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CASE REPORT

Fibrosing alveolitis in an infant

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Fibrosing alveolitis in an infant. J. Riedler, A. Golser, I. Huttegger.
ABSTRACT: A three month old female infant presented with unproductive cough, diffuse bilateral fine crackles, tachypnoea and failure to thrive despite a four month therapy with β_2-agonists and antibiotics. A chest radiograph showing bilateral perihilar infiltrates and a patchy infiltrate in the right upper lobe and lingula did not explain the physical examination with diffuse bilateral fine crackles.

As the condition did not improve and arterial oxygen tension (Pao_2) and oxygen saturation decreased during the following two months, an open lung biopsy was performed. The surgeon described the lungs as rubbery in consistency and histological findings showed patchy mild interstitial fibrosis and thickened alveolar septa.

A therapy with prednisone daily was started and given over a period of four months, but did not show sufficient improvement. Only after addition of azathioprine was clinical improvement and normalization of blood gases noted.
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Fibrosing alveolitis is a rare diffuse lung disease in children. The main symptoms are tachypnoea or dyspnoea, chest wall retractions, diffuse bilateral crackles, unproductive cough, poor weight gain and cyanosis [1]. The diagnosis is confirmed by lung biopsy. Histology demonstrates interstitial thickening of alveolar walls and the presence of large mononuclear cells in the alveolar spaces [2]. The term "fibrosing alveolitis" was proposed by SCADDING [3] in 1964. As early as 1944, HAMMAN and RICH used the term "diffuse interstitial fibrosis of the lungs" [4]. LIEBOW *et al.* [5] (1965) observed intra-alveolar desquamation of large mononuclear cells in the lungs of patients suffering from a chronic interstitial pneumonitis and called the disease "desquamative interstitial pneumonia" (DIP). They wanted this histological feature to be separated from that found in usual interstitial pneumonitis (UIP) [5]. By the use of electron microscopy it became apparent that the term "desquamated" was probably misleading because many of the cells were macrophages also seen in UIP varying mainly in relative numbers [2]. Therefore, many authors consider DIP and UIP to be part of the same disease and not specific disease entities [2, 6, 7].

We present the case of an infant with clinical and histological findings of fibrosing alveolitis, who improved slowly during the treatment with corticosteroids and azothioprine. Six months after discontinuation of therapy the patient is symptom free and thriving.

Case report

A three month old female infant was admitted to hospital presenting with marked tachypnoea, respiratory retractions, cough and failure to thrive. She was born after a normal pregnancy with a birth weight of 3.20 kg. Six weeks after birth she was noted to have tachypnoea and cough and was treated with antibiotics and β_2-agonists. Despite this therapy she did not improve and was, therefore, admitted to hospital. On admission she was at the 25th percentile for weight and the 50th percentile for height. Diffuse bilateral fine crackles were audible on physical examination. Chest radiographs showed bilateral perihilar infiltrates and a patchy infiltrate in the right upper lobe and lingula. Blood cell count, blood gas values, immunoelectrophoresis, immunological studies, sweat chloride concentration and results of routine biochemical studies were normal. Cultures for viruses from the nasopharyngeal swab as well as serum titres for virus, *Mycoplasma pneumoniae* and *Chlamydia* were negative. Results of serological tests for autoimmune diseases were also negative. Bronchoscopy and lung scan were normal. A computer tomograph of the lung gave no further information.

During the following eight weeks the clinical condition did not improve, the physical examination with diffuse fine crepitations over both lungs remained unchanged, the patient's weight fell from the 25th to less than the 3rd percentile, arterial oxygen tension

(Pao_2) decreased to 60 mmHg and oxygen saturation reached 87% during sleep. Therefore, an open lung biopsy was performed. The surgeon described the lungs as rubbery in consistency. Histological findings showed patchy mild interstitial fibrosis, thickened alveolar septa and patchy replacement of the usual flat alveolar lining cells by plump round cells, which were identified as hyperplastic type II pneumocytes by electron microscopy. Some alveolar spaces contained desquamated cells, which turned out to be macrophages. Histiocytic infiltration and collagen deposition contributed to the thickening of the wall (figs 1 and 2). These histological findings, although mild, confirmed the diagnosis of fibrosing alveolitis and the therapy with prednisone daily (2 $mg \cdot kg^{-1}$) was started and given for four months. As the child showed no real improvement azathioprine (4 $mg \cdot kg^{-1}$) was added. Clinical improvement was noted within some weeks. The prednisone was gradually discontinued during the following eight months.

