Interstitial Lung Disease in Children – A Report of Four Cases

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Summary

Interstitial lung disease (ILD) is very rare in children. In the majority of cases the aetiology is unknown. Very little is known about the clinical course of this condition in children. Prognosis may be influenced by sex, age of onset of symptoms, radiographic features, presence of right ventricular hypertrophy and histopathology.

We report our experience in managing four children with interstitial lung disease. All these children presented in early infancy with cough, respiratory distress, cyanosis and failure to thrive. Three of these children had finger clubbing and right ventricular hypertrophy. All patients received oral steroids. Chloroquine was added in two patients who showed no response. A trial of oral cyclophosphamide was started in one patient who failed with both drugs. One child is oxygen independent while another is on home oxygen therapy. The other two patients eventually died.

Key Words: Interstitial lung disease, Oxygen therapy, High resolution computed tomogram

Introduction

Interstitial lung disease (ILD) is rare in children and the exact prevalence is unknown Current knowledge is based solely on case reports and small series of patients. Despite the many publications available in adults it remain to be determined whether this information can be applied to children.

The diagnosis requires a high index of suspicion. The clinical presentation can be subtle, nonspecific and insidious in onset. Thus the diagnosis may be delayed.

The chest radiograph remains an important tool for diagnosis despite its inability to correlate with clinical and functional impairment. In 10% of adults it is reported to be normal. High resolution computed tomogram (HRCT) is better in defining the extent and severity of the disease in addition to identifying the optimal site for a lung biopsy. Open lung biopsy remains the diagnostic tool for ILD[1] but may not be possible in many cases.

Corticosteroids remain the drug of choice. Other forms of therapy have been used including hydroxychloroquine and cyclophosphamide. The results are unfavourable and the prognosis remains poor despite therapy.

Case 1

A 13-month-old Malay girl presented with recurrent cough at six months old. Three months later she was cyanosed, breathless with chest deformity and finger clubbing.

There was no evidence to suggest gastro-oesophageal reflux or recurrent aspirations. She had no symptoms of immunodeficiency syndrome. She was not exposed to toxin and pigeons.

Cardiac assessment showed elevated right ventricular pressure with pulmonary hypertension but no structural abnormality.

She was delivered full term normal delivery with a birth weight of 2.7 kg. Parents were nonconsanguinous. She was fully breast fed. Her immunisation was up to date. Her gross motor development was delayed. At thirteen months old she could only sit with support.

On examination her weight and height were below the third centile for her age. She was cyanosed in air with finger clubbing. She was tachypnoeic with subcostal and intercostal recessions. She had pigeon chest with marked Harrison sulci. There were fine crepitations on auscultation. Her liver was enlarged to 3.5 cm. The second heart sound was loud. She was hypotonic with normal reflexes.

Her full blood picture showed hypochromic microcytic anaemia. Her serum iron was 5.9 micromol/l (11.5-25.0 micromol/l). The arterial blood gas showed pH 7.46, pCo2 3.2 mmHg, pO2 39.4 mmHg, HCO3 33 mmol/l and oxygen saturation 76.7%. The nasopharyngeal aspirates for viral culture were negative. The antibody levels for measles, mumps, varicella, rubella and *Chlamydia pneumoniae* were insignificant. The IgM level for *Mycoplasma Pneumoniae was* 1/40 in the first titre. Fungal screening for *Candida albicans* and *Aspergillus* was negative. Serum alpha -1 antitrypsin was 3.36. (2-4 g/dl.) The sweat test was normal. Conjunctival scrapping for *Chlamydia trachomatis* was negative. The chest radiograph showed generalised fibrosis with haphazard arrangement of the lung structure. The HRCT of the chest showed generalised fibrosis with ground glass appearance which was consistent with the diagnosis of interstitial lung disease. Lung biopsy was not performed.

Oral prednisolone 2 mg/kg/day in two divided doses was started based on the radiological evidence of interstitial lung disease. She required two liters/min of oxygen to maintain saturation of 95%. She was discharged home after a month's stay in the hospital. She was readmitted two weeks later with bronchopneumonia and infectious hepatitis. Her total white count was elevated to 14.6 x 10^9/l and her liver enzymes were elevated. HbsAg was negative. The steroid was ceased temporarily till her liver enzymes returned to normal. She remained tachypnoeic and developed wheezing which responded to inhaled bronchodilator. In room air her oxygen saturation was 75%. Since she could not afford an oxygen concentrator she was discharged to a a peripheral hospital near her house with monthly follow-up to our hospital.

During the follow-up her growth, respiratory symptoms and oxygen requirement were monitored. Repeat echocardiogram showed mildly dilated right atrium and ventricle. The pulmonary pressure remained high. Her hyperactive airways were under control with inhaled bronchodilator and steroids. The prednisolone was tailed to 1 mg/kg/day for four weeks and further reduced to alternate days. She continued to require 1 liter of oxygen to maintain saturation of 95%. Her weight gain was poor. One year later we managed to obtain an oxygen concentrator for her and she was discharged home. She is presently oxygen independent.

