination showed gross splenomegaly extending almost to the right inguinal ligament and 10 cm hepatomegaly. The chest radiograph (fig 1) showed a coarse reticular pattern throughout both lungs, more prominent in the middle and lower zones; the proximal pulmonary arteries were enlarged but the cardiothoracic ratio was normal. Spirometry showed a restrictive ventilatory defect with an FEV<sub>1</sub> of 1.7 l (predicted 2.6 l) and FVC of 2.0 l (predicted 3.13 l). Arterial blood gas measurement showed: pH 7.43, oxygen tension (P<sub>O<sub>2</sub></sub>) 4.7 kPa, carbon dioxide tension (P<sub>CO<sub>2</sub></sub>) 3.1 kPa, bicarbonate concentration 15.2 mmol (mEq)/l. The haemoglobin was 17.1 g/dl with normal indices and the white cell count was normal. Serum alkaline phosphatase, acid phosphatase, urea, and electrolyte concentrations were all normal. The electrocardiogram showed right axis deviation, P pulmonale, and T wave

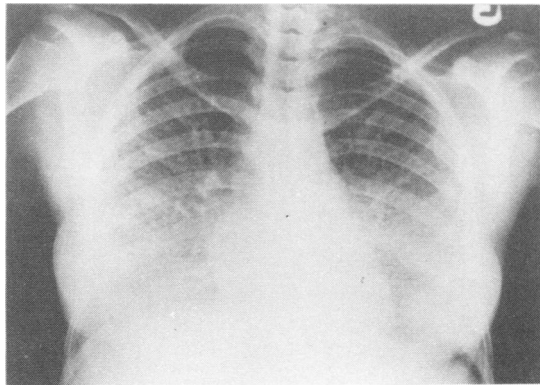


Fig 1 Chest radiograph showing extensive nodular pulmonary infiltrate.

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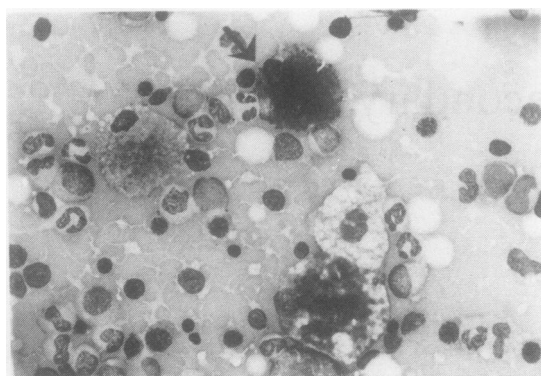


Fig 2 Bone marrow specimen showing enlarged histiocytes with a "foamy" appearance together with a "sea blue" histiocyte (arrowed), both characteristic of Niemann-Pick disease. (Leishman stain,  $\times 300$ .)

inversion in the right ventricular leads. The echocardiogram showed enlargement of both the right atrium and the right ventricle, dilated pulmonary arteries, and abnormal pulmonary valve motion, all of which were characteristic of pulmonary hypertension. Bone marrow examination was performed and this showed a normal background bone marrow with large numbers of histiocytes containing abnormal lipid deposits. Some of these had the appearance of "sea blue" histiocytes and others showed characteristic features of Niemann-Pick disease (fig 2).

### Discussion

Niemann-Pick disease is characterised by an absolute or relative deficiency of the enzyme sphingomyelinase, which

catalyses the reaction:

sphingomyelin +  $H_2O \rightarrow$  ceramide + phosphoryl choline.

Patients with the infantile form of Niemann-Pick disease have virtually no sphingomyelinase activity, whereas in the adult form there is detectable but reduced enzyme activity. This patient would appear to belong to the type B subclass,<sup>2</sup> with severe visceral disease, no neurological disease, and survival beyond childhood. The presence of small numbers of sea blue histiocytes is consistent with Niemann-Pick disease as these cells are found in several conditions besides so called sea blue histiocytosis.<sup>4</sup>

In the few previously reported cases normal lung volumes and considerably reduced carbon monoxide transfer factor have been found<sup>5</sup> but cor pulmonale has not previously been documented in this condition. The appreciable hypoxia in our patient is likely to have been an important factor in the development of pulmonary hypertension and right heart failure and control of the fluid retention has required increasing doses of diuretics.

We would like to thank Dr Stewart Hunter for performing the echocardiogram and Dr Mansur Qureshi for interpretation of the bone marrow appearances.

### References

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