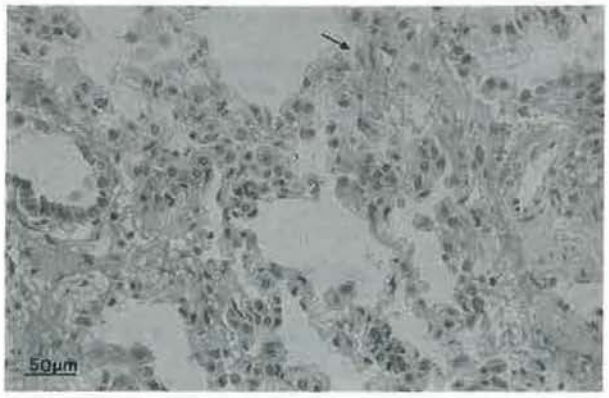

Fig. 1. – Irregular thickening of alveolar septa accompanied by little cellular desquamation into the alveolar spaces. On the left of the figure a normal bronchiolus can be seen. The arrow marks the detail shown in figure 2, (fuchsin-methylene blue).

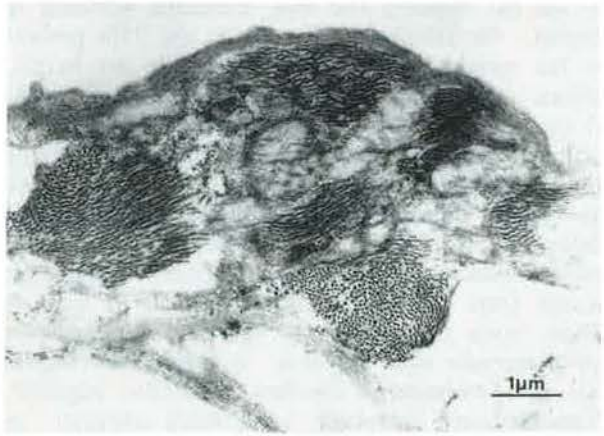

Fig. 2. – Marked thickening of alveolar septa by fibrous tissue (electronmicroscopy).

The chest radiograph showed little improvement. One year after the initiation of prednisone treatment and eight months after the addition of azathioprine, all medication was stopped. Six months after discontinuation of therapy the child's respiratory rate has normalized, she is no longer coughing, she has gained weight although slowly, her activity level and blood gas values have returned to normal. The shape of her thorax still shows deformities due to fixed retractions.

Discussion

Physical and histological findings in our patient satisfy the criteria for a diagnosis of mild fibrosing alveolitis. The abnormal physical signs were tachypnoea, cough, retractions and diffuse fine crepitations over both lungs. In general, the radiological findings involve both lungs equally but are often predominant in the lower zones. In the early course of the disease, localized linear or nodular densities are seen, whereas with progression reticular and reticulonodular patterns begin to appear [2]. Terminal stages usually show coarse reticulation often associated with cystic lesions and bullae [2]. On rare occasions however, chest radiographs can be normal or atypical, especially in early stages [1, 2, 8]. Also, in our patient the radiological findings were not typical for idiopathic pulmonary fibrosis and they did not progress.

CRYSTAL *et al.* [2] found a correlation between the degree of fibrosis on lung biopsy and the severity of disease estimated by chest film. The histological features of the lung are diagnostic and normally show different degrees of thickened alveolar septa and alveolar spaces filled with granular pneumocytes [2, 9]. Some authors find a histological subclassification into desquamative interstitial pneumonitis, lymphoid interstitial pneumonitis and usual interstitial pneumonitis useful because the three show different response to treatment and have different prognosis [10–12]. Our patient showed mild diffuse interstitial fibrosis with irregulary thickened alveolar septa and little cellular desquamation into the alveolar spaces resembling desquamative interstitial pneumonia according to the classification used by LIEBOW *et al.* [5]. The latter researchers found that this particular form of "chronic interstitial pulmonary disease" tended to follow a relatively benign course.

In general, the prognosis for patients with chronic interstitial pneumonitis is poor and the mortality rate is high, especially for those with usual interstitial pneumonitis [6, 11, 12]. Steroids, azathioprine, chlor-ambucil and cyclophosphamide have been used with varying success [6, 13–16]. The children reviewed by HEWITT *et al.* [6] who improved with corticosteroid, did so within six weeks of starting treatment. This was not the case in our patient, who seemed to show improvement only after azathioprine was added to the corticosteroid treatment. Since spontaneous resolution has been observed it would, however, be wrong to state categorically that the addition of azathioprine was the reason for the recovery. KEREM *et al.* [10] found high doses (pulses)

of methylprednisolone and daily oral doses of hydroxychloroquine to be effective in the treatment of infantile chronic interstitial pneumonitis.

From the course of the disease in our patient we learn: 1) that the addition of azathioprine may be effective if there is no improvement on steroid therapy alone, even after several months; and 2) that there may be no correlation between typical clinical findings and radiological and histological features.

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