Idiopathic pulmonary haemosiderosis: A rare cause of anaemia

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Idiopathic pulmonary haemosiderosis (IPH) is a rare pulmonary disease characterised by a triad of iron deficiency anaemia, haemoptysis and alveolar infiltrates on chest x-ray[1]. Death can occur suddenly after a massive pulmonary haemorrhage or due to chronic restrictive pulmonary insufficiency in those who survive for a longer period[2]. This report is to alert a clinician about the possibility of IPH in children who have unexplained anaemia, as seen in 2 children reported below presenting initially only with severe anaemia.

Case 1

An 8 year old boy was admitted with a history of increasing pallor and breathlessness for 1½ months. He had received blood transfusions and iron supplements in the past for severe anaemia. On examination he had severe pallor and mild hepatosplenomegaly. The haemoglobin (Hb) level was 1.9g% and the reticulocyte count 4%. The white cell count was 7.9 $x10^9$/L and the platelet count $300x10^9$/L. He had a microcytic, hypochromic anaemia. The direct Coomb test, sickling test, stool examination, Hb electrophoresis, bone marrow examination, parvovirus B19 antibodies, ultrasound scan of abdomen, 2-D echocardiogram of heart and Meckel scan were normal. Chest x-rays showed bilateral lung infiltrates. Haemosiderin laden macrophages were found in bronchoalveolar lavage (BAL). Lung biopsy showed alveolar spaces filled with haemosiderin laden macrophages without any vasculitis, necrosis or inflammation on light and electron microscopy. Immunofluorescence studies did not show any deposits. Blood transfusions were given and the patient was treated with prednisolone at 2mg/kg and iron supplements. He did not come for follow up but is reported to have died within a year of diagnosis.

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Case 2

A 4½ year old girl presented with complaints of increasing pallor, fever and easy fatiguability for 2 weeks, loss of appetite and weight loss of 3 kg in the past 7 months. She was admitted twice in the past to receive blood transfusions for severe anaemia and low serum iron. Her previous chest radiographs showed bilateral fluffy shadows. On examination she had pallor and tachycardia, the systemic examination being normal. Stool occult blood was positive; however chromium tagged red blood cell (RBC) scan did not reveal a gastrointestinal bleed. The Hb level was 3.7g% and the reticulocyte count 6.4%. The white cell count was $8.7x10^9$/L and the platelet count $420x10^9$/L. She had a microcytic, hypochromic anaemia. Anti-neutrophil cytoplasmic antibodies, anti-nuclear antibodies, anti-GBM antibodies and anti-dsDNA antibodies were negative. The sickling test, Meckel scan and cow's milk precipitin test were normal. Chest x-rays showed bilateral lung infiltrates. Haemosiderin laden macrophages were found in BAL. Lung biopsy showed alveolar spaces filled with haemosiderin laden macrophages without any vasculitis, necrosis or inflammation on light and electron microscopy. Immunofluorescence studies did not show any deposits. Blood transfusions were given and the patient was treated with prednisolone at 2mg/kg and iron supplements. Prednisolone was slowly tapered. She was asymptomatic and was maintaining stable haemoglobin levels 4 months after diagnosis after which she was lost to follow up.

Discussion

The onset of IPH usually occurs before 10 years of age[3]. Anaemia can be the solitary manifestation and is typically microcytic and hypochromic with elevated reticulocyte counts[4]. A delay of 30 months between onset of symptoms and diagnosis was found in one study[5] due to absence of the classic triad, an insidious onset and lack of awareness about this condition. IPH can mimic haemolytic anaemia: mean red cell survival time is reduced because of deposition of RBCs in the lung, and absorption of Hb from the lungs induces a rise in plasma bilirubin[6].

Haemoptysis is unusual as children swallow blood stained sputum (leading to positive stool occult blood) and alveolar bleeding does not readily gain access to central airways[7].

Though the gold standard for diagnosis is lung biopsy, unequivocal diagnosis can be made by presence of haemosiderin laden macrophages in BAL or gastric aspirate, sensitivity of which was found to be 92% and 30% respectively in one study[5]. A chest radiograph is an important diagnostic tool[8], which directed us to the definitive diagnosis in our patients. The most common finding is patchy alveolar infiltrates that are often perihilar or basilar and are usually bilateral. Lung biopsy shows 3 features– presence of intact/ minimally fragmented RBCs in alveoli (recent/active alveolar haemorrhage); multiple haemosiderin laden macrophages (subacute/ chronic or recurrent bleed) and absence of smooth muscle proliferation, vascular malformation, pulmonary infarct, vasculitis, granulomatous disease or infectious agent. Electron microscopy and immunofluorescence studies help to rule out immune complex deposition[9]. Corticosteroids are the mainstay of treatment in IPH. They decrease episodes of alveolar haemorrhage and may also decrease inflammation, thereby decreasing progression towards fibrotic disease[1]. Patients who fail to respond to steroids or develop unacceptable adverse effects may need other forms of immunosuppression, such as azathioprine, hydroxychloroquine or cyclophosphamide. Hydroxychloroquine treatment is found to have significant and lasting improvement in IPH[10]. However it requires periodic monitoring for retinal toxicity. IPH patients who receive long term treatment seem to have a better outcome (86% five year survival in one study[8]).

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