Here we summarise the clinical features, investigations, management and outcome of the four patients (Table I).

Discussion

We have described four children with interstitial lung disease who present in infancy Our fourth case presented very early in life since day one of life and such presentation was never being described in the literature. Two of our patients presented late by which time they were already hypoxic at rest with established cor pulmonale. Our first case had hyperactive airways and in the literature wheezing is reported in 40% of patients.

The diagnostic evaluations include chest radiograph and HRCT. HRCT can define the extent and severity of the disease which is helpful in diagnosing and managing these children in centers where open lung biopsy is not feasible. In addition, it helps to define and exclude questionable shadows on chest radiograph. It investigates dyspnoeic patient with abnormal lung function test values with apparently normal chest radiograph. It also describes coexisting disease eg. an emphysematous lung. Fan *et al* reported abnormalities of the chest radiographs

Table I
Summary of the clinical, radiological and management of the four patients with interstitial lung disease

Patients	1	2	3	4
Age of presentation	6 months	6 months	8 months	Birth
Sex	Female	Female	Male	Female
Clinical features				
Cough	Present	Present	Present	Present
Failure to thrive	Present	Present	Present	Present
Breathless	Present	Present	Present	Present
Physical signs				
Cyanosis	Present	Absent	Present	Present
Tachypnoea	Present	Present	Present	Present
Finger clubbing	Present	Absent	Present	Present
Chest deformity	Present	Present	Present	Present
Crepitations	Present	Present	Present	Present
Oxygen dependent	Yes	No	Yes	Yes
Radiological signs				
Chest x-ray	generalised, haphazard arrangement suggesting of fibrosis	opacities of both lung fields with interstitial involvement	opacities of both lung fields with fibrosis	interstitial damage with ground glass appearance
HRCT	generalised fibrosis with ground glass appearance	interstitial changes with ground glass appearance	not done	alveolitis of both upper lobes and right middle lobe
Echo cardiogram	Pulmonary hypertension	No pulmonary hypertension	Pulmonary hypertension	No pulmonary hypertension
Treatment	Oral prednisolone	Oral prednisolone	Oral prednisolone chloroquine	Oral prednisolone chloroquine
Outcome	alive	alive	dead	dead

at the time of initial assessment in 48 children evaluated for ILD over a period of 12 years. Thirty six children had predominantly interstitial infiltrates, six had interstitial and alveolar infiltrates, four had predominantly alveolar infiltrates and two showed non specific radiological changes[2].

The 'gold standard' for confirmation of diagnosis is a lung biopsy. The histologic marker of diagnosis is the alveolar thickening. Fan *et al* reported that a specific histologic diagnosis was made in 24 out of 30 lung biopsy procedures. The critical issue in the diagnostic evaluation of ILD diagnosis is the timing of the biopsy. The decision to perform should be individualised pertaining to the progression of disease, its severity, the radiological findings and the potential risks and benefits. In our patients no lung biopsies were performed. All patients were ill and parents were reluctant to consent to the procedure. We also needed to consider the risks involved in the procedure and whether the information obtained would alter our subsequent management.

Gautlier *et al* noted resting hypoxemia in 50% of 34 children with ILD of different types. This was associated with pulmonary hypertension by ECG and echocardiogram. 42% of these children were reported to have pulmonary hypertension in Leland's series[3].

The objective of therapy in ILD is to reduce the inflammatory process in the pulmonary interstitium and perialveolar structures. By doing this it will prevent or minimize pulmonary fibrosis. Corticosteroids are the mainstay of therapy. Patients who are unresponsive to steroids may benefit from immunosuppressive drugs such as cyclophosphamide, methothrexate and azathioprine. Cyclosporine A has been used in suppressing inflammation and has shown benefits in suppressing inflammation in children and adults with collagen and vascular disease. Chloroquine has been used in treating children with usual interstitial pneumonitis (UIP), desquamative interstitial pneumonitis (DIP) and lymphocytic interstitial pneumonitis (LIP). Only one of our patients responded to steroids while another showed partial response.

In children there are no proper guidelines to monitor the progress of the disease. Our overall experience in managing these children are limited. Our diagnosis depends on the clinical presentations with the aid of HRCT. When our patients did not respond to corticosteroids we had problems in deciding on the choice of anti-inflammatory drugs particularly when there was no histological support. Besides improvement in oxygen saturation there was no other indicator that can be used as an indicator of response.

Supportive therapy in these patients includes supplemental oxygen to alleviate hypoxemia, to prevent pulmonary hypertension and cor pulmonale. Adequate calories are required for the increased work of breathing and to support the normal growth of children. Finally in future we hope that we will be able to perform lung biopsies in our patients whom we suspect to have interstitial lung disease.

References

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