CASE REPORT

Anaemia and respiratory failure in a child: can it be idiopathic pulmonary haemosiderosis?

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SUMMARY

We present an 8-year-old male child admitted with cough and high-grade fever for 7 days and respiratory difficulty for 2 days. There was a history of blood transfusion at 2 years of age during a respiratory illness. The child was anaemic, tachycardic, tachypnoeic and hypoxic at presentation. Chest examination revealed equal air entry with fine crackles bilaterally. Blood reports were suggestive of anaemia (haemoglobin 6.5 g/dL), leucocytosis and high C reactive protein levels. Chest radiograph revealed bilateral air space opacities involving diffuse lung fields, right more than left. Relevant microbiological workup was negative. Based on the clinical scenario and investigations, a provisional diagnosis of pulmonary haemosiderosis was kept. The patient was started on intravenous pulse methylprednisolone. Fibre-optic bronchoscopy was done following recovery from the acute event. Bronchoalveolar lavage demonstrated a significant number of haemosiderin-laden macrophages confirming pulmonary haemosiderosis.

BACKGROUND

Idiopathic pulmonary haemosiderosis (IPH) is an uncommon disorder of unclear aetiology characterised by iron deficiency anaemia, recurrent or chronic pulmonary symptoms such as cough, and haemoptysis and diffuse pulmonary infiltrates.¹ IPH is a serious and potentially fatal disease, which occurs predominantly in infants and children <10 years of age.² Its clinical course is exceedingly variable, and delayed diagnosis is common. Often, haemoptysis may not be obvious or trivial and children may present with haematemesis and/or melaena or no such history at all. We report an 8-year-old child who presented with anaemia and respiratory failure. A high index of suspicion may help in the early diagnosis of this unusual disease and guide appropriate therapy and improving outcome.

CASE PRESENTATION

An 8-year-old male child, born of non-consanguineous parents, presented with cough and high-grade fever for 7 days and respiratory difficulty with tachypnoea for 2 days. Cough was non-productive with no diurnal variation. There was a history of passing dark brown stools. There was no history of recurrent fever, skin lesions, bleeding from any other site, arthritis, bone pains and significant drug intake. The child received blood transfusion at the age of 2 years, which was associated with a

brief respiratory illness. One month prior to the current illness, the child had a similar episode of lesser severity requiring hospitalisation. At that time, the child was treated with antibiotics, bronchodilators and oxygen supplementation. At admission, the child had marked pallor and respiratory distress. The respiratory rate was 55 breaths per minute, heart rate was 154 beats per minute and oxygen saturation was 85% on room air. The child was moderately built with a weight of 20 kg (WHO weight for age Z score: -1.79) and height of 112 cm (WHO height for age Z score: -2.71). Chest examination revealed equal air entry with fine crackles bilaterally. Abdominal, cardiovascular and nervous system examinations were unremarkable.

INVESTIGATIONS

Blood investigations revealed haemoglobin of 6.5 g/dL with hypochromic microcytic anaemia. The total leucocyte count was 20 800/mm³ (polymorph 82%, lymphocyte 15%, eosinophil 0.2% and monocyte 1.5%), reticulocyte count was 3.5%, platelets were adequate, C reactive protein was 21.8 mg/dL and erythrocyte sedimentation rate was 50 mm/h. Chest radiograph revealed bilateral air space opacities involving diffuse lung fields, right more than left (figure 1A). Liver and kidney functions were within normal limits. Consecutive samples for acid fast bacilli in gastric aspirates and induced sputum were negative. Nasopharyngeal swab for H1N1 real-time PCR and *Pneumocystis jirovecii* was negative. Clotting time, prothrombin time and activated partial thromboplastin time were in the normal range. Antinuclear antibody, antineutrophil cytoplasmic antibody, antiglomerular basement membrane antibody and Mantoux test were negative. Rheumatoid factor and thyroid profile were normal. C3 complement level was normal. Urinalysis was normal. Echocardiogram was normal. CT scan was suggestive of bilateral ground glass opacities (figure 1B). Based on the clinical scenario and investigations, a provisional diagnosis of pulmonary haemosiderosis was kept. Fibre-optic bronchoscopy was done

Figure 1 (A) Chest radiograph showing bilateral diffuse opacities. (B) CT scan showing bilateral ground glass opacities. (C) Normal chest radiograph at discharge.

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Figure 2 (A) Bronchoalveolar lavage showing ciliated columnar bronchial cells along with haemosiderin-laden macrophages (arrow). (B) Prussian blue stain positive in the haemosiderin-laden macrophages.

after recovery from the acute event. Bronchoalveolar lavage (BAL) demonstrated a significant number of haemosiderin-laden macrophages (figure 2). Coeliac serology (antitissue transglutaminase IgA) was performed and reported negative. Chest radiograph at discharge was normal (figure 1C).

DIFFERENTIAL DIAGNOSIS

Following possibilities were considered:

1. Severe pneumonia—bacterial, viral, pneumocystis and mycoplasma
2. Hypersensitivity pneumonitis
3. Diffuse alveolar haemorrhage
4. Alveolar proteinosis

TREATMENT

The child was managed with respiratory support using high-flow nasal cannula. Blood transfusion, bronchodilators, intravenous ceftriaxone and maintenance fluid were given. Once microbiological workup turned out to be negative, the child was started on steroids keeping a provisional diagnosis of IPH. Intravenous pulse methylprednisolone (dose of 25 mg/kg/day for 3 days) was given followed by oral prednisolone.

