Hepatitis C infection in a paediatric patient probably due to congenital infection

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Abstract

Hepatitis C Virus (HCV) occurs particularly in multitransfused children. Perinatal/ vertical HCV transmission rarely occurs (7%). We report a 9 month old Chinese girl presenting with severe unconjugated hyperbilirubinaemia since day 3 of life. She had septicaemia and received total parenteral nutrition(TPN) and fresh frozen plasma transfusion once (Donor Hepatitis B surface antigen (HbsAg) and Hepatitis C negative). She was referred for conjugated hyperbilirubinaemia at age 3 months with elevated alkaline phosphatase and liver enzymes. On examination, she was thriving, jaundiced with hepatosplenomegaly; stools and urine were yellow. Her mother had a history of tattooing and plastic surgery 10 years ago. There is no family history of autoimmune disease, liver disease, jaundice or blood transfusion. Blood film showed target cells; haemoglobin analysis was normal. Blood glucose, serum protein, albumin, prothrombin time and alpha-fetoprotein normal; raised aspartate transaminase (AST) 351 U/l, alanine transaminase (ALT) 288 U/l and alkaline phosphatase (ALP) 515 U/l. Serum bilirubin was raised (total 156, conjugated 107, unconjugated 49 µmol/l). Ultrasound abdomen showed normal liver and spleen echotexture. Liver biopsy showed features of neonatal hepatitis. Other investigations including thyroid function tests, red blood cell galactose-1-phosphate uridyl transferase, serum alpha-1-antitrypsin, ceruloplasmin, iron, congenital infection screen, urine culture and Hepatitis A IgM were negative. Screening for HbsAg and human immunodeficiency virus were negative for the patient and family. At age 3 months, anti-HCV were positive in both patient and mother. Serum HCV-RNA by PCR technique was detected in the mother but was false negative in the patient. The clinical impression then was maternal HCV infection with maternal transplacental anti-HCV IgG transfer to the patient; the hepatosplenomegaly being related to neonatal septicaemia/ TPN. At 6 months, jaundice had resolved but hepatosplenomegaly was still present. Serum ALP decreased to 340 U/l and ALT to 49 U/l. She had persistence of anti- HCV and developed HCV-RNA positivity. Hence, she has HCV viraemia and chronic HCV infection, probably congenitally (vertically) transmitted from maternal infection; HCV-RNA being falsely negative at age 3 months.

Key words: Hepatitis C; congenital; paediatric

Introduction

Hepatitis C virus (HCV) is a single-stranded Flavivirus-like RNA virus. HCV in children occurs more frequently in the multitransfused eg. thalassaemics, haemophiliacs, survivors of childhood cancers and haemodialysis patients. Congenital HCV transmission is rare (7%) (Nowicki, 1995) and it is still not clear whether transmission is mainly in-utero or perinatal. Intrafamilial spread is uncommon. We report here a 9 month old Chinese girl with Hepatitis C infection, probably due to congenital infection.

Case History

We present a 9 month old Chinese girl with a history of postnatal intensive care who developed severe indirect hyperbilirubinaemia on day 3 of life. She had methicillin- resistant *Staphylococcus* aureus septicaemia and received total parenteral nutrition (TPN) and fresh frozen plasma transfusion once. (Donor Hepatitis B surface antigen (HbsAg) and Hepatitis C antibody negative.) She is the 2nd of two siblings from a nonconsanguinous marriage. Her mother had a history of tattooing and plastic surgery 10 years previously. There was no family history of autoimmune disease, liver disease, jaundice or blood transfusion. She was referred for direct hyperbilirubinaemia at age 3 months with elevated alkaline phosphatase and liver enzymes. Physical examination at 3 months of age revealed that she was thriving (median weight 5.2kg, length 64cm, median head circumference 39cm), jaundiced and had hepatosplenomegaly (liver 6cm, spleen 4cm). Laboratory investigations showed target cells in the full blood picture, normal haemoglobin electrophoresis, blood glucose, serum protein, albumin, prothrombin time and alpha-fetoprotein. There was raised aspartate transaminase (AST) (351 U/l), ala-

nine transaminase (ALT) (288U/l) and alkaline phosphatase (ALP) (515U/l). Serum bilirubin was raised (total 156, direct 107, indirect 49 µmol/l). Ultrasound abdomen showed normal liver and spleen echotexture. Histopathological examination of the liver biopsy showed features of neonatal hepatitis with expanded portal tracts infiltrated by chronic inflammatory cells, piecemeal necrosis, giant cell transformation, ballooning degeneration and bile cholestasis (Figs. 1 & 2). Thyroid function tests, red blood cell galactose-1-phosphate uridyl transferase, serum alpha-1- antitrypsin, ceruloplasmin, iron, toxoplasmosis antibody, VDRL, urine cytomegalovirus, urine culture and hepatitis A IgM were negative. Screening for HbsAg and human immunodeficiency virus were negative for the patient and the family. At age 3 months, HCV antibodies were positive in both the ELISA and HCV Line Immunoassay (Fig. 3) but HCV-RNA was negative in the baby . Blood taken from the mother at this time showed HCV antibodies as well as HCV-RNA positivity. At age 6 months, the jaundice had resolved but the hepatosplenomegaly was still present in the baby. Serum ALP decreased to 340 U/l and ALT to 49 U/l. She had persistence of anti-HCV and developed HCV-RNA positivity.

Our conclusion is that there was active HCV infection in the mother resulting in transplacental HCV transfer during pregnancy to the patient with detection of anti-HCV IgG at age 3 months. The hepatosplenomegaly was related to neonatal septicaemia/total parenteral nutrition. At age 6 months, the patient had HCV viraemia and chronic HCV infection, probably congenitally (vertically) transmitted from maternal infection.

