Paediatric interstitial lung disease

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AIMS

At the end of the session, participants will know about important interstitial lung diseases in children including newly described entities.

Specifically, participants will understand
- epidemiology,
- classification,
- clinical presentation,
- diagnostic procedures,
- treatment strategies,
- prognosis regarding these diseases.

SUMMARY

Introduction

Paediatric interstitial lung diseases (ILDs) are rare, with no good prevalence data available. The estimated prevalence is around 1 in 100,000 compared to 60-80 in 100,000 in the adult population. Further, paediatric ILD comprises a much broader spectrum of disorders than in adults, linked to the fact that the various diseases occur in the context of lung growth. Around half of cases with paediatric ILD are diagnosed in the first two years of life, with a predominance of paediatric entities such as neuroendocrine cell hyperplasia of infancy (NEHI), pulmonary interstitial glycogenosis (PIG), genetic disorders of surfactant metabolism, and disorders of lung growth and development. In older children, the pathological conditions share similarities with the processes observed in adults. Around 10% of cases are familial.

Classification

More than ten years ago, a European Respiratory Society (ERS) Task Force on chronic interstitial lung disease in immunocompetent children collected the at that time largest series of children with ILD, a third of them below 2 years of age. Subsequent large series also distinguished between the groups 0-2 years of age and above 2 years of age. A novel detailed classification scheme was first applied to young children and subsequently evaluated in children 2-18 years of age. Disorders more prevalent in infancy include „diffuse developmental disorders“ (e.g. alveolar capillary dysplasia with misalignment of pulmonary veins), „growth abnormalities reflecting deficient alveolarization“ (e.g. chronic neonatal lung disease), „specific conditions of undefined aetiology“ (e.g. NEHI, PIG), and „surfactant dysfunction disorders“ (e.g. surfactant protein C mutations). The other four categories comprise „disorders related to systemic disease processes“ (e.g. immune-mediated/collagen vascular disorders), „disorders of the normal host - presumed immune intact“ (infectious/post-infectious processes), „disorders of the immunocompromised host“ (e.g. opportunistic infections), and „disorders masquerading as ILD“ (e.g. arterial hypertensive vasculopathy).
Management

The clinical presentation of paediatric ILD is non-specific, contributing to poor recognition of the disorders which may be confused with other diseases. There may be a history of cough, tachypnoea, respiratory distress, and failure to thrive. Physical examination may reveal tachypnoea, retractions, crackles, cyanosis, and allows to assess disease severity. The chest radiograph may be normal, or show non-specific findings, and has severe limitations. HRCT has higher diagnostic accuracy (sometimes a specific diagnosis can be made), offers more prognostic information and provides guidance for lung biopsy. Echocardiography is mandatory, to assess pulmonary hypertension and to exclude cardiac mimics of ILD. Laboratory tests should be streamlined according to clinical findings and/or imaging. Many children will require a lung biopsy to establish a diagnosis.

Supportive care includes administration of oxygen for chronic hypoxaemia, adequate nutrition, annual immunisation with influenza vaccine along with other routine immunisations against respiratory pathogens, aggressive treatment of infections, strict avoidance of tobacco smoke and other air pollutants, and the selective use of bronchodilators. In addition, the treatment of associated gastro-oesophageal reflux, whether it is a primary or secondary phenomenon, may be important in the management of children with ILD.

A few children with very mild disease do not require any pharmacologic treatment. In the majority of children with ILD, however, treatment with immunosuppressive, antiinflammatory, or antifibrotic drugs is required. As yet, there are no randomised controlled trials of treatment. Systemic corticosteroids (oral prednisolone, or intravenous methylprednisolone pulses), oral hydroxychloroquine, and oral azithromycin are the most commonly used drugs. However, responses to corticosteroids and hydroxychloroquine are highly variable in many types of ILD. If these options fail, other immunosuppressive or cytotoxic agents, such as azathioprine, cyclophosphamide, cyclosporine or methotrexate, may be used.

Prognosis

The prognosis for children with ILD is extremely variable, but paediatric ILD appears to be more responsive to therapeutic strategies than adult ILD. While patients with NEHI and PIG generally do well in the long term, many children with genetic abnormalities of surfactant function do poorly. For many disorders, there is no correlation between the response to treatment or the clinical outcome and the initial pattern of the chest radiograph or HRCT scan changes, or the histological findings in lung biopsy specimens.

Conclusions

Despite the rarity of these disorders, there has been considerable increase in our understanding of the genetic aetiologies, the mechanisms involved in the pathogenesis, and in the biology and prognostic significance of certain histologic patterns of paediatric interstitial lung disease. Further progress can be made through international collaborations and formation of research networks which will hopefully provide new insights into the understanding and management of these disorders.

FURTHER READING


*Collection of the at that time largest series of children with ILD.*
*Review with focus on pathophysiological mechanisms.*
*Current perspective.*
*Classification scheme of the ChILD Research Co-operative applied to children 0-2 years of age.*
*Classification scheme of the ChILD Research Co-operative applied to children 2-18 years of age, showing fewer diagnoses prevalent in infancy and more overlap with adult diagnoses.*
*Perspectives of parents of children diagnosed with ILD.*
*Description of pulmonary phenotypes in patients with brain-thyroid-lung syndrome.*
*Recent systematic review.*
*Description of clinical, radiological and pathological features of humidifier disinfectant-associated ILD.*
*Official ATS statement on classification, evaluation, and management of paediatric ILD with detailed protocols and recommendations.*
*Large cohort of paediatric sarcoidosis; differences compared with previous paediatric cohorts and with adult forms of sarcoidosis regarding presentation, management and outcome.*
*Extension of the chILD classification to 18 years of age, with additional entities included.*
*Series of 22 children with chronic lung disease associated with SP C mutations.*
*Series of 185 infants and children showing genotype-phenotype correlations.*

*Bombesin-positive neuroendocrine cells decrease with age, independent of disease type.*

**EVALUATION**

1. When comparing paediatric ILD with adult ILD, which of the following statements is false?
   a. The diversity of paediatric ILD is higher.
   b. The frequency of paediatric ILD is higher.
   c. The prognosis of paediatric ILD is better.
   d. The response to treatment of paediatric ILD is better.

Answer B

2. In children 0-2 years of age, the least common symptom of paediatric ILD is:
   a. Cough
   b. Failure to thrive
   c. Fever
   d. Tachypnoe

Answer C

3. Which of the following disorders is inherited in an autosomal dominant way?
   a. ABCA3 deficiency
   b. Pulmonary interstitial glycogenosis
   c. Surfactant protein B deficiency
   d. Surfactant protein C deficiency

Answer D