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CASE REPORT

Acute Idiopathic Pulmonary Haemorrhage in a 2 month old Infant

Case report and review of the literature

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نزيف رئوي حاد مجهول السبب عند طفل رضيع عمره شهرين

تقرير حالة مع مراجعة أدبيات

سالم التميمي ، حسين الكندي

الملخص: عادة ما يكون النزيف الرئوي بسبب مرض يصيب عدة أجهزة في الجسم يؤثر على الرئة ، وقد يكون في الرئة وحدها أو بمشاركة أجهزة اخرى. من جهة أخرى يكون تشخيص نزف الرئة المجهول بواسطة استبعاد الأسباب الأخرى ، وهو مرض نادر كما جاء وصفه في الأدبيات الطبية. في تقريرنا هذا نصف حالة طفل يبلغ من العمر شهرين، أحضر إلى قسم الطوارئ بمستشفى جامعة السلطان قابوس (عمان) في حالة فشل تنفسي مصحوبة بحالة صدمة من جراء نزيف شديد وحاد في الرئة. بعد التحري الدقيق في مختلف أجهزة الجسم لم نجد سببا لهذا النزيف. هذه الحالة بعرضها السريري وصورها الشعاعية تشبه ما هو موجود في المراجع بما يسمي النزيف الرئوي مجهول السبب. العلاج بالستيرويدات القشرية نتج عن شفاء عاجل من حالته التنفسية الحرجة.

مفتاح الكلمات: داء هيموسيديريني ، فشل تنفسي ، صدمة ، ستيرويدات قشرية ، تقرير حالة ، عمان.

ABSTRACT: Pulmonary haemorrhage is usually secondary to a systemic disease affecting the lung with or without other organ involvement. Idiopathic pulmonary haemorrhage is a diagnosis of exclusion; as described in the literature, it is a rare disease. We report a two months old infant who presented at the Emergency Department of Sultan Qaboos University Hospital, Oman, with respiratory failure and shock secondary to an acute severe pulmonary haemorrhage. Detailed investigations for pulmonary, cardiovascular, renal and systemic inflammatory causes were negative. His clinical presentation and radiological imaging were consistent with idiopathic pulmonary haemorrhage. Treatment with corticosteroids resulted in a remarkable and fast recovery from his critical respiratory status.

Keywords: Haemosiderosis; Respiratory failure; Shock; Corticosteroids; Case report; Oman.

Pulmonary haemorrhage (PH) and haemoptysis are rare in children and more so in healthy infants.[1] PH may be due to very rare conditions such as pulmonary-renal syndromes and idiopathic pulmonary haemosiderosis (IPH); it can be dangerous and life-threatening.[2]

It is also very challenging when presenting acutely in a baby who was previously well and found by parents to be covered with blood on face or nose and struggling to breathe. These infants need immediate medical attention, often ventilatory support and extensive investigations to find out the source of the bleeding and the cause.[3] Following a report from Cleveland, Ohio, USA,[4] acute idiopathic pulmonary haemorrhage (AIPH) in infancy was, in 2004, recognised as a diagnosis of exclusion by the US Centers for Disease Control (CDC). The current report is of a two month old infant who presented at the Emergency Department of Sultan Qaboos University Hospital, Oman, with the clinical and radiological features of acute idiopathic pulmonary haemorrhage.

Case Report

The male infant was born at 34 weeks of gestation and had an uneventful perinatal period. There was no family history of bleeding or rheumatologic disorders. At 2 months, the mother got up at 5 am to breast feed the baby who was sleeping next to her and found his face and clothing covered with blood. He was unresponsive, with shallow breathing,

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up-rolling of the eyes and stiff limbs. The parents rushed him to the Emergency Department of Sultan Qaboos University Hospital. On examination, he was still unresponsive with shallow breathing, the room air pulse oxymetry being 84% saturation. A chest examination showed bilateral diffuse crackles, with signs of respiratory failure and shock. His face and clothes were blood stained with no skin bruises, petechiae, or apparent vascular malformations. He was intubated and fresh blood was noted coming through the endotracheal tube. After resuscitation with intra-venous saline boluses, a first dose of broad spectrum antibiotics was given and he was transferred to the Paediatric Intensive Care Unit. He was ventilated with high pressure settings and 100% oxygenation. The arterial blood gas after intubation and ventilation showed severe metabolic acidosis and low pCO_2 due to hyperventilation (pH = 7.2; pO_2 = 38.5 KPa; pCO_2 = 2.9 KPa, HCO_3 = 8.3, mmol/l, BE =18). The metabolic acidosis was corrected with the intravenous (IV) fluids and IV sodium bicarbonate.

