

Primary pulmonary hemosiderosis-a rare cause of Microcytic hypochromic anemia

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Vol. 15, No. 1 (2011-01 - 2011-06)

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Abstract

Iron deficiency anemia (IDA) is the most common cause of anemia in children. In developing countries, the underlying nutritional deprivation makes IDA the most commonly diagnosed condition and empirical iron supplementation is more or less a norm. Peripheral blood smear picture of microcytic, hypochromic anemia gives an appropriate lead. However, failure of iron therapy and exclusion of its common causes prompts us to look at other diagnostic possibilities. Idiopathic pulmonary hemosiderosis is one such rare condition. We report a two-year female child with persistent microcytic hypochromic anemia with recurrent hospitalizations for respiratory symptoms not attributable to anemia. The purpose of this paper is to create awareness about Idiopathic Pulmonary Hemosiderosis as a possible but rare cause of microcytic, hypochromic anemia associated with respiratory distress and to delineate diagnostic difficulties and possible pitfalls.

Keywords: Primary pulmonary hemosiderosis; Microcytic hypochromic anemia

Accepted April 11 2010

Case report

A 2-year female child from rural south India was brought to our outpatient department with complaints suggestive of acute lower respiratory tract infection and severe pallor. Past history revealed similar complaints warranting three hospitalizations, and thrice blood transfusions. Physical examination revealed a Grade II Protein energy malnutrition, hypopigmented hairs, platynychia. The child was in congestive cardiac failure. Auscultation of chest revealed occasional rhonchi and crepitations. The liver was palpable 5 cm below the right costal margin with a span of 12 cm. The rest of the systemic examination was normal. Investigation revealed hemoglobin of 6.3 gm/dl; Red blood cell indices and peripheral blood picture was suggestive of microcytic hypochromic anemia. Iron profile revealed an increase in Total iron binding capacity. In view of pallor, failure to thrive and recurrent respiratory symptoms, gastroesophageal reflux study was done which was negative. Stool examination was negative for ova, cyst and occult blood. Chest X-ray revealed bilateral diffuse non-homogenous infiltrates. The child was transfused with 10 ml/kg of packed red blood cells. She was discharged on oral iron therapy (6 mg/kg/day of elemental iron) and antihelminthics. At discharge, her hemoglobin level had risen to 9.5 gm/dl.



Figure 1. Chest radiography showing bilateral pulmonary infiltrates

Two months later, she presented again with low grade fever, cough and respiratory distress. Examination revealed severe pallor, congestive cardiac failure. Investigations showed Hb of 7.6 gm which had dropped by 1.9 gm/dl despite good compliance to iron supplementation. Chest X-Ray showed bilateral reticulogranular pattern (Fig 1).

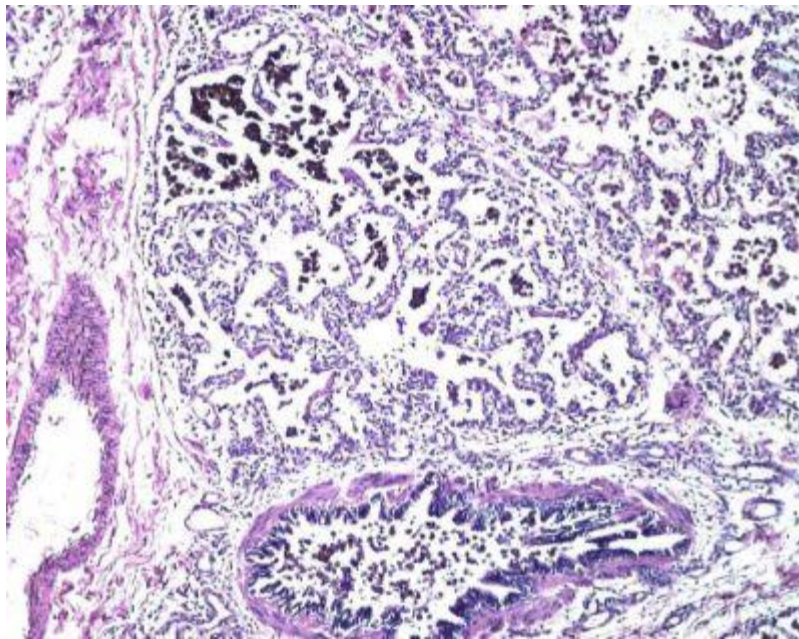


Figure 2. Photomicrographs (H&E x 250) showing lung parenchyma with hemosiderophages in the alveolar space and in the lumen of the bronchiolar lumen but sparing the interalveolar septae. Note the normal histology of the peribronchial blood vessel.

