Parvovirus B19 Infection as a Rare Cause of Fulminant Liver Failure: A Case Report

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ABSTRACT

Parvovirus B19 infection is common in childhood. The clinical presentations range from benign to life threatening. The literature shows that the clinical presentation is influenced by the patient's age and the presence of chronic disease such as chronic hemolytic disorders and immunosuppressed conditions. As the majority of patients with liver failure are diagnosed as indeterminate, knowledge about parvovirus B19 associated liver disease is limited. We examined 3 children with parvovirus B19-induced fulminant liver failure, 2 of whom underwent liver transplantation. Although the presented patients received standard corticosteroid and tacrolimus therapy as an immunosuppressive regimen, acute rejection, parvovirus B19 persistence, or any other complications due to parvovirus B19 were not observed. Physicians should be aware of the parvovirus B19 infection in association to acute liver diseases.

PARVOVIRUS B19 infection is frequently associated with mild clinical findings except chronic illness [1]. According to the data from the literature, fulminant liver failure secondary to parvovirus B19 infection is very rare [2,3]. As parvovirus B19 infection is common in childhood, liver involvement is expected to occur more frequently. However, reports about the liver involvement associated with parvovirus B19 is very limited [2–8]. In this paper, we present the clinical features of 3 children with parvovirus B19-induced fulminant liver failure.

CASE REPORT

Case 1

A 5-year-old girl was admitted because of elevated liver enzymes and coagulopathy. It had been detected during an evaluation for a febrile illness 6 days prior. The family said rashes, thought to be related to infection, on the chest, abdominal wall, and cheeks had been present for the first days of the fever. The rashes had disappeared 3 days prior to the examination. Her consciousness was clear, and her physical examination was normal except for the jaundice in the sclera and skin. Laboratory parameters were as following alanine aminotransferase (ALT) 3014 U/L, aspartate aminotransferase (AST) 4548 U/L, gamma glutamyl transferase 124 U/L, total bilirubin 7.9 mg/dL, direct bilirubin 4.9 mg/dL, and international normalized ratio (INR) 1.8. Parvovirus B19 IgM antibody and parvovirus B19 polymerase chain reaction (PCR) were positive. Wilson disease, alpha-1 antitrypsin deficiency and other metabolic liver diseases, autoimmune hepatitis, and other causes of viral hepatitis were excluded (Table 1). The liver color Doppler ultrasonography was normal. On the sixth day of admission, plasma exchange was started because of the progressive increase in INR (INR = 2.6). A total of 4 sessions were applied, and 1.5 to 2 plasma volumes were removed in each session. Despite the ongoing plasmapheresis sessions, hepatic encephalopathy developed on the ninth day of the admission, and a liver transplantation was performed using a living donor. The patient received methylprednisolone at the intraoperative anhepatic and postreperfusion phases and tacrolimus as immunosuppressive therapy. Methylprednisolone was given−100 mg intraoperatively and 60 mg at the first day of transplantation. When the patient started oral intake, methylprednisolone was switched to prednisolone. She was discharged on the 18th day after the successful transplantation. She was given prednisolone, which was tapered to 5 mg within the next 2 months and stopped at the sixth month. Acute rejection did not develop. Parvovirus B19 DNA was not detected in the serum at the third month. Now in the fourth year of liver transplantation, no complications, due to parvovirus B19 or any other reason, have been observed.

Case 2

A 14-year-old boy was admitted with fatigue and jaundice to a state hospital. He had an upper respiratory tract infection 2 weeks prior

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Table 1. Patients' Initial Laboratory Parameters

Parameter	Case 1	Case 2	Case 3
Hemoglobin (g/dL)	14.1	12.6	14.4
WBC count (m^3)	11,800	8800	7500
Thrombocyte count (m^3)	218,000	226,000	243,000
ALT (U/L)	3014	1810	2491
AST (U/L)	4548	1680	1960
GGT (U/L)	124	88	112
ALP (U/L)	388	194	256
LDH (U/L)	990	632	1020
Albumin (g/dL)	3.4	3.2	3.3
Total bilirubin (mg/dL)	7.9	17.5	28
Direct bilirubin (mg/dL)	4.9	13	21
PT (min)	19.4	24	32
INR	1.8	2.8	2.75
EBV IgM	Negative	Negative	Negative
EBV PCR	Negative	Negative	Negative
Hepatitis A IgM	Negative	Negative	Negative
Hepatitis E IgM	Negative	Negative	Negative
Hbs ag	Negative	Negative	Negative
HBc IgM	Negative	Negative	Negative
Hbs ab	Positive	Positive	Positive
HCV ab	Negative	Negative	Negative
Parvovirus IgM (U/mL)	43 (positive)	63.8 (positive)	42.2 (positive)
Parvovirus IgG (U/mL)	0.4 (negative)	0.2 (negative)	0.3 (negative)
Parvovirus PCR (U/mL)	312,580	279,700	284,020
Ceruloplasmine (mg/L)	324	386	352
24-hour urine copper (mcg/d)	42	62	66
Autoimmune antibodies (ANA, ASMA, anti-LKM)	Negative	Negative	Negative
IgG (g/L)	8	9.6	10