OUTCOME AND FOLLOW-UP

The child was tapered off respiratory support within 72 hours of starting steroids. The child was discharged after 7 days of hospitalisation on oral prednisolone (1 mg/kg/day) for 4 weeks followed by taper over 2 weeks. Subsequently, the child was put on inhaled corticosteroids (budesonide 400 µg/day) using a metered dose inhaler and spacer. The child is being followed every 3 months in the paediatric chest clinic and is doing well at 1 year of follow-up.

DISCUSSION

IPH is characterised by a triad of recurrent haemoptysis, iron deficiency anaemia and presence of pulmonary infiltrates on chest radiograph. The underlying pathology is diffuse alveolar haemorrhage. Following haemorrhage, haemoglobin's iron is converted to haemosiderin within 2–3 days by the alveolar macrophages.¹ IPH is diagnosed by the presence of haemosiderin-laden macrophages in BAL, gastric aspirate and lung tissue. IPH is more common in children with an equal incidence reported in both sexes and may manifest at any age.¹ IPH is a diagnosis of exclusion and can be diagnosed after other causes have been ruled out. The differential diagnosis of alveolar haemorrhage includes: pulmonary capillaritis associated with Goodpasture's syndrome, systemic lupus erythematosus, Wegener's granulomatosis, microscopic polyangiitis and other connective diseases.

Aetiology of IPH is unknown. There are certain theories involving autoimmune, allergic or environmental basis.¹ Previously, most cases of diffuse alveolar haemorrhage were labelled as IPH, but with increasingly available diagnostic studies, most

of them have been found to be having an underlying pathology. Some authors recommend a mandatory lung biopsy in children with a negative workup.³ The lung biopsy in IPH demonstrates red blood cells in alveoli and interstitium with no evidence of vasculitis and fibrosis in the case of chronic haemorrhage.³ Children with isolated pulmonary capillaritis have the presence of capillaritis, that is, inflammation of pulmonary capillaries and alveolar interstitium. Children with capillaritis more often need cytotoxic therapy and have a poorer prognosis.³ We offered lung biopsy to our patient, but in view of the invasiveness of the procedure, parents did not give consent.

The presentation of IPH is exceedingly variable in children.^{4–7} Because it mimics common respiratory illnesses including asthma and pneumonia, diagnosis is often delayed. Children may present with unexplained anaemia and growth failure. Haemoptysis often may not be observed in children just as in our case. Therefore, children presenting with anaemia, chest radiographic abnormalities and respiratory failure should be evaluated for IPH. During an acute episode, patients with extensive bleeding may need respiratory support including mechanical ventilation. Response to therapy is often dramatic with rapid improvement in oxygenation and clearing of infiltrates within 3–5 days. Children with chronic low-grade bleeding may present with recurrent respiratory illnesses with clubbing and features of chronic lung disease. Diagnosis of such cases needs a high index of suspicion. Diagnosis of IPH is based on suggestive history, imaging findings and presence of haemosiderin-laden macrophages on BAL. Children with minimal bleeding often do not have radiographic abnormalities.

As IPH is a rare disease, no randomised controlled trials are available comparing different therapies. Most evidence is from observational studies.² Recommended therapy is systemic corticosteroids for an acute episode. Therapy is usually tapered and stopped once disease is in remission for few months. Other options include hydroxychloroquine, azathioprine and cyclophosphamide in children unresponsive to corticosteroids. We treated our patient with pulse methylprednisolone initially followed by low-dose prednisolone for few months. A retrospective review of 26 children suggested that inhaled corticosteroids could be effectively used in follow-up period in combination with hydroxychloroquine for tapering and stopping corticosteroids.² We also used a similar strategy and put the child on inhaled corticosteroids while tapering steroids. The child is doing well in follow-up in inhaled corticosteroids.

No large studies are available on the follow-up of IPH. One of the studies with the largest follow-up (median 5.5 years) showed that 28% children had complete recovery and corticosteroids could be stopped, 20% had a satisfactory course but needed continuation of corticosteroids and remaining 52% had an unsatisfactory course needing immunosuppressants other than corticosteroids.⁸

Learning points

- Idiopathic pulmonary haemosiderosis (IPH) is a rare disorder which can mimic common respiratory illnesses including asthma and pneumonia.
- The characteristic triad of recurrent haemoptysis, iron deficiency anaemia and presence of pulmonary infiltrates on chest radiograph is not seen in most patients.
- Children with unexplained anaemia and respiratory failure should be evaluated for IPH.
- The diagnosis of IPH is confirmed by the presence of haemosiderin-laden macrophages in bronchoalveolar lavage after excluding other causes of pulmonary haemorrhage.

An increasing number of cases of IPH are now being diagnosed as having an autoimmune aetiology with a systematic autoimmune workup and a lung biopsy. It seems pertinent to highlight the usefulness of evaluating them again for autoimmune antibodies during follow-up. One follow-up study reported one-fourth of the patients turning up positive for autoimmune antibodies later in follow-up.⁸ IPH has also been found to be associated with coeliac disease and Down's syndrome.^{8,9} Workup for coeliac disease is mandatory in all patients with IPH. Institution of gluten-free diet has been shown to improve the respiratory symptoms in these children.¹⁰

Contributors All authors: involved in the clinical management of the patient. AK and AsK: performed literature search. DR and MA: involved in manuscript writing.

Competing interests None declared.

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