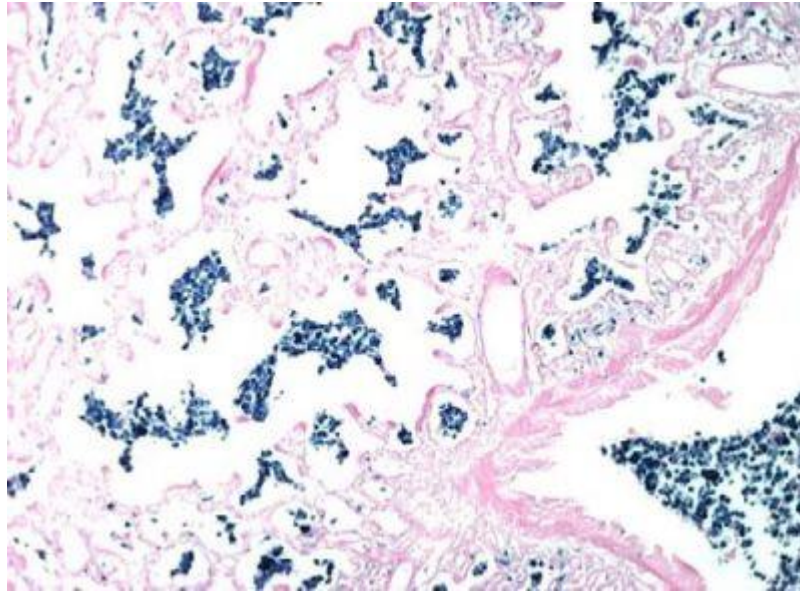


Figure 3. Perls' stain highlighting the presence of he-mosiderin by the blue staining of the the macrophages noted in the alveolar spaces.

Serum bilirubin was 2.1 mg/dl with indirect fraction of 2 mg/dl. The reticulocyte count was 2.8%. The peripheral smear showed no evidence of hemolysis. Bone marrow aspiration and biopsy were normal. In view of failed re-sponse to oral iron therapy, Upper GI endoscopy, colono-scopy and RBC scan was done to rule out occult bleeding all of which were negative. On direct questioning, the parents gave history of sudden onset of respiratory dis-tress and at the end of each of these episodes, the patient required blood transfusion. This happened three times in a span of 6 months. In view of definite temporal correlation of acute onset of respiratory distress and pallor, a diagno-sis of Pulmonary hemosiderosis, probably idiopathic (IPH) was considered. After initial stabilization, a thora-coscopic lung biopsy was done. At microscopy, the archi-tecture of lung parenchyma was intact but exhibited dense aggregates of macrophages with intracellular brown pig-ment which was Perls' positive confirming it as he-mosiderin. These hemosiderophages were also noted in the lumina of the adjacent bronchioles (Figs. 2 & 3). The interstitium showed evidence of fibrosis. The blood ves-sels were histologically normal ruling out vasculitis. No granulomatous inflammation was noted in the lung tissue examined. These features confirmed a histologic diagno-sis of primary pulmonary hemosiderosis by correlation with the clinical, laboratory and histological data.

Discussion

Idiopathic pulmonary hemosiderosis (IPH) is a rare disor-der of unknown etiology characterized by iron deficiency anemia, recurrent or chronic pulmonary symptoms such as cough and hemoptysis and diffuse pulmo-nary infil-trates [1]. The incidence is reported from 0.24 to 1.23 cases per million in selected populations(2). The clinical course of IPH is exceedingly variable; anemia, cough and radiological evidence of pulmonary infiltrates are seen in most of the affected individuals but in the absence of pulmonary problems diagnosis and treatment may get delayed. Individuals of any age can be affected and it occurs with equal frequency in males and females(3,4). Although its etiology remains unknown, IPH is consid-ered to be an immune mediated disease.

The presence of ANCA is thought to be a sign of poor prognosis for pulmonary progression. The presence of other antibodies seems to be the predictor for develop-ment of an immune response. Several cases were reported with iron deficiency anemia, pulmonary symptoms in-cluding cough, dyspnea and hemoptysis, diffuse paren-chymal infiltrates on chest radiographs(2,5). Diagnosis can be delayed in patients without pulmonary symptoms [6,7]. Despite presence of pulmonary symptoms, diagno-sis was delayed in our case by 2 months as we did not correlate the two symptoms and attributed the low hemo-globin to iron deficiency anemia. The diagnosis can be confirmed by demonstration of hemosiderosin-laden macrophages in the gastric aspirates or BAL. Biopsy is essential for diagnosis if BAL results are not confirmatory [8]. In our patient, IPH was confirmed by the finding of hemosiderin filled macrophages in lung biopsy material as in other studies [2,7]. A diagnosis of primary pulmo-nary hemosiderosis was considered at histology taking into consideration, the age of the patient, negative history for exposure to iron compounds, and the presence of pig-ment accumulation predominantly in the alveolar air spaces rather than in the

interstitial peribronchial vascular distribution associated with fibrosis which is the feature associated with secondary pulmonary hemosiderosis. [9]. Our patient was started on oral iron supplementation and oral prednisolone(2mg/kg/day).

We conclude that IPH should be considered when investigating a possible cause of iron deficiency anemia with respiratory symptoms especially in patients who require multiple blood transfusions. A more rapid diagnosis in the form of cytology of sputum or examination of bronchoalveolar fluid could have helped us in the early diagnosis of pulmonary hemosiderosis.

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Curr 4 Pediatr Res 2011 Volume 15 Issue 1