A CASE OF IDIOPATHIC PULMONARY HEMOSIDEROSIS PRESENTING WITH PULMONARY HEMORRHAGE DURING EPSTEIN-BARR VIRUS INFECTION

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SUMMARY
Pulmonary hemorrhage, a rare and life-threatening event in children, results from various disorders. Idiopathic pulmonary hemosiderosis characterized by repeated episodes of pulmonary hemorrhages is a rare disease with unknown etiology. It has also been reported that pulmonary hemorrhage may be seen during Epstein-Barr virus infection. In this report we present 2 year-old girl complained with respiratory distress, pallor, fever and sore throat. She diagnosed Epstein-Barr virus infection, anemia and pneumonia. Because she had anemia and respiratory distress simultaneously, we highly suspected from pulmonary hemorrhage. But hemosiderin-laden macrophages were not demonstrated in gastric aspirates. The girl treated symptomatically and healed uneventfully. After one uneventfully year, she was admitted with pallor and respiratory distress, and pulmonary hemorrhage was demonstrated on lung biopsy. The diagnosis of idiopathic pulmonary hemosiderosis was established. Three other pulmonary hemorrhage attacks were observed at the follow-up. We suggest that Epstein-Barr virus infection might be one of the possible factors responsible from idiopathic pulmonary hemosiderosis.

Key Words: Epstein-Barr Virus, Pulmonary Hemorrhage, Idiopathic Pulmonary Hemosiderosis

ÖZET
Epstein-Barr Virus Enfeksiyonu Sırasında Akciğer Kanaması ile Ortaya Çıkan İdiopatik Pulmoner Hemosiderosis Olguşu


Anahtar Kelimeler: Epstein-Barr Virus, Pulmoner Kanama, İdiopatik Pulmoner Hemosiderosis

Pulmonary hemorrhage in children is rare but can be life threatening. Infections, trauma and foreign bodies are probably the most common causes of pulmonary hemorrhage in children. However, pulmonary hemorrhage results from various disorders such as cardiovascular, toxic, neoplastic, vasculitic, and idiopathic (1). We recently treated a 2 year-old girl who had pulmonary hemorrhage during Epstein-Barr virus infection. Because bleeding diathesis including pulmonary hemorrhage has been reported in Epstein-Barr virus infection (2, 3), it was also

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possible that her pulmonary hemorrhage was related to Epstein-Barr virus infection. However, she experienced other pulmonary hemorrhage attacks at the follow-up, and the diagnosis of idiopathic pulmonary hemosiderosis was established. To our knowledge, this is the first article reported a case of idiopathic pulmonary hemosiderosis presenting with pulmonary hemorrhage during Epstein-Barr virus infection.

Case Report

A 2-year-old girl was admitted to our hospital with a 3-day history of fever, sore throat, cough, dyspnea, and pallor. She was well until three days prior to admission when her complaints had appeared abruptly. She was being followed by a pediatrician regularly, and her physical examination and complete blood count was uneventful during the last visit performed one month ago.

On admission, the child had severe dyspnea and pallor. Her breathing rate was 60/min; there were retractions in intercostal, subcostal and suprasternal regions. Her breath sounds were decreased especially in the right hemithorax. Her body temperature was 38.3°C. Pharyngeal examination revealed severe inflammation, swelling and exudate in tonsillar area. Enlarged, tender lymph nodes were noted in cervical, axillary, and inguinal regions. The liver and spleen were palpable 4 and 5 cm from the costal margins, respectively. Her transcutaneous oxygen saturation was 94% while receiving 6-l/min nasal oxygen.

Laboratory examinations included hemoglobin level of 5.2 g/dl, leucocyte count of 17.300/mm³ (20% neutrophils, 54% lymphocytes, 24% atypical lymphocytes, and 2% monocytes), and platelet count of 318.000/mm³. Sedimentation rate was 26 mm/h and C-reactive protein level was 0.58 mg/dl. Blood chemistry was normal except for slightly elevated transaminases (ALT: 65 U/L, AST: 50 U/L, normal range <35 U/L). Chest X-ray examination showed bilateral perihilar consolidation (Figure 1). Epstein-Barr virus viral capsid antigen IgM and IgG were positive. The diagnosis of infectious mononucleosis related to Epstein-Barr virus infection, pneumonia and anemia was established. Intravenous fluid and nasal oxygen therapy were started.

On the second day of hospitalization, respiratory distress of the patient increased and her hemoglobin value decreased to 4.7 g/dl. After blood was taken for laboratory investigations, she was transfused with concentrated erythrocytes and her hemoglobin value increased to 9.3 g/dl. According to the results obtained from pretransfusion blood specimens; MCV: 71 fl, MCH: 22 pg, MCHC: 31 gr/dl and RDW: 16.7. Reticulocyte count was 2.3%. Serum bilirubin values were normal. Direct Coombs test was negative. The hemoglobin electrophoresis was normal. Investigation of stool for blood was negative. Coagulation tests were within normal limits. Serum iron profile was consistent with iron deficiency (serum iron: 28 mg/dl, unsaturated iron binding capacity: 480 mg/dl, transferrin saturation: 5.5%), while serum ferritin and serum haptoglobin were normal. Bone marrow aspiration was normal.

