An additional clinicohistopathological observation of neonatal pulmonary interstitial glycogenosis is described, confirming the findings in the original description by Canakis and coworkers [1]. The most striking finding is the presence of glycogen-laden cells within the interstitium of the lung. The outcome is favourable relative to other chronic interstitial lung diseases. We propose an alternative term as “glycogenosis” refers to a group of inborn errors of metabolism that are not related to this disease.

A few hours after birth, a term infant developed signs of respiratory distress and was transferred with supplemental oxygen. Congenital heart disease was ruled out. In the hours after admission, the respiratory condition deteriorated and the baby was intubated and treated with surfactant, high frequency oscillation and nitric oxide inhalation for 12 days. Tracheal aspirate showed normal surfactant protein C and B. Chest X-ray films showed progressive hyperinflation and evolution to a mixed interstitial and alveolar pattern.

Owing to chronic oxygen dependency and obvious tachypnoea, a high resolution CT scan of the chest was performed on day 55 demonstrating distortion of the lung architecture with the presence of linear opacities, mixed with areas of overinflation/emphysema and ground glass opacity. In the further work-up, cystic fibrosis was excluded and serum alpha-1-antitrypsin was normal. An infectious cause including Chlamydia, adenovirus, coxackievirus, influenza, parainfluenza, Epstein-Barr virus, cytomegalovirus and Mycoplasma could not be demonstrated. Bacterial cultures remained sterile. A Mantoux test was negative.

On day 68, an open lung biopsy was performed. Haematoxylin and eosin stained sections revealed diffuse thickening of the alveolar septae (Fig. 1A,B), while frozen sections showed the presence of abundant glycogen in the cytoplasm of the interstitial cells (Fig. 1C,D). Ultrastructural analysis of lead-contrasted ultrathin sections showed interstitial cells containing intracytoplasmic pools of high contrast granular material compatible with monoparticulate glycogen.

Methylprednisolone pulse therapy was initiated at 10 mg/kg per day once daily for 3 days every month. There was no effect on oxygen need after 4 monthly treatments. The child was discharged home on supplemental oxygen at the age of 6 months and steroid therapy was continued monthly. Oxygen requirement decreased gradually and could be stopped at the age of 10 months, as was steroid therapy. He remained well except for a brief hospitalisation at the age of 1 year for a viral respiratory infection and 10 days hospitalisation at the age of 19 months because of bronchiolitis due to respiratory syncytial virus.

Canakis and coworkers described seven cases of chronic interstitial lung disease (ILD) presenting with an atypical respiratory disorder during the neonatal period [1]. Most patients were symptomatic within 24 h after birth. Infectious or inflammatory causes of respiratory insufficiency were ruled out. All patients showed uniform histological features: thickened interstitium with immature interstitial cells containing abundant cytoplasmic glycogen. Although cytoplasm of occasional type 2 cells may contain residual aggregates of
glycogen particles in full-term neonatal lungs, large cytoplasmic pools of glycogen are normally undetectable in pulmonary interstitial cells either during fetal development or post-natally. The authors proposed the term “pulmonary interstitial glycogenosis” for that new variant of neonatal ILD and suggested an abnormal differentiation of pulmonary mesenchyme as pathogenic mechanism.

This case could also be diagnosed as pulmonary interstitial glycogenosis, principally based on the presence of abundant diastase-sensitive glycogen both in cryo-sections and at the ultrastructural level. We emphasize the importance of PAS-staining and electron microscopy in the histopathological work-up of neonatal interstitial lung disease. Since the PAS signal was barely visible on formalin-fixed paraffin-embedded material, one should always store snap-frozen tissue pieces, as well as material for ultrastructural analysis when considering the abovementioned diagnosis.

The radiological abnormalities, although non-specific, are congruent with the findings of Canakis et al. [1]. It remains to be determined whether the accumulation of glycogen is specific enough and unequivocally diagnostic, making it an entity distinct from cellular interstitial pneumonitis (CIP). Schroeder et al. [4] did not perform special stains for glycogen on the tissue samples of their patients with CIP.

Pathogenically, an abnormality in lung differentiation involving interstitial mesenchymal cells has been postulated [1]. The term “glycogenosis” is a provocative denomination as it refers to a group of inborn errors of metabolism with well known aetiology; however, there is no deficiency of any of the enzymes related to the glycogenoses [1]. As there is no link to the metabolic disease, we suggest that the term “pulmonary interstitial glycogen accumulation disorder” should probably be preferred to “pulmonary interstitial glycogenosis”.

In about 40% of cases of ILD, a favourable response to corticosteroids is observed regardless of the clinical presentation or histological appearance of the disease [2]. In this patient, oxygen requirement gradually decreased after the fifth methylprednisolone pulse dose. As there is almost no inflammation in this interstitial disease, corticosteroid therapy could exert its effect, if any, by acceleration of glycogenolysis [3]. In the near term lung glycogenolysis in the alveolar epithelium is accelerated by the action of steroids. It remains speculative whether the same applies to glycogen abnormally stored in mesenchymal cells. Finally, the slowly progressive amelioration may merely reflect the natural course of the disease.

The clinical course of our case confirmed the favourable prognosis of pulmonary interstitial glycogenosis, different to most other forms of neonatal interstitial pneumopathy [1, 2]. There is progressive clinical and radiological amelioration over the first months of life, but subclinical expansion of the lungs may persist for years.

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References