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ACUTE RESPIRATORY DISTRESS SYNDROME IN A CHILD WITH HUMAN PARVOVIRUS B19 INFECTION

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Abstract

A 6-year-old girl developed shock and multiple organ dysfunction including acute respiratory distress syndrome in association with parvovirus B19 infection. The diagnosis was based on positive antibodies and the detection of parvovirus 19 DNA in serum, bronchial secretions and skin biopsy. It seems likely, but it was not proved, that the parvovirus infection caused acute respiratory distress syndrome.

Keywords

human parvovirus B19; multiple organ dysfunction syndrome; acute respiratory distress syndrome; nitric oxide

Human parvovirus B19 (PB19) usually causes erythema infectiosum, a common childhood benign condition with a typical slapped-face rash.^{1,2} Infection can be asymptomatic¹ or uncommonly give rise to a variety of clinical manifestations: chronic anemia; arthritis; transient aplastic crisis; thrombocytopenia; neutropenia; myocarditis; hepatitis; meningitis; encephalitis; atypical rash; hydrops fetalis; and congenital anemia.^{1,2} PB19 can cause a mild respiratory tract illness with no rash, but there are also reports of acute obstructive respiratory disease and severe pneumonia.^{3,4}

CASE REPORT

A 6-year-old girl presented with fever, sore throat, abdominal pain and myalgia. She had a history of asthma controlled with montelukast. Two weeks previously she had a slapped-face rash, and on the second day of disease she developed a maculopapular exanthema over the thighs. Hemoglobin, platelet and white blood cell (WBC) count were normal but C-reactive protein was 30.5 mg/dL. The urine analysis revealed >50 WBC per high power field. After blood and urine bacterial cultures, therapy was started with ceftriaxone for probable urinary tract infection.

On the third day, the patient was admitted to her local emergency department. The exanthema was petechial and spread over the abdomen, arms and legs, reaching the soles and palms, resembling rickettsiosis. She developed labored respiration, poor perfusion, hypotension, lowered consciousness and conjunctival hemorrhage. Her respiratory condition deteriorated with bronchospasm and increasing needs for oxygen. She was transferred to a university hospital and admitted to the Pediatric Intensive Care Unit, requiring tracheal intubation and mechanical ventilation. Chest radiograph and PaO₂:FiO₂ ratio were consistent with acute respiratory distress syndrome (ARDS).

Initial treatment included aggressive pressure-controlled ventilation, salbutamol, sedatives, analgesics, inotropic support and cefotaxime, clarithromycin and ciprofloxacin. On admission, hemoglobin had dropped to 8.4 g/dL requiring 2 red blood cell transfusions, and platelets reached a minimum value of $86 \times 10^9/L$. A coagulation study revealed a prolonged activated partial thromboplastin time and prothrombin time: 47.1 and 16.8 seconds, respectively. Liver function tests were abnormal; maximum total bilirubin and transaminases were 4.5 and 2.1 times normal, respectively. Total WBC counts remained normal with lymphocytopenia during first 5 days. C-reactive protein continued to rise until day 6 to a maximum of 50.6 mg/dL.

On the fourth day, the rash was more confluent with target lesions. A skin biopsy revealed angiocentric dermatitis with moderate mononuclear perivascular infiltrate of the dermis and intravascular polymorph margination. Intravenous immunoglobulin (IVIG) 400 mg/kg/d was administered for 5 days. The liver was slightly homogeneously enlarged by abdominal ultrasonography. A transthoracic echocardiogram was normal. The respiratory condition did not improve, and inhaled nitric oxide was delivered for 6 days (maximum, 20 ppm; methemoglobin, <1%).

Blood, urine and bronchial secretion bacterial cultures remained negative. *Rickettsia conorii*, *Borrelia burgdorferi*, *Coxiella burnetii*, *Ehrlichia*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Leptospira*, *Pneumocystis carinii*, respiratory virus, cytomegalovirus, Epstein-Barr virus, herpes simplex virus and human immunodeficiency virus were excluded by serology and/or direct (antigen or nucleic acid) detection.

IgM and IgG antibodies against PB19 were positive (indirect immunofluorescence), and PB19 DNA by polymerase chain reaction (PCR) was detected in plasma (virus load, 4.8×10^4 genome copies/mL) bronchial secretions and skin biopsy (real time PCR; Real Art ParvoB19 RG).

An immunologic evaluation on day 6 showed decreased CD8⁺ and CD4⁺ lymphocytes, decreased IgG and total complement hemolytic activity. Antinuclear and cytoplasmic antineutrophil antibodies and circulating immunocomplexes were negative. She progressively improved, and ventilatory support ceased on day 13. The exanthema subsided after the first week. She was discharged from the Pediatric Intensive Care Unit after 16 days with no respiratory distress and no neurologic sequelae.

Five weeks after hospitalization, serum PB19 DNA remained detectable by PCR, (virus load, 10^3 genome copies/mL); IgM and IgG antibodies were positive. Immunologic evaluations (total lymphocyte and neutrophil counts, lymphocyte subpopulations, immunoglobulins including IgG subclasses and specific IgG antibodies, complement, phagocytosis and oxidative burst) 5 weeks and 3 months later were normal.

PB19 DNA remained detectable by PCR during 6 months after acute disease.

The patient was enrolled in an investigation of the efficacy and safety of Dotrecogin Alfa (activated) in Paediatric Severe Sepsis (Eli Lilly and Co.).

DISCUSSION

This is a case of shock with multiple organ dysfunction syndrome and ARDS in a child with evidence of recent PB19 infection.

The detection of IgM and PB19 DNA in serum, skin tissue and bronchial secretions and the failure to detect other pathogens make it likely that parvovirus was the cause of disease, but proof of lung tissue infection was not possible.

The full spectrum of PB19 induced disease is not yet defined, and evidences of persistence, association with autoimmune diseases and atypical evolutions are increasing.^{1,2} PB19 can infect and persist in both T and B lymphocytes, up-regulate cytokine expression and alter host cellular immunity.²

Treatment with IVIG in persistent infection results in decreased viremia and improvement of symptoms and has a potentially curative role.¹ We believe that IVIG was beneficial in this case because some apparently immune-related manifestations like the erythema improved.

Respiratory involvement to this degree caused by PB19 has been documented in only 2 immunocompetent women and in a pediatric case after heart transplantation.^{3–5} A milder pleuropneumonitis was also reported in a healthy man.⁶

It is uncertain whether lung injury results from direct infection or from immune damage. The cellular receptor for PB19, erythrocyte P antigen, is expressed not only in erythroid cells but also in other tissues including the lung. Local viral replication might therefore represent a primary pathogenic mechanism.²

In our case as in the case reported by Wardeh and Marik,³ the detection of DNA in respiratory tract secretions suggests a direct effect of the virus.

To the best of our knowledge, an association among human PB19 infection, multiple organ dysfunction syndrome and ARDS in immunocompetent children has not been previously reported.

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