Mast cells in pulmonary haemosiderosis

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SUMMARY A case of childhood pulmonary haemosiderosis with a fourfold increase in mast cells in the lung is described. This finding is discussed in relation to the pathogenesis of the disease. Comparison is made with controls, and the use of disodium cromoglycate is advocated.

Pulmonary haemosiderosis (PH) represents the final common pathway of a variety of diseases,1 some of which such as passive venous congestion have been recognised for many years, while others such as immune complex deposition have been recently delineated.2 A large core of cases of unknown aetiology and pathogenesis remains, however, classified as idiopathic pulmonary haemosiderosis (IPH) and characterised clinically by recurrent episodes of dyspnoea, cough, haemoptysis, pulmonary infiltrates, and anaemia. Within this group the childhood and adult forms differ to a degree that suggests they may be different entities.

Case history

A three year old boy developed recurrent respiratory distress and pallor. In the 6 weeks before admission he had suffered three episodes of dyspnoea and reduced exercise tolerance, each lasting one week. There was a history of mycoplasma pneumonia at 5 months of age, with a normal chest radiograph three months later. The child was clinically anaemic but otherwise normal. Shortly after admission, episodes of tachypnoea and cough developed and he became increasingly pale. He had iron deficiency anaemia and radiographs showed widespread pulmonary infiltrates. Other investigations including serum protein electrophoresis, antibody screen, mycoplasma titre, cold agglutinins and serum C3 and C4 were normal.

Treatment consisted of blood transfusion and short courses of prednisolone during 6 acute episodes. On this regimen a favourable response was obtained rapidly within two or three days in each instance. Because of the possibility of an underlying infective process, an open lung biopsy was performed. In addition to the features of IPH shown by light and electron microscopy,2 the biopsy showed increased numbers of mast cells in the alveolar walls.

Treatment with disodium cromoglycate began and resulted in regression of dyspnoea, maintenance of a steady haemoglobin value, and clinical cessation of pulmonary bleeding for a period of 14 weeks. An episode of massive intrapulmonary haemorrhage then occurred and the patient died. At necropsy the lungs showed the characteristic brown induration with superimposed recent bleeding. Abnormalities shown by light and electron microscopy were similar to those seen in the lung biopsy, with alterations in the mast cells consistent with cromoglycate treatment.3 The other organs, in particular the kidneys, were normal. Lung tissue from this child was compared with that from three adults with PH (one case each of mitral stenosis, immune complex mediated PH, and adult IPH) and three normal adult controls (Fig. 1) using light and electron microscopy.

Fig. 1. Number and percentage of mast cells in our patient's lung (before and after treatment) and in adult controls (three with PH and three healthy controls).
microscopy, and including quantitative mast cell analysis as described by Fox et al.\textsuperscript{4}

Materials and methods

The diagnosis of IPH in this patient and the adult control patient with IPH was established according to the criteria of Thomas and Irwin.\textsuperscript{1} Tissue was processed in the usual fashion for light microscopy and stains used included toluidine blue for mast cell metachromasia. Electron microscopy was carried out on a Jeol 100CX. In each case the number of mast cells per unit area, the area of lung occupied by mast cells, and the number and type of granules within the mast cells were assessed. Techniques used included image analysis quantification and direct counting of mast cell granules in random electron microscopy fields. To avoid sample error due to regional variations in tissue morphology, observations were confined to subpleural lung parenchyma in all cases.

Results

The number of mast cells in the child's lung before administration of disodium cromoglycate was four times greater than that of controls, although the number of granules/cell was the same. After disodium cromoglycate treatment the average number of granules/cell doubled with a concurrent fall in the total number of cells (Fig. 1). The proportion of different granule types (scroll, reticular, mixed, and empty) did not alter with treatment. There was, however, considerably more pleomorphism of the granules after disodium cromoglycate treatment (Fig. 2).

Discussion

Our knowledge of the role played by the mast cell in health and disease remains incomplete in spite of much investigation.\textsuperscript{5} Apart from passing reference to a slight increase in mast cell numbers in IPH by early workers in this field,\textsuperscript{6} individual cases with increased mast cell populations have not been described. There was no evidence in this child that the mast cell accumulation was caused by atopy or was part of a systemic mastocytosis. The relevance of the serologically and radiologically documented mycoplasma pneumonia some years previously is unclear.

While we are unable to show an aetiological relation between the high mast cell count and pulmonary haemorrhage in our patient we suspect

Fig. 2. Random view of alveolar wall before treatment with disodium cromoglycate, showing mast cells (MC) and a haemosiderin-laden macrophage (PLM) in the alveolar wall. Inset lower right is a mast cell after treatment. Note increase in number of granules and their pleomorphic appearance. ALV=alveolar space. (× 4000).
that heparin, the principal product of human mast cells, was pathogenetically implicated, probably by aggravating and prolonging bleeding. The stimulus which initiates pulmonary haemorrhage in childhood IPH remains unknown but because of the increased granulation of the mast cells in the lung at necropsy it is obvious that in this child it was not mast cell degranulation that precipitated the terminal haemorrhage.

Assessment of the therapeutic effect of disodium cromoglycate in this disease is bedevilled by the known tendency of childhood IPH to relapse and remit. We feel that further cases must be investigated for mast cell accumulation in the lung and that disodium cromoglycate should, in the meantime, be added to the empiric treatment regimens that are currently used.

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References

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Congenital pulmonary lymphangiectasis associated with pleural effusions

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SUMMARY We report a case of congenital pulmonary lymphangiectasis in which pleural effusions were shown antemortem by thoracentesis. We suggest that disordered lymphatic drainage led to the production of the effusions.

Congenital pulmonary lymphangiectasis is a rare congenital anomaly most often presenting as intractable respiratory distress from birth. The lungs show diffuse dilatation of the interlobular and subpleural lymphatics. It has been suggested that pleural effusions might occur in association with congenital pulmonary lymphangiectasis due to disordered lymphatic drainage, but such an association has not hitherto been reported, although congenital pulmonary lymphangiectasis has been found in babies with hydrops.

Case report

A boy weighing 2.7 kg was delivered after the fifth pregnancy of a 34 year old Caucasian woman who had previously had three normal children and one miscarriage. The pregnancy had been complicated by rhesus isoimmunisation, but examination of amniotic fluid at 31 weeks' gestation suggested that the fetus was only mildly affected. At 34 weeks' gestation there was spontaneous rupture of the membranes and drainage of copious golden-yellow liquor. Caesarean section was performed because of a transverse presentation. Delivery was uneventful and the infant had no oedema or other external abnormalities. The cord blood haemoglobin value was 18.3 g/dl and cord blood bilirubin was 45 μmol/l (2.63 mg/100 ml). A Coombs's test was not done. The infant was cyanosed, made poor respiratory efforts, and there was poor chest expansion during artificial ventilation. At 7 minutes of age approximately 30 ml of clear yellow fluid was aspirated from each hemithorax, but there was no improvement. Bilateral pneumothoraces developed and were drained, but ventilation did not improve and he died aged 3 hours.

Chest radiograph at 2 hours of age showed noticeable alveolar shadowing, changes suggestive of bilateral interstitial emphysema, and bilateral pneumothoraces despite the presence of chest drains. The pleural fluid contained red blood cells, (8200/mm³), and white blood cells (100/mm³) most of which were lymphocytes and had a protein content of 13 g/l of which 11 g/l was albumin. No organisms were seen on direct examination and no bacteria were cultured. Cultured blood lymphocytes had a normal male karyotype.