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Short Communication

Childhood Interstitial Lung Disease: What have we Learned So Far?

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Childhood interstitial lung disease (chILD) comprises > 200 rare heterogeneous respiratory disorders that can affect infants, children, and adolescents [1]. The prevalence (1.5 - 3.8 cases per million [2] and incidence (1.3 cases per million children [3]) of chILD may vary across different studies/analyses depending on study design [1].

Children's interstitial lung diseases, sometimes labelled diffuse parenchymal lung diseases (DPLD), cover many rare conditions that mainly affect the lung parenchyma, leading to impaired alveolar gas exchange. Aetiology and pathogenesis are broad. The leading clinical symptoms are tachypnoea, hypoxemia, retractions, crackles, and failure to thrive [4].

A separate classification for chILD has been developed and updated most recently in 2013 by the chILD Research Network and recommended in the official American Thoracic Society clinical practice guideline on classification, evaluation, and management of chILD in infancy [5].

chILD includes disorders that occur in adults as well as those unique to children, such as neuroendocrine cell hyperplasia of infancy and diseases attributed to genetic conditions and developmental processes [6]. Fibrosing forms of interstitial lung disease (ILD) involve an injurious process that can occur in both children and adults [7]. It is not clear, however, whether the mechanism of fibrosis in the adult lung is similar to fibrosis in children who have ongoing alveolarization [7].

Though fibrosing ILD in children has not been extensively studied and characterised, underlying conditions or contributing factors include surfactant dysfunction disorders such as mutations in SFTPC, ABCA3 and NKX2.1, connective tissue disease-related ILD, and radiation- or drug induced fibrosis [7]. Similar to adults, subgroups of patients with fibrosing chILD exhibit a progressive phenotype characterised by worsening symptoms, lung function decline and increased morbidity [6].

ChILD is usually diagnosed if three of the following features are present: 1) respiratory symptoms (cough, rapid and/or difficult breathing, and exercise intolerance), 2) respiratory signs (tachypnea, adventitious sounds, retractions, digital clubbing, and failure to thrive or respiratory failure), 3) hypoxemia, and 4) diffuse abnormalities on a chest radiograph or computed tomography (CT) scan [5,6].

The choice of which specific diagnostic test to use depends on a variety of factors, including the clinical context and disease severity and duration [2]. Clinical evaluation includes chest radiography, chest CT, pulmonary function testing, infant pulmonary function testing, bronchoscopy with BAL, echocardiography, genetic testing, and/or lung biopsy [5].

Currently, high-resolution computed tomography (HRCT) remains the imaging investigation of choice for the evaluation of ILD [8] HRCT is helpful not only in the diagnosis of ILD but also in monitoring disease activity and severity. However, the main concern with HRCT is the potentially harmful radiation, particularly considering chronicity of ILD and requirement for frequent follow-up examinations. Magnetic resonance imaging MRI is an attractive, nonionizing radiological alternative study to CT. Recent technical advances and refined pulse sequences have increased the diagnostic quality of lung MRI. Various studies in paediatric population have highlighted the role of lung MRI in the diagnosis of pulmonary infections [9,10]. Most of these studies have emphasized on detection of parenchymal abnormalities by lung MRI. In addition, the role of MRI in evaluation of airways has also been suggested [11,12].

A pilot study shows that lung MRI, with current routinely available sequences, is not currently near to replacing HRCT with MRI for the evaluation of paediatric ILD in the immediate future. However, this is only a pilot study, and larger studies are required in this field [13].

There are no approved therapies for ILD treatment in children and, based on anecdotal evidence, the current standard of care comprises the empiric use of systemic steroids, other (steroid-sparing) immunosuppressants, hydroxychloroquine (HCQ) or azithromycin [14,15].

HCQ can inhibit the production of inflammatory cytokines (e.g. IL-1, IL-6, TNFα and INFγ) and the degradation of intracellular cargo via the autophagy pathway [16]. It can interfere with aberrantly produced proteins in cells affected by pathogenic variants in the genes for surfactant protein C [17], ABCA3 [18], COPA [19] and others.

Currently an industry sponsored phase 3 trial of nintedanib in children with fibrosing chILD (ClinicalTrials.gov: NCT04093024) is ongoing, aiming to include at least 30 patients [20]. This points out the extraordinary logistic effort and financial power necessary to recruit such a relatively small number of subjects in this condition.

Preventing infections might reduce morbidity and mortality in chILD. Some study centres use passive immunisations against the human respiratory syncytial virus during the cold season for patients diagnosed with chILD. Furthermore, the use of face masks was highly effective, reducing respiratory tract infections during the COVID-19 pandemic [21].

Several studies stated that achieving an optimal nutritional status is important to maintain better pulmonary function, physical performance, fewer complications, and to prolong survivals among these patients with chronic respiratory illness [22,23].

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