Parvovirus B19 Seropositivity and Its Laboratory and Clinical Effects in PICU Admitted Children at Mofid Children Hospital

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Abstract

Background: Acute parvovirus infection may cause different complications and comorbidity in Pediatric Intensive Care Unit (PICU) patients. This study was conducted to investigate the effect of parvovirus infection on death, Hb, WBC count, and liver function tests in patients admitted to Mofid Children Hospital PICU from September 2015 to September 2016.

Methods: 66 children admitted to Mofid Children Hospital PICU were selected. Data on age, sex, underlying disease, anti-parvovirus IgG and IgM antibody, death, Hb, WBC count, AST, and ALT were gathered by questionnaire and data analysis was performed by the SPSS 21.

Results: Age range of children was 1-156 [Mean: 36.5(±41.3 SD)] months. Underlying diseases were gastrointestinal disease (13 cases), respiratory tract illnesses (14 cases), urinary tract diseases (6 cases), nervous system diseases (3 cases), hematological and oncological diseases (7 cases) and other diseases (3 cases). Quantitative results on IgG and IgM were analyzed. IgG and IgM were not significantly associated with Hb and WBC count. ALT over 12.5 *IU* was more significant in IgM positive cases and AST over 67 *IU* in IgG positive cases. IgM positivity was significantly associated with death ($p<0.05$).

Conclusion: Parvovirus serologic antibody can be an important measure in PICU patients because it can be associated with anemia, neutropenia, and LFT tests.

Keywords: Child, Intensive Care Units, Parvoviridae infections, Pediatric

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Introduction

Parvovirus B19 is a DNA virus from the Parvoviridae family and Erythrovirus genus. A wide range of clinical symptoms are attributed to parvovirus infection. The virus is the cause of a wide range of clinical syndromes from erythema infectiosum (Fifth disease), arthritis and arthropathy as a risk factor for autoimmune diseases and aplastic crisis in patients with increased turnover of red blood cells (1). The virus affects blood cells in children with hematologic malignancies and also may be the cause of cytopenia with no other explanation and no clinical symptoms of erythema infectiosum (2). Elevated ALT and alkaline phosphatase levels may occur in acute parvovirus infection (3). Fifty cases of parvovirus worldwide have been reported to be associated with hepatitis, including both healthy and rheumatological and hematological patients. Hepatic involvement ranges from transient elevation of hepatic enzymes to fulminant hepatitis (4). Hepatitis severity may be higher in children (5). Since children admitted to Pediatric Intensive Care Units (PICUs) may concurrently develop organ failure and the complication of the underlying disease, parvovirus infection may lead to significant morbidities in them. This study investigated Hb, WBC count, liver enzymes, and death in parvovirus B19 seropositive patients admitted to Mofid Children Hospital PICU from September 2015 to September 2016.

Materials and Methods

Sixty six patients randomly selected from children admitted to Mofid Children Hospital PICU from September 2014 to September 2015 were included in the study. A questionnaire was filled for each patient including age, gender, underlying disease, liver enzyme tests, Hb, WBC count, serologic IgG and IgM antibody measurement and death. Serologic test was performed by an ELISA kit [Datis Tashkhis Teb (IgG and IgM), Germany]. Based on a 42% estimate of anti-IgM positivity (6), the sample size for the study included 66 cases. Blood sampling was carefully done on the first day of admission in order to avoid lysis in blood samples. Children with a history of blood and blood product transfusion up to 3 months before were excluded from study. Informed consent was obtained from parents of study case.

All data analyses were carried out by the SPSS version 21 (SPSS Inc., Chicago). Descriptive analysis was done by bivariate analysis using chi-squared test at significance level (p) of 0.05, and correlation coefficients were estimated at two-tailed significance level of 0.05.

Results

A total of 66 children with age range of 1-156 [Mean: 36.5 (±41.3 SD), median: 18] months were included in the study. Thirty cases (45.5%) were male. Underlying diseases were gastrointestinal disease (13 cases), respiratory tract illnesses (14 cases), urinary tract diseases (6 cases), nervous system diseases (3 cases), hematological and oncological diseases (7 cases) and other diseases (3 cases) (Table 1). Fourteen cases (21.5%) were IgG positive and 5 cases (0.07%) IgM positive.

IgG antibody range was 1-105 [Mean: 29.1 (±38.1 SD)] and IgM antibody range 0.03-0.5 [Mean: 0.12 (±0.108 SD). No significant correlation was observed between IgG and IgM, and Hb (Two-tailed p>0.05). Fourteen patients died. There was also no significant correlation between IgG and death but a significant correlation between IgM and death (two-tailed p=0.02) was observed. The correlation between IgG and IgM, and WBC count was not significant as well. Student's *t*-test between IgG antiparvovirus and ALT>12 *IU/ml* was done. The test result was significant between IgM antiparvovirus and ALT>12 *IU/ml* (p=0.03). The result of student's *t*-test between IgM antiparvovirus and AST>67 *IU/ml* was significant (p=0.03), but not between IgG antiparvovirus and AST>67 *IU/ml*.

