

Clinical Challenge Number 10

A 16-year-old boy was transferred from a district general hospital with few days' history of jaundice, ascites and hepatic encephalopathy. 7 years ago, he had developed idiopathic haemolytic uremic syndrome leading to end stage renal failure, despite treatment with plasmapheresis and steroids. Renal transplantation was performed 5 years ago. Immunosuppression consisted of Tacrolimus, Mycophenolate mofetil, and prednisolone. Patient had good adherence to treatment and Tacrolimus levels were in the range his transplant team wanted to maintain. There was no evidence of liver disease prior to the renal transplant. About 9 months after renal transplant, the patient developed anicteric chronic hepatitis with consistently elevated ALT and AST ranging from 90 to 470 U/L, and 60 to 400 U/L, respectively. Serologic tests for hepatitis B, hepatitis C, hepatitis E, Epstein-Barr virus, and cytomegalovirus, autoimmune serology as well as blood HBV and HCV PCR analyses were repeatedly negative. Serum concentrations of α 1 antitrypsin, copper, and caeruloplasmin were normal. Liver biopsy showed pericellular fibrosis with incomplete cirrhosis as well as minimal steatosis and mild inflammatory activity suggesting underlying steatohepatitis. Iron and copper concentrations in the liver tissue were normal. Right ventricular failure, constrictive pericarditis, and Budd-Chiari syndrome were ruled out. Despite intensive therapy the patient lapsed into hepatic coma and died before liver transplantation could be performed.

What is the most likely diagnosis?

PS: This is not a real case; hence we are circulating this via email to all our members. Even though this activity is mainly for our trainees, a multi-disciplinary approach to solve this clinical challenge is very welcome.

Answer to Clinical Challenge Number 10

Many thanks for your participation in this clinical challenge. The correct answer is **Hepatitis E Virus (HEV) infection**. No one has sent the correct answer this time.

HEV serology is not very reliable in immunocompromised patients. Autochthonous HEV genotype 3 (GT3) infection is an underdiagnosed problem that is emerging in western world. In immunocompetent individuals HEV infection runs a self-limited course, in solid organ transplant recipients (SOTR) it can progress to chronicity in $\leq 60\%$ owing to impaired HEV-specific T-cell responses. Although in SOTR symptoms are often mild and ALT levels only moderately increased, chronic HE can rapidly lead to progressive cirrhosis. HEV PCR in serum or stools should be tested if unexplained hepatitis occur in solid organ transplant recipients. Timely diagnosis of HEV infection is very important because dose reduction of immunosuppressants or antiviral therapy with ribavirin can lead to a sustained virologic response and thereby halt or reverse disease progression.

In this patient blood PCR analysis showed a positive result for HEV-RNA GT3. To identify whether this was a chronic or acute infection, a retrospective analysis of stored blood samples was performed using quantitative HEV PCR. HEV-RNA was already detectable 2

days after transplantation and persisted over the following years showing chronic HEV infection (no pre-transplant samples were available).