Parvovirus B19 in an immunocompetent adult patient with acute liver failure: An underdiagnosed cause of acute non-A-E viral hepatitis

J Kee Ho MB MRCPI¹, Susan PL Tha MD PhD FRCPC², Robert Coupland MD FRCPC², Bakul I Dalal MD FRCPC², William R Bowie MD FRCPC¹, Gayatri M Sreenivasan MD FRCPC¹, Mel Krajden MD FRCPC³, Eric M Yoshida MD MHSc FRCPC¹

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There are occasional pediatric reports of parvovirus B19-associated transient acute hepatitis and hepatic failure. A case of a 34-year-old immunocompetent woman who developed severe and prolonged but self-limited acute hepatitis and myelosuppression following acute parvovirus B19 infection is reported. Parvovirus B19 may be the causative agent in some adult cases of acute non-A-E viral hepatitis and acute liver failure.

Key Words: *Hepatitis; Liver failure; Parvovirus B19*

Parvovirus B19 (PVB19) is a common infection that usually occurs in childhood, with 50% of adolescents having specific anti-PVB19 antibodies by 15 years of age. It is transmitted by respiratory droplets and blood products. Most infections are asymptomatic, and the clinical presentation ranges from erythema infectiosum to nonspecific influenza-like symptoms (1). In adults, particularly middle aged women, it may cause polyarthropathy that resembles rheumatoid arthritis or systemic lupus erythematosus (2). In the immunocompromised host, it can result in chronic or recurrent bone marrow suppression (2). Transient mild elevations in transaminases without jaundice commonly occur with acute parvovirus infection. In children, acute hepatitis can be severe, with manifestations of acute liver failure (ALF), but it is usually self-limited (1).

CASE PRESENTATION

A 34-year-old immunocompetent woman from China presented with a six-week history of polyarthrititis, prior sore throat, anorexia, fever greater than 38.5°C and four weeks of right upper quadrant discomfort and jaundice. She gave no history of previous liver disease and had no risk factors for viral hepatitis. There was no history of consumption of herbal remedies. She drank minimal alcohol and was a smoker. On examination, she was markedly icteric, and there was hepatosplenomegaly, ascites

Infection à parvovirus B19 chez une patiente adulte immunocompétente présentant une insuffisance hépatique aiguë : Cause sous-diagnostiquée de l'hépatite virale non-A-E aiguë

Il arrive qu'on rencontre des cas pédiatriques d'hépatite aiguë transitoire et d'insuffisance hépatique associées au parvovirus B19. On présente ici le cas d'une femme immunocompétente de 34 ans qui a développé une hépatite aiguë sévère et prolongée, mais spontanément résolutive, et un problème de myélosuppression après une infection à parvovirus B19 aiguë. Le parvovirus B19 peut donc être un agent causal dans certains cas d'hépatite virale non-A-E aiguë et d'insuffisance hépatique aiguë chez l'adulte.

and bilateral pleural effusions; she showed no peripheral stigmata of chronic liver disease and she was not encephalopathic.

Laboratory investigations revealed leukocytes $2.8 \times 10^9/L$ (normal values $4 \times 10^9/L$ to $11 \times 10^9/L$); neutrophils $0.59 \times 10^9/L$ (normal values $2 \times 10^9/L$ to $8 \times 10^9/L$); lymphocytes $1.7 \times 10^9/L$ (normal values $1.2 \times 10^9/L$ to $3 \times 10^9/L$); hemoglobin 98 g/L (normal values 135 g/L to 175 g/L); platelets $79 \times 10^9/L$ (normal values $125 \times 10^9/L$ to $350 \times 10^9/L$); international normalized ratio 2.3; partial thromboplastin time 66.7 s (normal values 25 s to 38 s); total bilirubin 418 $\mu\text{mol/L}$ (normal values 0 $\mu\text{mol/L}$ to 18 $\mu\text{mol/L}$); alanine aminotransferase 711 U/L (normal values 25 U/L to 80 U/L); aspartate aminotransferase 994 U/L (normal values 10 U/L to 38 U/L); alkaline phosphatase 282 U/L (normal values 50 U/L to 200 U/L); gamma-glutamyltransferase 296 U/L (normal values 15 U/L to 80 U/L); and serum albumin 18 g/L (normal values 34 g/L to 50 g/L). Tests for HIV, hepatitis A, B, C and D serology, and monospot were negative. The patient's smooth muscle antibody, antimitochondrial antibody, antinuclear antibody and screen for Wilson's disease were all negative.