Discussion

Parvovirus, a single stranded DNA virus, is known as the etiologic agent of erythema infectiosum in children without hematological diseases (7). Polyarthropathy may be seen in female cases with acute symmetric arthritis lasting 1-3 weeks. Sometimes arthritis may be prolonged and lead to presentations of rheumatoid arthritis (8). Parvovirus is a pathogen known to be responsible for transient red cell aplasia in children with sickle cell disease (9), severe aplastic anemia (10), hemolytic anemia and polyneuropathy in children without any underlying diseases (11) and autoimmune hemolytic anemia and

Table 1. Baseline disease distribution in PICU admitted children (MCH 2014-15)

Disease type		
Gastrointestinal diseases	Stress ulcer	1
	Rectorrhagia	1
	Necrotizing enterocolitis	1
	Injury to esophagus	1
	Hematochezia	1
	Gastrointestinal bleeding	1
	Esophagus stricture	1
	Esophageal dilation	1
	Esophageal atresia	1
	Diaphragmatic hernia	1
	Choanal atresia	1
	Biliary atresia	2
Pulmonary diseases	Pulmonary collapse and consolidation	1
	Pulmonary hypoplasia	1
	Respiratory distress	5
	Cystic fibrosis	1
	Lung hydatid cyst	1
	Interstitial lung disease	1
	Pneumonia	1
	Asthma attack	1
	Bronchiolitis	3
	Cystoid pneumatosis	1
Urinary tract system	Chronic kidney disease	1
	Hemolytic uremic syndrome	1
	Posterior urethral valve	1
	Urolithiasis	2
	Nephrotic syndrome	1
Central nervous system	Spinal muscular Atrophy	1
	Hydrocephalus	2
	Reflex sympathetic dystrophy syndrome	1
	Brain anomaly	1
	Craniosynostosis	1
	Convulsion	6
	Asphyxia	1
	Brain tumor	1
Endocrine	Methylmalonic acidemia	1
	Diabetes	3
Infectious diseases	Meningoencephalitis	1
	Septic shock	2
Hematology and oncology	Hemophagocytic lymphohistiocytosis	1
	Chronic granulomatous disease	2
	Lymphangioma	1
	Hemophilia	1
	Hepatoblastoma	1
	Neuroblastoma	1
Others	Psychological problems	1
	Chromosomal abnormality	2
Total		66

hemophagocytosis (12). This study estimated the serologic parvovirus infection in critically ill children with diseases of different types. Parvovirus infection is a cause of bone marrow failure of erythroid type.

In a study on children under 5 years in Tanzania, acute parvovirus infection was associated with 1.1 *mg/dl* decrease in Hb level (13). Myelosuppression and vasculitis may be a response to acute parvovirus infection in patients with myelodysplastic syndrome (14). In our study, no decline in Hb in patients with acute parvovirus infection was observed, which may be due to different pathological agents in our patients. The findings on WBC count and acute parvovirus infection are inconsistent. Hematological findings in patients with parvovirus infection do not show typical changes in WBC count (15). Two cases of paroxysmal nocturnal hemoglobinuria and neutropenia were reported in patients with aplastic crisis (16). The study of Liu *et al* in critically ill children showed higher rate of anemia and thrombocytopenia in the parvovirus B19-positive group, which was not the case in neutropenia and lymphopenia ($p>0.05$) (6). This is consistent with our study as no effect of parvovirus infection on WBC count was observed. Sufficient evidence in the literature indicates that parvovirus can be a replicate in hepatocytes and pronormoblasts and may cause hepatic damage from transaminase elevation to fulminant liver failure, macrophage activation syndrome and fibrosing cholestatic hepatitis (17). Autoimmune hepatitis may occur as a complication of acute parvovirus hepatitis (18). In our study, patients with acute parvovirus infection had comparatively higher levels of ALT and AST, which could be attributed to parvovirus infection. Our results are confirmed by the study of Liu *et al* reporting impaired hepatic function in critically ill children (6). The effect of parvovirus infection on fetal and neonatal erythroid cells is known as well. Parvovirus is the most common cause of non-immune hydrops fetalis (19), and also the cause of spontaneous abortion and intrauterine fetal death (20, 21). Parvovirus infection in critically ill patients may lead to many complications in different organs such as liver and reticuloendotelial system (16,17), and is likely to substantially influence prognosis, mortality and morbidity. Because children who are admitted to PICUs may have various underlying diseases and therefore are likely to undergo invasive procedures, surgery and intubation, acute parvovirus infection may lead to more severe complications and even increase the likelihood of death in them. In the current study, no significant correlation between IgG and death was observed but the correlation between IgM and death was significant. This is an important finding that deserves paying further attention. Parvovirus infection is transmitted *via* aerosolized droplets by coughing and sneezing, or may occur due to blood transfusion and be transmitted from mother to fetus (22). Based on interpretation of antibody, parvovirus in Mayo Clinic laboratory (23), both IgG and IgM against parvovirus may be present at or soon after onset of illness and reach peak titers within 30 days. Because IgG antibody may persist for years, diagnosis of acute infection is made by the detection of IgM antibodies. So antibody can detect acute infection, although viral load has more accuracy. Because of importance of this infection in critical patients and its novelty, this study can be the first impression for other studies in this field. In our PICU settings, sporadic and epidemic transmission of this virus is likely. Because there was no specific concern about this virus, no measures were taken on a routine basis to detect it in the critically ill patients routinely. Our study highlights the importance of this virus and its effect on patients' mortality. Patients in this study suffered from different diseases. One limitation of our study was lack of considering the potential effect of children's underlying diseases on anti-parvovirus antibody level. Seven of our patients had hematological and oncological diseases that could be the reason for lack of pronounced elevation of antiparvovirus antibody level in them. The strength of our study was the focus on acute parvovirus infection and potential associated effects on the clinical and laboratory characteristics of children admitted to the PICU. Although the study sample is limited and 5 deceased patients comprise a low number for powerful statistical results, significant statistical measurements show the importance of parvovirus infection in critically ill patients. This result can be confirmed or rejected by other studies.

Conclusion

Parvovirus infection is an important disease and may cause decrease in level of Hb, aplastic crisis, elevation of transaminase level and increase the likelihood of death. Therefore, acute parvovirus

infection should be further investigated as there is ample evidence necessitating directing more attention to acute parvovirus infection in critically ill children especially in Iranian population.

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