Investigations included: complete blood count (CBC) which showed leukocytosis of 33.8 x 10^9/L; lymphocytosis of 26.2 x 10^9/L; a neutrophil count of 7.2 x 10^9/L; platelets 555 x 10^9/L; haemoglobin 9.8 g/dL; haematocrit 31.6%; reticulocyte 1.4%; mean cell volume 75.2 fl; mean cell haemoglobin 23.3 pg and red cell distribution width 18.4. His coagulation profile showed a mildly elevated prothrombin time (PT) of 15.8 sec (normal range 10.5-14.9); activated partial thromboplastin time (APTT) 40 sc (range 25.0-39.0) and international normalised ratio (INR) 1.3 (range 0.800-1.200) that corrected when mixed with normal plasma. The liver enzymes were slightly raised: serum aspartate aminotransferase (S-ASAT) was 153 u/l (normal range 22-58); serum alanine aminotransferase (S-ALAT) 54 u/l (range 11-39); serum alkaline phosphatase (S-ALP) 176 u/l (n range 110-302); serum bilirubin 44 umol/l (range 4-17); total protein 62 g/l (range 64-83); serum albumin 40 g/l (35-50); serum ferritin 162ng/ml (range 20-300); plasma ammonia 56 umol/l (range 11-35), and serum lactic acid 1.44 mmol/l (range 0.50-2.20). His urea at 4.5 mmol/l (range 2.5-6.4) and creatinine at 43 umol/l (range 27-53) were both normal; the urine analysis was negative for blood. He received fresh frozen plasma, packed red blood cell transfusion and vitamin K. His chest X-ray showed a bilateral ground glass appearance [Figure 1]. A computed tomography (CT) scan of the chest showed bilateral alveolar opacities [Figure 2]. The CT scans of the brain and abdomen were normal. The electroencephalogram (EEG) did not show any epileptic activities. Both the electrocardiogram (ECG) and echocardiography were normal. Blood, sputum, urine and stool cultures were negative for bacteria and fungus. The auto-antibodies screen was negative including for anti-nuclear antibodies, rheumatoid factor, anti-mitochondrial antibodies, anti-smooth muscle antibodies, anti-reticulin antibodies, anti-neutrophil nuclear anti-bodies (C-ANCA), myloperioxidase (MPO-ANCA) and proteinase-3 (PR3-ANCA). A specific immunoglobulin E (IgE) to cow's milk was negative, an IgG to cow's milk was not feasible. Haemosiderin laden macrophages were negative on the gastric aspirate that was done on day 9 of the illness. An interview with both parents showed that there were no smokers at home or a source of moulds since they live in a new house with no water leakage or heating system.

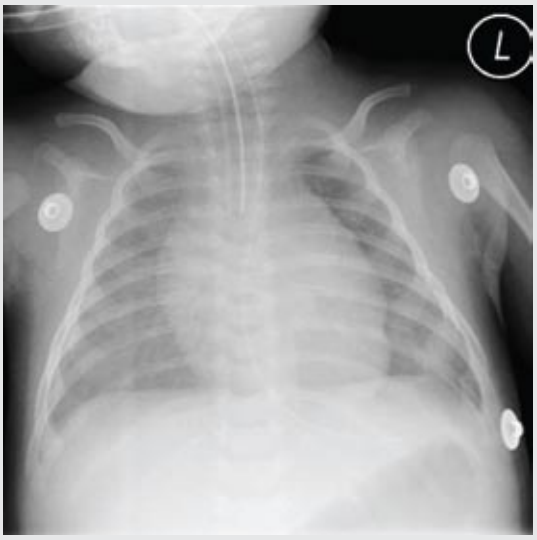

Figure 1: Chest X-rays showing bilateral diffuse opacification of both lung fields, ground glass appearance suggestive of pulmonary hemorrhage

