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CASE REPORT

Parvovirus B19 induced hepatic failure in an adult requiring liver transplantation

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Abstract

Parvovirus B19 induced acute hepatitis and hepatic failure have been previously reported, mainly in children. Very few cases of parvovirus induced hepatic failure have been reported in adults and fewer still have required liver transplantation. We report the case of a 55-year-old immunocompetent woman who developed fulminant hepatic failure after acute infection with Parvovirus B19 who subsequently underwent orthotopic liver transplantation. This is believed to be the first reported case in the literature in which an adult patient with fulminant hepatic failure associated with acute parvovirus B19 infection and without hematologic abnormalities has been identified prior to undergoing liver transplantation. This case suggests that Parvovirus B19 induced liver disease can affect adults, can occur in the absence of hematologic abnormalities and can be severe enough to require liver transplantation.

Key words: Parvovirus B19; Fulminant hepatic failure; Orthotopic liver transplant; Fulminant hepatitis

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INTRODUCTION

Parvovirus B19 is a common infection that often occurs in childhood, with 50% of adolescents having antibodies to the virus by 15 years of age[1]. The infection is transmitted by respiratory droplets and through blood products derived from viremic donors. Most acute infections in children do not result in symptoms, but the clinical presentation can range from erythema infectiosum to non-specific febrile symptoms. In adults, a polyarthropathy that can resemble rheumatoid arthritis or systemic lupus erythematosus has been reported, particularly in middle aged women[2]. In patients with hemoglobinopathies the infection can cause a clinically relevant drop in hemoglobin, which may require transfusion. In the immunocompromised patient, this infection can result in bone marrow suppression and transient mild transaminase elevations commonly occur. In children there have been several reports of severe acute hepatitis and acute liver failure, which are most often self-limited[1]. There is, however, at least one reported case of parvovirus B19 induced fulminant hepatic failure in a child that required urgent liver transplantation[3].

The majority of published cases of parvovirus B19 induced hepatitis in adults have suggested that hepatic involvement by the virus is less severe than in the pediatric population[4]. We report the case of a 55-year-old immunocompetent woman with no previous history of liver disease who developed fulminant hepatic failure secondary to acute infection with parvovirus B19 and required urgent liver transplantation.

CASE REPORT

A 55-year-old immunocompetent woman who was born in Canada presented to her family physician and subsequently a local emergency room with a two week history of fatigue, general malaise, nausea with emesis,

anorexia, dark urine and pruritus. She was noted to be jaundiced and complained of mild arthralgias in her upper extremities. One week prior to developing these symptoms, she was a passenger on a commercial airplane flight and assisted an ill jaundiced passenger who had vomited. She was a retired registered nurse with no risk factors for viral hepatitis. She denied the use of herbal remedies and acknowledged minimal alcohol consumption. On initial assessment, she was afebrile with marked icterus, no hepatosplenomegaly or ascites and mild asterixis.

Initial laboratory investigations revealed a hemoglobin 161 g/L (normal: 115-155 g/L), white blood cell count 6.6×10^9/L (normal: 4×10^9-11×10^9/L), platelet count 236×10^9/L (normal: 150×10^9-400×10^9/L), creatinine 62 μmol/L (normal: 40-95 μmol/L), aspartate aminotransferase 1838 U/L (normal: 10-38 U/L), alanine aminotransferase 1398 U/L (normal: 20-65 U/L), alkaline phosphatase 304 U/L (normal: 50-160 U/L), γ-glutamyl transpeptidase 179 U/L (normal: 10-55 U/L), direct bilirubin 166 μmol/L (normal: 0-5 μmol/L) and total bilirubin 359 μmol/L (normal: 0-18 μmol/L), international normalized ratio 1.9 (normal: 0.9-1.1), partial thromboplastin time 34 s (normal: 24-34 s), albumin 29 g/L (normal: 35-48 g/L). Hepatitis A IgG was positive and IgM was negative, hepatitis B surface antigen was negative and hepatitis C serology was negative and investigations excluded hepatitis E. Acetaminophen level was < 66 μmol/L (normal: < 66 μmol/L). An urgent abdominal ultrasound demonstrated a normal appearing liver with no focal lesions.

Two days after admission to a local hospital she was transferred to the regional liver transplantation centre for assessment. On arrival, she remained icteric and demonstrated evidence of mild hepatic encephalopathy and ascites. Her liver enzymes continued to deteriorate and her liver function tests became increasingly abnormal. Her Model for End-stage Liver Disease (MELD) score was 28[5]. Further investigations revealed a serum ceruloplasmin of 301 mg/L (normal: 215-540 mg/L), IgA 3.24 g/L (normal: 0.7-4.0 g/L), IgG 13.4 g/L (normal: 6.7-15.2 g/L), IgM 1.09 g/L (normal: 0.4-2.3 g/L). The patient's anti-nuclear antibody, anti-smooth muscle antibody and anti-mitochondrial antibody were negative and iron studies were within normal limits. Serology for human immunodeficiency virus and cytomegalovirus were negative, Epstein Barr virus IgG was positive and IgM was negative. Serology for parvovirus B19 was positive, with both IgG and IgM being detected by ELISA (Biotrin).

