Clinical Brief

Laryngitis and Neutropenia from Parvovirus-B19

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ABSTRACT

Parvovirus-B19 has been reported a rare cause of acute laryngitis. Here, we described an 11-month-old girl who had prolonged acute laryngitis and neutropenia associated with parvovirus-B19 infection. Intravenous immunoglobulin therapy resulted in resolution of her symptoms, except neutropenia. We concluded that parvovirus-B19 can cause prolonged laryngitis and intravenous immunoglobulin treatment should be considered. **[Indian J Pediatr 2007; 74 (10) : 950-952]** *E-mail: ozlemozbek@superonline.com*

Key words : *Children; Laryngitis; Neutropenia; Parvovirus-B19 infection*

Symptoms and signs caused by Parvovirus-B19 (PV-B19) infection, which depend on the hematopoietic and immune status of the infected host, can range from the absence of any overt sign of disease to life-threatening illness. Erythema infectiosum, transient aplastic crisis, chronic anemia, neutropenia, thrombocytopenia, myocarditis, hepatitis, encephalitis, arthritis and arthralgia are some of the diseases and clinic manifestations associated with PV-B19.[1] However, it has rarely been a cause of acute laryngitis.[2] We report an 11-month-old girl with a long-standing history of stridor and neutropenia associated with PV-B19 infection.

CASE REPORT

An 11-month-old girl with stridor and a barking cough was referred to our hospital. She had been treated with oral dexamethasone 0.5 mg/Kg/d for 2 days and ampicillin-sulbactam 50 mg/Kg/d during the prior week because of acute laryngotracheobronchitis. Despite that treatment, her respiratory distress, hoarse voice, and inspiratory stridor did not resolve.

Physical examination on admission revealed a body temperature of 36.8°C, a blood pressure of 90/60 mmHg, a pulse rate of 136 bpm, and an oxygen saturation value of 97%. Her weight and height were within normal limits for age. She was tachypneic and dyspneic and exhibited inspiratory stridor. Auscultation of the chest revealed coarse breath sounds.

The results of initial hematologic tests were as follows: hemoglobin, 12.4 g/dL; hematocrit, 34.7%; white blood cell count, 10.1×10^9/L; platelet count, 449×10^9/L; mean corpuscular volume, 77.3 fL; and absolute neutrophil count, 1×10^9/L. A peripheral smear showed 81% lymphocytes, 11% neutrophils, and 8% monocytes, but no atypical cells. The results of blood biochemistry analyses including C-reactive protein were within the reference ranges. Chest radiography showed bilateral hyperinflation of the lungs. Plain radiographic studies of the neck revealed the classic steeple sign. The results of nasopharyngeal swab analysis for influenza, adenovirus, and respiratory syncytial virus were negative.

To treat the patient's laryngitis, we initiated therapy with oral dexamethasone, the dose of which was adjusted up to a maximum of 1 mg/Kg/d according to the clinical manifestations of disease. Nebulized budesonide (2 mg/d) and ampicillin-sulbactam were also administered. Because the symptoms were persistent, we evaluated the supraglottic region *via* fiberoptic endoscopy, which showed inflammatory edema of the vocal cords. The results of 2-dimensional echocardiography (ECO) and computed tomographic angiography of the neck, which were performed to examine the subglottic tissue for extrinsic compression of the airway and intraluminal obstruction by a mass, were within normal limits. Esophageal pH monitoring for gastroesophageal reflux yielded normal results.

On the third day of the patient's hospitalization, gastroenteritis and severe neutropenia with fever developed. The results of hematologic tests showed the

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following values: hemoglobin, 11.6 g/dL; hematocrit, 34.4%; white blood cell count, 2.9×10^9/L; platelet count, 518×10^9/L, and absolute neutrophil count, 0.087×10^9/L. A peripheral smear showed 89% lymphocytes, 3% neutrophils, and 8% monocytes. Virus-induced lymphocytes were noted on peripheral smear. The level of C-reactive protein was 1.1 mg/dl. Neither rotavirus nor adenovirus antigens were detected in the stool. The results of stool and blood cultures remained negative. However, *Candida albicans* was identified in a throat culture. A second laryngeal endoscopy revealed no fungal lesion under the subglottic region. The results of serologic tests for the Epstein-Barr virus, herpes simplex virus, and cytomegalovirus were negative. Nevertheless, the results of testing for PV-B19 immunoglobulin (Ig) M and IgG positive, after 1 month only PV-B19 IgG positive. Age-related levels of serum IgA, IgG, and IgM were within normal limits; and total IgE was 53.2 IU/mL (normal range, 0-40 IU/mL). The results of testing for egg-specific and milk-specific IgE in serum were negative. The results of complements 3, and 4, and C1q esterase levels were within normal limits. Treatment was initiated with imipenem for the neutropenic fever. Nebulized budesonide treatment was stopped because of oral moniliasis, and treatment with oral nystatin and fluconazole therapy was begun. The patient's fever resolved after 2 days of imipenem therapy and did not persist.