During the first 36 hours of admission, the child was treated with parenteral antibiotics and mechanical ventilatory support, however, he continued to be critically sick with fresh blood coming through the endotracheal tube. A bronchoscopy could not be performed because of his critical status, but it was clinically clear that he had a pulmonary haemorrhage with no identifiable cause. As it was suspected that he might have an

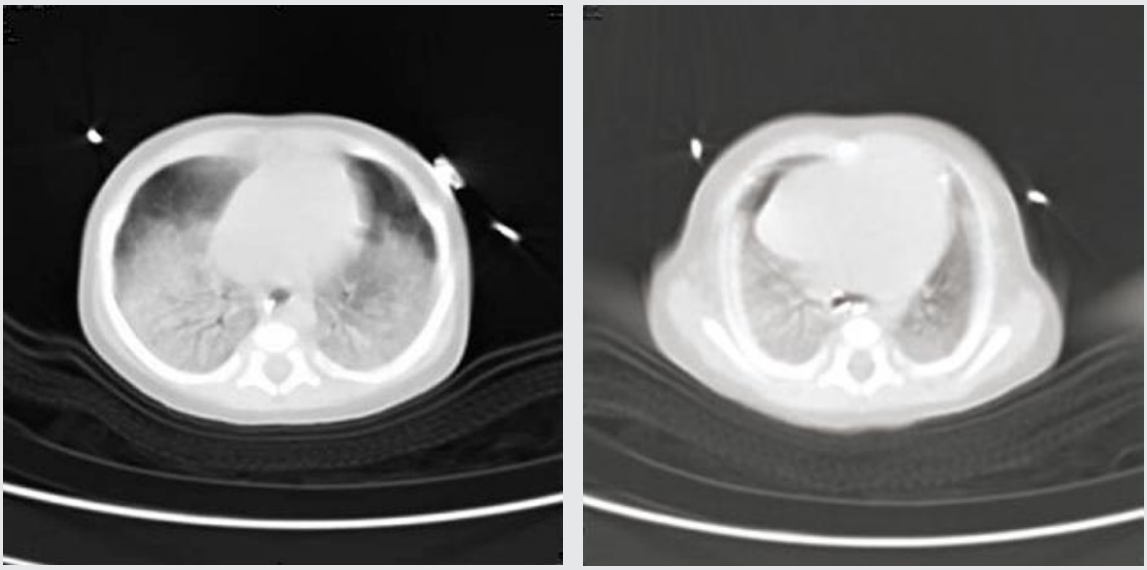

Figure 2: Computed tomography scans of the chest showing bilateral alveolar opacities

idiopathic pulmonary haemorrhage, he was started on methylprednisolone 2mg/kg/day IV divided into 4 doses every 6 hours for 3 days. Within few hours of the second dose there was a clear response to steroids seen in a decrease in oxygen need from 70% to 30% and a decrease in mechanical ventilation pressures. He was extubated on the fourth day of admission and was discharged on the ninth day on oral prednisone that was tapered over a 6 month period. No follow-up bronchoscopy was done because the child remained well. A CBC done one month after the illness showed a normal Hb of 12.0 g/dL; white blood count (WBC) 15.3 x 10^9/L, and platelets were 535 x 10^9/L. There were no more bleeding episodes on subsequent clinic visits up to two years of age; however, he had viral induced wheezes several times between the age of 9 months and 14 months which are now resolved.

Discussion

Pulmonary haemorrhage and haemoptysis in children are uncommon. In a major case review by Coss-Bu et al.,[1] it was found that among 228 children and young adult patients, who presented to Texas Children's Hospital over 10 years, 65% had cystic fibrosis and 16% had congenital heart disease and the remaining 19% had a range of other causes. Pulmonary haemosiderosis is defined as an abnormal accumulation of haemosiderin in the lungs that results from a diffuse alveolar haemorrhage. It may occur as a primary process in the lung (idiopathic) or secondary to cardiac diseases, bleeding disorders, collagen vascular diseases, or systemic vasculitis.[2]