Abbreviations: ab, antibody; ALP, alkaline phosphatase; ALT, alanine aminotransferase; ANA, anti-nuclear antibody; ASMA, anti-smooth muscle antibody; AST, aspartate aminotransferase; EBV, Epstein-Barr virus; GGT, gamma glutamyl transferase; HBc, hepatitis core; Hbs ag, hepatitis B surface antigen; HCV, hepatitis C; INR, international normalized ratio; LDH, lactate dehydrogenase; LKM, liver kidney microsomal antibody; PCR, polymerase chain reaction; WBC, white blood cell.

to admission. Because of the progressive regression of his consciousness, he was admitted to our intensive care unit. The patient was in grade 1 hepatic encephalopathy. Laboratory parameters were as following: ALT 1810 U/L, AST 1680 U/L, total bilirubin 17.5 mg/dL, direct bilirubin 13 mg/dL, and INR 2.8. Parvovirus B19 IgM antibody and parvovirus B19 PCR were positive. Other causes of acute hepatic failure were excluded (Table 1). Double volume plasma exchange was started. Despite the ongoing plasmapheresis sessions, hepatic encephalopathy progressed and a successful liver transplantation was performed from a living donor during the grade 2 hepatic encephalopathy phase. Patient received methylprednisolone and tacrolimus. Parvovirus B19 DNA did not persist in the serum and disappeared at the tenth week. Acute rejection or any other complication due to parvovirus B19 did not observed.

Case 3

A 16-year-old boy was admitted for evaluation in terms of jaundice. He was the brother of the Case 2 patient. He had an history of upper respiratory tract infection like his brother. The patient was conscious. He had elevated liver enzymes (ALT 2491 U/L, AST 1960 U/L) and bilirubin levels (total bilirubin 28 mg/dL, direct bilirubin 21 mg/dL). The INR was 2.75. A 1.5 to 2 volume plasma exchange was started. Hepatic encephalopathy did not develop. Plasma exchange was completed after 3 sessions. The patient recovered spontaneously. Parvovirus B19 IgM antibody and parvovirus B19 PCR were positive. Other causes of acute and chronic liver failure were excluded (Table 1) during in-hospital follow-up.

DISCUSSION

Parvovirus B19 infection is common in childhood. Patients frequently recover without any complications, but it can also result in life-threatening clinical conditions. The best-known clinical presentations of parvovirus B19 infections are erythema infectiosum (fifth disease), fetal infection leading to nonimmune hydrops fetalis, arthralgia or arthritis, transient aplastic crisis in those with chronic hemolytic disorders, and pure red blood cell aplasia in immunocompromised individuals [1].

Our cases show that parvovirus B19 infection can also cause fulminant liver failure in healthy children. There are a few case reports of parvovirus B19-induced hepatitis and liver failure in the English literature [2–4]. Yoto et al [4] described 7 children who had parvovirus B19-induced hepatitis in their retrospective investigation of children with acute hepatitis. None of the children required liver transplantation. Kim et al [5] reported parvovirus B19 infection associated with acute hepatitis in an infant that resolved spontaneously. Krygier et al [6] reported an immunocompetent adult who developed fulminant hepatic failure during an acute infection with parvovirus B19 who subsequently underwent orthotopic liver transplantation. So et al [7] reported an urgent liver transplantation for acute liver failure due to parvovirus B19 infection, which was complicated by

the primary Epstein-Barr virus, cytomegalovirus infections, and aplastic anemia in an 11-year-old boy. Langnas et al [8] investigated the explanted livers and serum samples of 6 pediatric patients who underwent liver transplantation due to non-A, non-B, and non-C fulminant liver failure associated with aplastic anemia. They determined parvovirus B19 DNA in 4 of 6 liver tissues, and all 6 had parvovirus B19 IgG. In these cases, the presence of the active parvovirus B19 infection is unclear because the IgG antibody exhibits latent infection.

In children with infectious fulminant liver failure, the reason is mostly due to the hepatitis A virus. Infrequently reported etiologies are the hepatitis B virus, Epstein-Barr virus, non-A to non-E hepatitis, and hepatitis E virus [9]. Our cases suggest that there should be more patients with fulminant liver failure due to parvovirus B19. Due to our observations, we now routinely investigate the parvovirus B19 infection in etiological evaluation of pediatric fulminant liver failure in our clinic.

None of the cases developed acute rejection. Any other clinical presentation related to parvovirus B19 infection, such as aplastic anemia, rash, and arthritis, was observed after transplantation. Also, the parvovirus B19 DNA load rapidly decreased and disappeared in a short time after transplantation. These observations also indicate that postoperative immunosuppressive treatment at standard doses does not have a negative effect on the resolution of parvovirus B19 infection.

In conclusion, our cases indicate that in etiological evaluation of fulminant liver failure in children, parvovirus B19 infection should be investigated. Pediatricians should be aware of the parvovirus B19 infection in case of acute liver diseases.

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