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Methylprednisolone pulse therapy rescued life-threatening pulmonary hemorrhage due to idiopathic pulmonary hemosiderosis

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ABSTRACT

Idiopathic pulmonary hemosiderosis (IPH) is an extremely rare cause of massive pulmonary hemorrhage in children. During the acute phase, death due to massive alveolar hemorrhage and subsequent severe respiratory failure. We report two cases of IPH children who developed hypoxemic respiratory failure and massive pulmonary hemorrhage. One case of a 10-year-old boy was treated with methylprednisolone pulse therapy (10 mg/kg/d) for the first three days and followed by systemic steroid therapy, he successfully decannulated 10 days later and discharged with a favorable quality of life. Another case of a 4 year-old female child with Down's syndrome diagnosed as IPH for over one year and treated with oral corticosteroids for maintenance therapy. She sudden suffered severe hypoxemia with rapid falls in the hemoglobin level. We applied methylprednisolone pulse therapy (10 mg/kg/d) for three days and other supportive therapies, the girl survived through complicated with oxygen dependence. We suggest that methylprednisolone pulse therapy provides a chance of recovery and survival for patients with IPH at the acute phase, even if accompanied by severe pulmonary hemorrhage.

1. Introduction

Idiopathic pulmonary hemosiderosis (IPH) is a relatively rare chronic respiratory disorder, which is classically characterized by the triad of recurrent hemoptysis, iron deficiency anemia and diffuse parenchymal infiltration on chest radiographs [1]. Although with an estimated incidence of 0.24–1.23 per million children, the mortality rate of IPH can be as high as 50% [2,3]. Pulmonary hemorrhage, generally accepted as an extremely rare complication, is a major life-threatening condition in the pediatric populations [2,4,5]. Among all possible therapeutic strategies of severe pulmonary hemorrhage complicated with IPH, first-line conventional treatment is traditionally based on corticosteroids. However, using corticosteroids pulse therapy in childhood IPH has rarely been well defined. Herein, we presented two cases of the successful use of pulse methylprednisolone therapy (MPT) during an overwhelming pulmonary hemorrhage occurred in a 10-year-old boy and a 4-year-old girl with IPH, they survived in these life-threatening situation.

2. Case 1

A 10-year-old boy was admitted to our pediatric intensive care unit with complaints of cough, dyspnea and fatigue for >1 years. He had been hospitalized for several times during this period and was diagnosed with α-thalassemia. Repeated intravenous infusion of antibiotics, intermittent oral prednisone and transfusion of erythrocyte suspending liquid were given due to anemia and symptoms of airway inflammation, but no significant improvement had been seen. The child's vital signs were as follows: temperature, 36.8 °C (98.2 °F); heart rate, 98 bpm in a sinus tachycardia; respiratory rate, 24 breaths/min in tachypnea; blood pressure, 112/65 mm Hg. Skin and mucous membrane pallor, crepitating rales and wheezing were also detected on physical examination. Although respiratory effort was increased, no strong evidence of dyspnea and respiratory failure was found. Laboratory investigation on admission suggested hypochromic microcytic anemia (hemoglobin of 103.3 g/L, mean corpuscular volume 71.5 fL, mean corpuscular hemoglobin 21.38 pg, mean corpuscular hemoglobin concentration 299.1 g/L), increased platelet level (581.5×10^9/L), low immunoglobulin light chain kappa level (6.03 g/L), decreased complement C3 (726 mg/L), elevated Serum IgE concentration (26,620 IU/mL). White

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blood cell count, fibrinogen level and prothrombin time were within normal limits. Chest X-ray revealed prominent perihilar and bibasilar consolidation while bilateral ground-glass infiltrates in both lung fields compatible with a long-term bleeding was showed through computer tomography (CT) scan (Fig. A.1). Microscopic examination of the BAL slide smear revealed large amount of hemosiderin-laden macrophages (Fig. B.1 and 2).On the 6th hours after admission, the patient presented sudden paleness, cyanosis of lips, dry cough, increased capillary refill time, tachypnea (respiratory frequency raised to 65 bpm), tachycardia (cardiac frequency raised to 145 bpm) and acute hypotension (85/46 mm Hg). Diffuse wheezing was heard in physical examination. The hemoglobin dropped from previous 103.3 g/L to 61.4 g/L and fibrinogen level dropped to 1.65 g/L while prothrombin time raised to 15.7 s. Chest X-ray indicated bilateral marked airspace consolidation and increased density areas, (Fig. A.2). He was intubated for mechanical ventilation support immediately due to respiratory failure and overwhelming bleeding was observed in the cannula during intubation. Massive pulmonary hemorrhage complicated to IPH was considered. However, his condition deteriorated and had persistently poor oxygenation, a blood gas analysis showed a PH of 6.88, a PCO_2 of >115 mm Hg, a PO_2 of 47 mm Hg with FiO_2 100%.We have to applied a very high positive-pressure ventilation treatment (EvitaXL; Drager, Lubeck, Germany; maximum peak inspiratory pressure (PIP)/positive end-expiratory pressure (PEEP): 50/20 cm H_2O) to arrest the bleeding and provide adequate ventilation and oxygenation. Since the ventilator parameters have been exhausted for children, treatment should be comprehensively considered by controlling pulmonary hemorrhage. We treated pulse MPT (10 mg/kg/d) and transfusion of red blood cell suspension.24 h after the comprehensive treatment schemes, the boy's condition was improved with blood pressure (103–110/56–62 mm Hg) and cardiac frequency (110–116 bpm), PIP and PEEP were going low at this time point. Index of blood gas suggested magnificent improvement with a PH of 7.35, a pCO_2 of 52 mm Hg, a pO_2 of 147 mm Hg. Pulse MPT (10 mg/kg/d) was lasted for 3 consecutive days since admission. With a good early response including improved respiration and oxygenation (PaO_2/FiO_2 88, oxygen index 23.6) on the 3rd day of treatment, dosage of cortical steroid was then down-titrated to 2 mg/kg/d for 1 week (from day 4 after admission to day 10). On the 8th day, chest X-ray demonstrated marked significant improvement (Fig. A.3). The patient was extubated 10 days after initiation of mechanical ventilation, subsequently transferred to the ward in stable condition on an oral taper of prednisone for 1 mg/kg/d on the 12th day and successfully discharged home 6 days later with a favorable quality of life. The patient remains on a steroid taper and further fellow-up (Fig. C).