An abdominal computed tomography scan confirmed bilateral pleural effusions, hepatosplenomegaly with a prominent portal vein (1.5 cm) and moderate ascites. Doppler examinations of the portal and hepatic venous systems were normal. Her echocardiogram was normal apart from a small pericardial effusion.

Departments of ¹Medicine and ²Pathology, University of British Columbia; ³British Columbia Centre for Disease Control, Vancouver, British Columbia

Correspondence: Dr Eric M Yoshida, Vancouver General Hospital, Division of Gastroenterology, 100-2647 Willow Street, Vancouver, British Columbia V5Z 3P1. Telephone 604-875-5371, fax 604-875-5447, e-mail eyoshida@interchange.ubc.ca

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Figure 1) Bone marrow aspirate (A); bone marrow biopsy (B). Erythroid hypoplasia with maturation arrest at the stage of proerythroblasts. The proerythroblasts are larger than normal; many bilobed forms are seen. Note intranuclear inclusions (arrows, inset). Hematoxylin and eosin stain, original magnification $\times 200$

A transjugular liver biopsy showed evidence of regenerative changes without fibrosis and significant lobular hepatitis. The portal tracts showed scattered mononuclear cells without piecemeal necrosis, and ductular proliferation accompanied by neutrophilic cholangiolitis. There was spotty hepatocyte necrosis with relatively minor mononuclear inflammation, minor hepatocyte ballooning and steatosis, but obvious Kupffer cell hyperplasia. Stains for herpes and cytomegalovirus were negative, as was the cytomegalovirus rapid culture.

She became progressively pancytopenic and required multiple transfusions of blood products. She was commenced on intravenous immunoglobulin (Ig). Her bone marrow biopsy revealed large proerythroblasts containing nuclear inclusions and a paucity of mature erythroid precursors, consistent with parvovirus infection (Figure 1). She was found to be positive for IgG and IgM to PVB19. Serum and bone marrow polymerase chain reaction for PVB19, performed toward the end of her illness, were negative. The patient subsequently recovered fully with normalization of her liver enzymes and hematological parameters. The IgM to PVB19 became nonreactive, with persistence of IgG at follow up. The total duration of illness was slightly more than 10 weeks.

DISCUSSION

PVB19 has been proposed as the causative agent of ALF or hepatitis-associated anemia (HAA). However, there are still conflicting opinions as to the role of this virus and its pathogenesis. One small series (3) ($n=6$) reported detectable PVB19 DNA by polymerase chain reaction in liver tissue in 66% of patients with ALF associated with HAA and 50% of patients with ALF without HAA. PVB19 DNA was not detected in the

serum in any of the subjects, a situation similar to our case. In another small series ($n=16$) (4), PVB19 DNA was detected in 83% of livers from patients with idiopathic non-A-E ALF associated with HAA and 75% of livers without HAA. In contrast, however, another study (5) reported the presence of PVB19 DNA in liver tissues of four of 15 patients (27%) with acute hepatitis versus three of 22 (14%) with nonviral liver disease. Furthermore, this study found no difference in prevalence of PVB19 in liver tissue in patients with ALF or HAA compared with those with chronic hepatitis C and hepatitis B infection.

CONCLUSIONS

PVB19 is not universally accepted as a cause of acute viral hepatitis, with both supporting and dissenting studies reported in the literature. Our clinical experience, however, would suggest that PVB19 may be a cause of some nonpediatric cases of non-A-E hepatitis and ALF.

REFERENCES

1. Young NS, Brown KE. Parvovirus B19. *N Engl J Med* 2004;350:586-97.
2. Naides SJ. Rheumatic manifestations of parvovirus B19 infection. *Rheum Dis Clin North Am* 1998;24:375-401.
3. Langnas AN, Markin RS, Cattral MS, Naides SJ. Parvovirus B19 as a possible causative agent of fulminant liver failure and associated aplastic anemia. *Hepatology* 1995;22:1661-5.
4. Karetnyi YV, Beck PR, Markin RS, Langnas AN, Naides SJ. Human parvovirus B19 infection in acute fulminant liver failure. *Arch Virol* 1999;144:1713-24.
5. Wong S, Young NS, Brown KE. Prevalence of parvovirus B19 in liver tissue: No association with fulminant hepatitis or hepatitis-associated aplastic anemia. *J Infect Dis* 2003;187:1581-6.