Five days after transfer, she was placed on the waiting list for liver transplantation. Ten days after transfer she developed worsening encephalopathy and was moved to the top of the transplant list. Twelve days after her transfer she underwent an orthotopic liver transplant. One day post-transplant she was extubated and by the following day she was transferred to the solid organ transplant ward in stable condition.

Histopathologic analysis of the explanted liver demonstrated massive hepatic necrosis consistent with viral induced fulminant hepatitis. A sample of the explanted liver was ground up with a mortar and pestle in a 2 mL volume of Minimal Essential Medium. After clarifying by centrifugation, the preparation was extracted for nucleic acid using the EasyMag platform (from bioMerieux). The extracted DNA was then tested by a parvovirus specific PCR using the forward primer CCAGGAATGACTACAAAAGGCAAATAC and the reverse primer GGTAATGCGGGGTTTCTTG. The reaction was carried out for 40 cycles, each consisting of 95℃ for 0 s, 52℃ for 30 s and 72℃ for 30 s. The PCR products were analyzed by electrophoresis on agarose gel containing ethidium bromide and visualized under UV light. A band corresponding to a 191 base pair amplicon, diagnostic for Parvovirus B19, was seen. The finding of Parvovirus B19 by PCR in the explanted liver therefore confirmed the serological diagnosis of acute Parvovirus B19 infection.

DISCUSSION

Parvovirus B19 has been proposed as a causative agent of hepatitis, hepatitis-associated anemia and acute liver failure. There are several cases reported in the literature of patients with abnormal liver biochemistry, with and without associated anemia, caused by acute infection with parvovirus B19. One small series reported detectable parvovirus B19 DNA by polymerase chain reaction in liver tissue from 4 of 6 (67%) pediatric patients with acute liver failure accompanied by hepatitis-associated anemia and in 2 of 4 (50%) of those with acute liver failure in isolation[6]. Viral DNA was not detected in any of the patients' sera. A second small series found that parvovirus DNA was detected in 5 of 6 (83%) livers from patients with idiopathic non-A-E acute liver failure with hepatitis-associated anemia, 2 of 3 (67%) livers in patients with isolated acute liver failure and 1 of 6 (17%) livers from patients with acute liver failure of known non-parvovirus etiology[7]. So *et al*[3] (2007) have recently published a case report describing an 11-year-old boy who presented with fulminant hepatic failure secondary to acute parvovirus B19 infection who required urgent liver transplantation.

The majority of the available literature regarding acute parvovirus B19 induced fulminant hepatic failure has described cases involving children. Despite this, however, there are several published reports of acute parvovirus B19 infection in adults associated with the development of acute hepatitis[8-11]. Interestingly, in virtually every case reported the patients have had a complete and spontaneous remission. This has led to speculation that the syndrome in adults is not only less common than in children, but that it has a much less severe course with better patient outcomes. The case described in this report appears to be the first reported in which an adult patient has been recognized as having acute parvovirus B19 induced fulminant hepatic failure prior to liver transplantation. There remains a

remote possibility that she acquired the infection in childhood and that this acute episode was precipitated by an immune response to viral reactivation. In any event, it demonstrates that adults may also develop fulminant hepatic failure in the absence of hematologic abnormalities and may ultimately require liver transplantation as a potential life saving intervention.

It is worth noting that the notion of parvovirus B19 as a cause of acute viral hepatitis is not universally accepted and that there is also literature published that questions this association. A small study by Wong *et al*[12] documented the presence of parvovirus B19 DNA in the liver tissue of 4 of 15 (27%) patients with acute hepatitis as compared to 3 of 22 (14%) patients with non-viral liver disease. They concluded that no difference exists in the prevalence of parvovirus B19 in liver tissue in patients with acute liver failure or hepatitis-associated anemia as compared to those with chronic hepatitis B and C infection. Despite this study's findings, evidence continues to mount in favour of parvovirus B19 as a causative agent of acute hepatitis and fulminant hepatic failure.

In conclusion, there is growing evidence that Parvovirus B19 may cause acute viral hepatitis, which can result in fulminant hepatic failure requiring liver transplantation. Although this infection is most commonly acquired in childhood, adults who become acutely infected can develop liver dysfunction as a result. The liver disease can occur independently from the often-associated hematologic abnormalities, as illustrated by the case described in this report. Fulminant hepatic failure induced as a result of acute infection with parvovirus B19 remains a rare clinical entity, however it may be underreported due to infrequent testing that results from a lack of awareness about this syndrome. A wider recognition of parvovirus B19 as a potential cause of severe liver disease is expected to augment our ability to make a definitive diagnosis of the etiology underlying such severe clinical presentations.

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