3. Case 2

A 4-year-old girl, previously diagnosed with Down's syndrome, at the age of 3 developed weakness, fatigue and anemia. Physical examination at that time revealed profound skin and mucous membrane pallor. Hemogram on admission showed hemoglobin of 5.0 g/dL, MCV of 85.1 fL, and MCH of 24.9 pg/cell. The levels of serum iron and transferritin were decreased, and the reticulocyte rate was elevated (5.3%). Autoimmune antibody panel, direct and indirect antiglobulin tests were all negative. The renal and liver functions were normal. Nucleated cells in bone marrow smears showed marked hyperplasia of active proliferation of erythroid, myeloid and megakaryocytic obvious. The patient received a red cell transfusion and hemoglobin climbed to 11.1 g/dL. Despite of a routine clinical work-up, the cause of anemia was not established. After a 10 days' observation, the patient developed anemia again. X-ray showed infiltration over bilateral lung fields (Fig. D). It led to the suspicion of pulmonary hemorrhage. BAL fluid was acquired by bronchoscopy, and abundant hemosiderin-laden macrophages were discovered in it using Prussian stain (Fig. E). Immunologic and cardiogenic disorders predisposing to pulmonary hemorrhage were excluded by immunologic and echocardiography examinations. With the diagnosis of IPH, intravenously administered methylprednisolone (2 mg/kg/d) was instituted for the first three days and followed with oral prednisolone for maintain therapy (2 mg/kg/d). She received regular follow-up at the outpatient department for the following 1 year. Her hemoglobin ranging from 8.8 g/dL to 11.0 g/dL during this period of follow-up. This time the girl was admitted to our hospital on Dec 5th, 2016 because of pale appearance and exertional dyspnea 3 days and hemoptysis 2 h triggered by bacteria infections of the upper respiratory tract before admission. Upon arrival at the hospital, physical assessments showed tachypnea (40 breaths/min) and diffuse fine crackles. Her vital signs included blood pressure of 106/62 mm Hg, heart rate of 150 bpm, and body temperature of 36.1 °C. She had mottled skin with delayed capillary refill time (4 s) and the pulse oximetry showed 75% on room air. Laboratory investigation was showed hemoglobin dropped from 10.5 g/dL (Dec 1st, 2016) to 6.9 g/dL while admission, with normal platelet counts. The coagulation profile showed a mildly increased international normalization ratio for prothrombin time, but normal partial prothombin time. Disseminated intravascular coagulation profile showed increased fibrinogen, fibrin degradation products and D-D dimer, positive 3P test. On imaging, diffuse pulmonary infiltrates suggestive of alveolar hemorrhage (Fig. F) and a diagnosis of pulmonary hemosiderosis complicated to IPH was made. The patient was given continuous positive airway pressure (PEEP 8 cm H_2O) therapy because her parents refused intubation for mechanical ventilation support. Arterial blood gas data were indicated respiratory failure (pH 7.21, PCO_2 48 mm Hg, PO_2 58 mm Hg with FiO_2 50%). Considering that she did not well respond to standard dose corticosteroid treatment (2 mg/kg/d) this time, Pulse MPT (10 mg/kg/d × 3d) was performed, and followed 5 mg/kg/d × 3d. Partial clinical remission (no episodes of hemoptysis, reduced paleness, and fatigue) and improvement of anemia (stable hemoglobin values after transfusion) after the therapy. Respiratory distress improved with the pulse oximetry showed 92–95% though oxygen supplement with FiO_2 40%.The patient survived in the acute phase. However, she developed oxygen dependent.

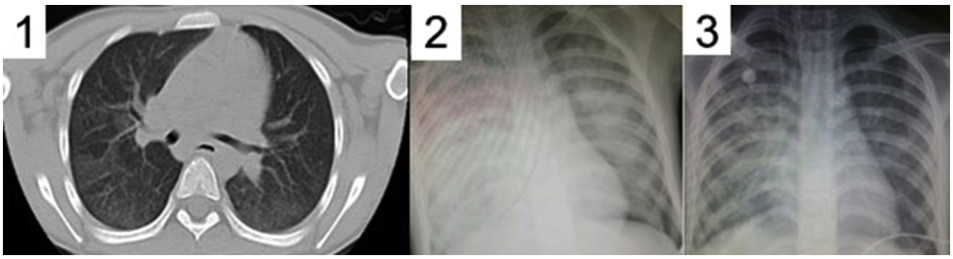

Fig. A. Series imaging of case 1. (A.1) Chest computed tomography shows bilateral ground-glass infiltrates in both lung fields on high resolution computed tomography; (A.2) chest radiography (postero-anterior view) on 1 day after admission revealing bilateral lobe consolidation with areas of profound confluence in the right lung during an acute phase of massive pulmonary hemorrhage; (A.3) chest radiography on 8 day showed marked clearing of infiltrates.

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