Idiopathic pulmonary haemosiderosis (IPH) is a rare diagnosis of exclusion. It is distinct from the pulmonary-renal syndrome in that the pathology is confined to the lungs and there is no renal or systemic involvement.[2] The incidence in paediatric age groups has been estimated to be very low; for example, during the three decades 1950-1979, IPH occurred in 10 Swedish children which indicates that the yearly risk of onset is 0.24 case per million children.[5] In Japan, there were 39 cases of IPH in children in a 20 year time span (1974-1993) which gives an incidence of 1.23 cases/year per million children.[6] The diagnosis is suggested by the symptom triad of haemoptysis, anaemia and pulmonary infiltrates and is secured by the finding of haemosiderin-laden macrophages (siderophages) in bronchoalveolar lavage fluid (BAL).[7] In the years 1993-2000, there were reports of an epidemic of an unusual form of IPH which affected 30 very young infants in Cleveland, Ohio. These babies mostly presented with severe diffuse alveolar haemorrhage; 75% of them required blood transfusion and ventilatory support in the acute stage. All known causes of pulmonary haemorrhage were excluded by investigations. In most of the infants, the bleeding either stopped or lessened with the use of steroids.[3] Following these reports, the US CDC investigated the cases and came up with a recommendation of

case definition in their 2004 report [4,8] as a clinically confirmed case of "Acute Idiopathic Pulmonary Haemorrhage"(AIPH). This was defined as an illness in a previously healthy infant aged < 1 year with a gestational age of > 32 weeks, no history of neonatal medical problems that might cause pulmonary haemorrhage, and whose illness is consistent with the following criteria:

1. Abrupt or sudden onset of overt bleeding or frank evidence of blood in the airway.
2. Severe presentation leading to acute respiratory distress or respiratory failure resulting in hospitalisation in a paediatric intensive care unit with intubation and mechanical ventilation.
3. Diffuse, bilateral pulmonary infiltrates on a chest radiograph or computed tomography of the chest.

It has been suggested by some authors that IPH can be due to immunological causes.[9-11] Yao et al. stated in their case report that a positive perinuclear neutrophil cytoplasmic antibody (p-ANCA) at the initial assessment may indicate the presence of alveolar capillary or glomerular vasculitis which may be a sign of poor prognosis, and that a measurement of anti-neutrophil cytoplasmic antibodies (ANCA) is recommended for all patients with pulmonary alveolar haemorrhagic syndromes.[11] In our patient, an extensive immune workup did not reveal any evidence of autoimmune disease.

Environmental or toxic factors may precipitate the disease in genetically predisposed individuals. Haemolysin stachylysin, a toxin produced by the fungus *Stachybotrys chartarum*, was associated with pulmonary haemorrhage/haemosiderosis in 10 infants of Cleveland community;[6] however, an actual cause-and-effect relationship between it and pulmonary haemorrhage has not been definitively established.[8,12,13] and the significance of stachylysin in IPH is still under investigation.[13,14] In our case, we did not make a home visit; however, the interview with the parents did not reveal any source of toxins in the home environment.

Conclusion

Our patient met the criteria defined by the CDC for IPH. He was two months old at presentation and his gestational age was 34 weeks. He was normal until the day of presentation when he was found to be covered with blood on his face and was in respiratory failure when presented to the hospital for which he was immediately intubated and mechanically ventilated. He had clear evidence of pulmonary haemorrhage: the frank blood in the endotracheal tube and the findings in both the plain and CT chest radiography. Our patient responded very well to methylprednisolone 2mg / kg/day IV, which resulted in fast improvement and probably prevented further pulmonary bleeding as in many of the patients reported from Cleveland.[6] A bronchoscopy to obtain bronchoalveolar lavage could not be done because of the critical status of the patient during the first 72 hours and then we had to extubate him since he responded very dramatically to the steroids. A follow-up bronchoscopy may well have detected continued low grade alveolar bleeding, but it was not done since he was doing well and his haemoglobin remained normal. During the two years of follow up he had no recurrence of pulmonary haemorrhage.

In summary, this two months old patient presented as a typical case of acute pulmonary haemorrhage as defined by the CDC criteria and has done very well with corticosteroid therapy for 6 months with no clinical recurrence in 2 years.

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