On the fourth day of hospitalization, her respiratory status deteriorated and concomitantly her hemoglobin value decreased to 4.8 g/dl. She was transfused with concentrated erythrocytes

Figure 1: Bilateral perihilar consolidation is shown in the X-ray graphy of the thorax. Apex and basal areas are partially conserved.
again and her hemoglobin value increased to 12.9 g/dl. A computed tomography scan of the thorax revealed bilateral perihilar consolidation (Figure 2). Because of poor condition of the patient, teicoplanin and meropenem were started. Reticulocyte counts, serum bilirubin values, direct Coombs test, and investigation of stool and urine for blood, serum haptoglobin, and coagulation tests remained within normal limits. A broad viral serology panel was negative except for Epstein-Barr virus. Serology for antinuclear, anti double stranded DNA, antinuclear cytoplasmic, and antiglomerular basement membrane antibodies were negative. No pathogens were isolated from throat swab and blood specimens. Tuberculin skin test was negative and acidoresistant bacteria were not found in gastric aspirates. Otolaryngorhinological examination did not reveal a bleeding focus.

Since patient’s dyspnea did not respond to the antimicrobial therapy teicoplanin and meropenem were discontinued in the seventh day of treatment. On the fifteenth day of hospitalization while receiving supportive care, patient’s breathing difficulty had decreased. During that time her hemoglobin value had stayed between 9.4-10 g/dl, and her hepatosplenomegaly and lymphadenopathies had resolved. Because of the unexplained abrupt decrease in hemoglobin value and the concomitant increase in breathing difficulty we considered the possibility of pulmonary hemorrhage or pulmonary hemosiderosis. Radionuclide scan performed on the twentieth day of hospitalization showed no active pulmonary hemorrhage. Repeated computed tomography scan of the thorax revealed decrease in perihilar consolidation (Figures 3 and 4). Hemosiderin-laden macrophages were not demonstrated in gastric aspirates. The girl treated symptomatically and healed uneventfully. After twenty-two days of hospitalization, she was discharged from the hospital. Although evaluation for milk-protein allergy was negative we offered milk-free diet.

Figure 2: Bilateral perihilar consolidation is shown in the computed tomography of the thorax.

Figure 3: Two weeks later, partially resolution is seen in perihilar consolidation.

Figure 4: In computed tomography of the thorax performed two weeks later, complete resolution is seen in perihilar consolidation.
After one uneventfully year, she admitted with complaints of cough, dyspnea, hemoptysis and pallor. She had tachypnea, retractions, and bilateral diminished breathing sounds. Her hemoglobin level was 5 g/dl. She did not have any physical and laboratory finding concordant with Epstein-Barr virus infection. A computed tomography scan of the thorax revealed bilateral perihilar consolidation. She was transfused with concentrated erythrocytes and her hemoglobin value increased to 9.8 g/dl. After written consent from her family, an open lung biopsy was performed. Microscopically, typical features of idiopathic pulmonary hemosiderosis were seen including recent intra-alveolar hemorrhage, large numbers of intra-alveolar hemosiderin-laden macrophages, and mild diffuse interstitial fibrosis. The diagnosis of idiopathic pulmonary hemosiderosis was established. Although she received inhaled corticosteroid therapy, three similar attacks were observed.

Discussion

Infectious mononucleosis, which is the most commonly caused by Epstein-Barr virus infection, is manifested typically by fever, exudative pharyngitis, lymphadenopathy, hepatosplenomegaly, and atypical mononucleosis (4). The spectrum of disease is variable, ranging from asymptomatic to fatal infection. Bleeding is a rare complication of infectious mononucleosis and manifested by various clinical pictures. Pulmonary hemorrhage (2, 3), tonsillar hemorrhage (5), hematuria (6), retinal hemorrhage (7), subarachnoid hemorrhage (8), cerebral hemorrhage (9), and subcapsular splenic hematoma (10) have been reported in patients with Epstein-Barr virus infection. Although bleeding diathesis has been ascribed to various factors such as thrombocytopenia (11), coagulopathy related to hepatic dysfunction (12), vessel wall erosion (5), and friability of the enlarged spleen (10), exact mechanism of bleeding remains obscure in some cases.

Our patient had Epstein-Barr virus infection in the first pulmonary hemorrhage attack proved by computed tomography scans of thorax. If we had performed a radionuclide scan or bronchoscopy in the acute period, pulmonary hemorrhage could have been demonstrated. In the first attack we could not explain why pulmonary hemorrhage occurred. She did not have thrombocytopenia, and her coagulation tests including bleeding time were normal. Her pulmonary hemorrhage might have been caused by changes in vascular integrity as speculated by Weinstein and O’Hare (3). However, pulmonary hemorrhage attacks recurred in our patient and the diagnosis of idiopathic pulmonary hemosiderosis was established.

Idiopathic pulmonary hemosiderosis is a rare disease, predominantly occurring in children and young adults, with a markedly variable clinical course characterized by repeated episodes of multifocal pulmonary hemorrhages. The condition occurs in the absence of primary cardiac disease, glomerulonephritis, or other disorders associated with intrapulmonary bleeding. Idiopathic pulmonary hemosiderosis is defined clinically by the triad of hemoptysis, diffuse pulmonary infiltrates on the chest roentgenogram, and iron deficiency anemia. Despite numerous experimental morphologic, immunologic, and ultrastructural studies, the etiology and pathogenesis of idiopathic pulmonary hemosiderosis are not known (13).

Based on evidence obtained from our patient and the other cases in literature, we suggest that pulmonary hemorrhage may be a potential complication in Epstein-Barr virus infection. However, pulmonary bleeding may result from various factors other than Epstein-Barr virus infection. For this reason, patients with Epstein-Barr virus infection associated with pulmonary hemorrhage must be followed for other possible causes such as idiopathic pulmonary hemosiderosis. Furthermore, it is an attractive assumption that Epstein-Barr virus infection may be one of the several possible factors for the development of idiopathic pulmonary hemosiderosis.
REFERENCES


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