Although dexamethasone therapy was extended for 1 month, stridor recurred when the dexamethasone dose was decreased to 0.1 mg/Kg/d, and the patient's neutropenia persisted. In an attempt to treat both laryngitis and neutropenia, which were attributed to an immune reaction resulting from PV-B19 infection, we administered intravenous immunoglobulin (IVIG) 1 g/Kg/d for 3 consecutive days. After IVIG treatment, the patient's laryngitis improved dramatically and the stridor resolved. Treatment with dexamethasone was tapered off over a 2-week period. Unfortunately, the neutropenia persisted for 1 year after IVIG treatment had been terminated. Her bone marrow aspiration showed normal findings as well as normal granulopoiesis. We did not attempt to treat the patient's neutropenia during that period because it caused no adverse effects.

DISCUSSION

Acquired acute upper-airway obstruction in children is a life-threatening situation and usually caused by infection, a foreign body in the airway, or trauma. PV-B19 infection rarely causes that disorder. To our knowledge, the largest reported patient group with acute respiratory disease caused by PV-B19 infection consisted of 21 children.[2] Of those subjects, 3 toddlers had acute subglottic laryngitis. According to the authors of that report, PV-B19 can provoke acute respiratory disease in children who have a specific endogenous predisposition (such as thin or unstable bronchial walls or bronchial or tracheal mucosal hyperreactivity) to respiratory disorders. In another report, a 6-year-old girl with acute respiratory distress syndrome, multiple organ dysfunction, and shock was described.[3] Parvovirus-B19 DNA was identified in her serum and bronchial secretions and in the results of a skin biopsy. Our patient also experienced prolonged stridor in addition to neutropenia as a result of PV-B19 infection.

The gold standard in the workup of a patient with suspected stridor is upper and lower airway endoscopy.[4] During the week after our patient was admitted to the hospital, we evaluated her upper airway with endoscopy, which revealed laryngeal edema. The results of computed tomographic angiography of the neck and ECO, were also normal. We considered whether the candidal infection identified in a throat culture could be a cause of the laryngeal stridor in this patient, but a second endoscopic examination of the larynx did not reveal a fungal infection in the subglottic region, and her symptoms did not resolve after systemic antifungal treatment. We concluded that the oral candidiasis was a concomitant infection that resulted from immunosuppression and inhaled steroid treatment.

Our patient had severe neutropenia (absolute neutrophil count $<0.5\times10^9$/L) that was associated with PV-B19 infection. Blood cells other than erythrocytes, such as neutrophils or platelets, can be affected by PV-B19 infection.[5] An autoimmune disorder has been implicated as a cause of neutropenia in patients with PV-B19.[6] However, some investigators suggested that parvovirus-B19–specific cytotoxic T-lymphocytes recognize and destroy nonproductively infected granulocyte precursor cells in the bone marrow rather than autoimmune destruction.[7] Since her bone marrow showed normal granulopoiesis, we concluded that her neutropenia was a result of immune reaction unresponsive to IVIG.

Oral corticosteroids are the drugs most often recommended to treat moderate-to-severe croup because of its ease of administration, availability, and low cost.[4] Nebulized budesonide is another effective treatment option.[4] We treated our patient with both oral dexamethasone and nebulized budesonide; however, her clinical findings did not improve. Recently, IVIG has been used for treatment of chronic PV-B19 infection.[8,9] The dramatic resolution of respiratory symptoms after IVIG therapy in our patient may support the efficacy of this treatment.

We concluded that PV-B19 can cause acute and/or prolonged respiratory disease and that because of its immunomodulatory effect, IVIG treatment should be considered for patients with PV-B19 infection.

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