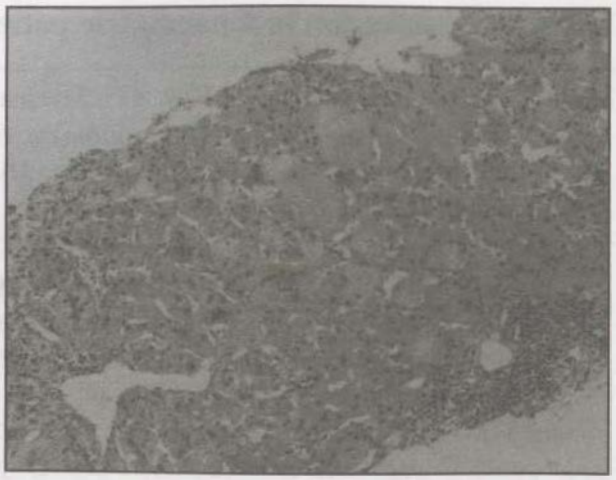

Fig. 2. Histopathology of liver biopsy showing giant cells.

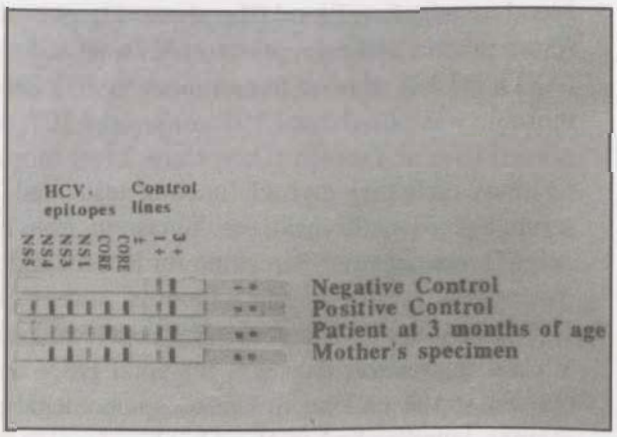

Fig. 3. HCV line immunoassay showing antibody bands to HCV.

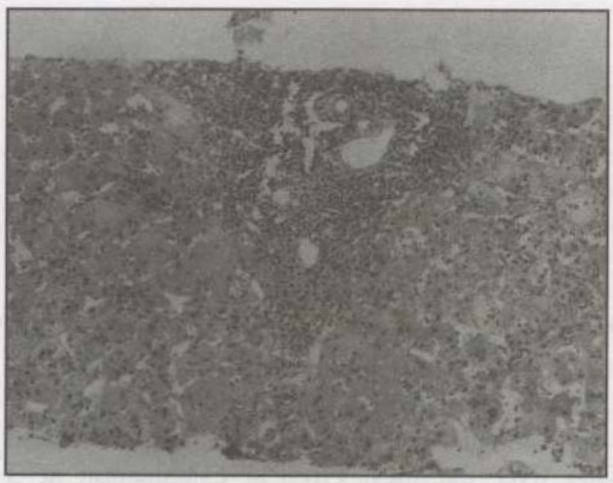

Fig. 1. Histopathology of liver biopsy showing portal tract inflammatory infiltrate

Discussion

Chronic HCV infection is a serious disease with progression to chronic active hepatitis (35%) and cirrhosis (20%) and although fulminant hepatic failure is rare, there is a 4-fold increased risk of bepatocellular carcinoma especially in prolonged viral exposure in paediatrics. There is little data on alpha-interferon (IFN) treatment in paediatric HCV infection (Bortolotti *et al.*, 1995). Current studies of IFN treatment in children show a response rate of 36% and relapse rate of 50% in responders (Ruiz-Moreno *et al.*,1992). Response is reported to be better if pretreatment levels of ALT and HCV-RNA are low, cirrhosis is absent and HCV infection is due to genotype (2a, 3 better than 1b). The greatest

benefit and cost effectiveness is achieved in the youngest children because of lower dosage (body weight), prevention of complications, shorter duration of infection, longer life expectancy (hence, morbidity from chronic HCV) and children tolerate IFN better (Jonas, 1996).

Longer duration of infection is said to increase the likelihood of viral integration into the host genome; once this occurs IFN may be less effective (Lai *et al.*, 1987). Hence younger children with short duration of infection benefit best from IFN treatment.

Congenital HCV infection in babies of HCV antibody positive mothers usually have raised liver enzymes during their first year of life and the majority progress to chronicity. However, the liver disease is usually asymptomatic during infancy and is likely to be mild throughout infancy and childhood (Bortolotti *et al.*, 1997). From previous early studies, HCV has been reported to be prevalent in Malaysian populations, the risk factors for HCV transmission being sharing of needles in parenteral drug users, unscreened blood/blood products and perhaps also the sexual route. The HCV antibody prevalence is known in some Malaysian groups eg. intravenous drug users (85%) and commercial female sex workers (9%); multiple transfused patients (58%), liver cirrhosis (28%) (Sinniah, 1992; Sinniah & Ooi, 1993), and healthy bood donors in Kuala Lumpur (1.49%) (Duraisamy, 1994). While routine HCV screening nationwide has been a policy for all blood and tissue donors in Malaysia since 1994, it is perhaps too preliminary to advocate such routine HCV screening for pregnant women. Routine HCV screening in pregnant women may be considered if an effective treatment regimen or effective HCV vaccine becomes available (Zein, 1997). Meanwhile, we recommend selective anti-HCV screening for women at high risk for HCV and for babies of HCV infected mothers.

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