Transient nephritis during resolution phase of acute virale hepatitis E

Abstract

Hepatitis E Virus is a causative agent of hepatitis. Viral E hepatitis is responsible for various clinical manifestations. However, immune reactions due to hepatitis E virus are rarely encountered. A case of membranoproliferative glomerulonephritis associated with hepatitis E virus is reported her.

Introduction

Viral Hepatitis is a major public health problem worldwide. The hepatitis is a disease that can be caused by five unrelated human viruses, namely, hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D (HDV) and hepatitis E (HEV). Table 1 summarizes the outcome of the different viruses. Hepatitis E was not recognized as distinct clinical entity until 1980, previously known as enterically transmitted non-A, non-B hepatitis (NANBH). Hepatitis E is caused by infection with the hepatitis E Virus, a non-enveloped single-stranded, linear, positive sense, polyadenylated RNA (7,5kb). Structural and physiochemical properties, the hepatitis E virus have been classified in the family Caliciviridae, genus Calicivirus. The hepatitis E virus is seen in epidemic outbreak in regions where low standards of sanitation promote the transmission of the virus. Epidemics of hepatitis E have been reported in Southern and Central asia, North and West Africa, Middle East, an in parts of Mexico. It is also seen as sporadic disease in many parts of the world often in travellers returning from abroad. The incubation period following exposure to hepatitis E virus range for 2 to 10 weeks. It is a self – limiting disease followed by recovery and typically lasts 1-4 weeks, chronic infection was until recently thought not to occur. Typical signs and symptom of hepatitis include jaundice, anorexia, hepatomegal, abdominal pain and tenderness, fever, mild chills, nausea, vomiting, clay-coloured stools, dark coloured urine, diarrhoea, arthralgia, although the disease may range in severity from sub clinical to fulminant form with overall patient population mortality rates ranging between 0,5-4%, and as 10-40% among pregnant women. During outbreaks the infection is most common among adults aged 15-40 years (3-30%) than among children (0,2-10%). Hepatitis B and C Virus infection is associated with membranoproliferative glomerulonephritis. Membranoproliferative glomerulonephritis is a kidney disorder that may be related to immune system function. There has only once, been reported membranoproliferative glomerulonephritis due to acute hepatitis E virus. We report a patient with acute hepatitis E virus that developed membranoproliferative glomerulonephritis.

Case Report
A 25 year old man was admitted to Ullevål University Hospital on March 14, 2008, with a thirty day history of mild diarrhoea and 10 days dark urine, on control 3 days later the patient had fever, loss of appetite, nausea, vomiting and upper abdominal pain. He was of Arabic origin, lived in Norway and with recently travel history to an endemic area within six to eight weeks prior to symptom onset. The patient had a non-organised individual travel to India and Nepal in December, January and February, the length of his stay ranged 9 weeks. The patient had been healthy during the travel, however 1 week prior to departure, after staying three days along the Varanasi River in North-India, the patient had a history of reported vomiting and flu-like syndrome, cough, low grade fever and night sweats, this condition lasted for three days. The patient was hepatitis A and hepatitis B vaccinated.

Physical examination revealed splenomegaly, tenderness in the right hypochondrium, and severe jaundice. Abnormal laboratory findings included an International Normalized Ratio (INR) at 2.1. Liver dysfunction was seen, with an increase in levels of aspartate aminotransferase (5665 U/L), alanine aminotransferase (6959 U/L), lactate dehydrogenase (617 U/L), alkaline phosphatase (363 U/L), glutamyltranspeptidase and total bilirubin (468 umol/l). Serum immunoglobulinG levels were relatively elevated (15.3 g/L). No antibodies against human immunodeficiency virus (HIV), hepatitis C virus (HCV), hepatitis B virus (HBV), Cytomegalovirus (CMV), Epstein Barr Virus (EBV) were not detected, instead Anti-HEV IgG was detected with Genelabs Diagnostics HEV Elisa. Antibodies against smooth muscle (SMA) were detected, and SMA titer revealed 64, however ANA ELISA, AMA, Anti-LKM1, RF, IgA RF ELISA, IgM RF ELISA, Anti-CCP, C-ANCA screen, P-ANCA screen, Anti-PR3, Anti-MPO where all negative. Chest X-ray was normal. Abdominal ultrasonography taken 18.03.08, showed hepatomegaly, no thickened gallbladder and splenomegaly. The kidney basement membrane showed no pathology. The patient was treated conservatively.

On the twentieth day the patient improved considerably. His liver function test showed serum aspartate aminotransferase (143 U/L), alanine aminotransferase (522 U/L) and bilirubin (94 umol/l). However the patient started to describe the manifestation of kidney pain (severe back ache). Ibux medical treatment relieved immediately the symptoms of kidney pain. Urine Microbiological Bacterial Cultures revealed no bacterial nephritis. A new abdominal ultrasonography taken 01.04.08 demonstrated normal sized kidneys with widespread thickening of the kidney basement membrane, compatible with renal membranoproliferative glomerulonephritis. A renal biopsy was not performed. The patient’s initial urinalysis was positive for blood and leukocytes. Dipstick urinanalysis revealed blood +++++, and leukocytes +(+), Urine light microscope provided further confirmation of haematuria and leukocytes. He had no hypertension and no decline in renal function. Full blood count revealed no other than hepatitis E virus infection.

He was discharged from hospital, followed up, and received no other medication than Ibux. During follow up of six months, the patient kept well and liver function, kidney function test where normal.

**Discussion**

Most autochthonous hepatitis E virus infections are selflimiting, acute icteric hepatitis; however, follow-up studies of 40 hepatitis E virus infected patients demonstrated that six (15 %) patients developed complications. The clinical features of autochthonous hepatitis E infection range from asymptomatic infection to mild hepatitis, to subacute liver failure. Study based on affected individuals have presented a range of other non-hepatic symptoms, however this studies have not yet reviled infected patient with acute hepatitis E virus, that develop membranoproliferative
glomerulonephritis. Although one of the most frequent kidney diseases associated with chronic hepatitis C virus (HCV) and B virus is membranoproliferative glomerulonephritis. Membranoproliferative glomerulonephritis due to hepatitis virus is still a poorly understood disease. To our knowledge Hepatitis E Virus causing membranoproliferative glomerulonephritis, has only once been reported in a case report. Many associated infections have been reported to cause membranoproliferative glomerulonephritis, but none have been found in this patient. It is believed that the persistent infection with the hepatitis E virus (HEV) is responsible for an immune complex-mediated glomerulonephritis in this patient. Development of membranoproliferative glomerulonephritis in this patient with clinical hepatitis and positive serology for Anti-HEV IgG makes the cause and effect relationships of membranoproliferative glomerulonephritis with hepatitis E most likely.

The principal clinical manifestations of glomerulus’s disease in hepatitis virus infected patients are the presence of proteinuria and microscopic haematuria with or without impaired kidney function, this patient had also demonstrated widespread thickening of the kidney basement membrane.

The clinical manifestations of membranoproliferative glomerulonephritis may be so variable that the disease is often diagnosed only if it has been systematically considered. Many times, it is diagnosed as a form of back pain. In a UK hospital-based study, 40 patient with autochthonous hepatitis E were identified, with affected individuals presenting a range of other non-specific symptoms, 2% describe the manifestation of back pain.

**Conclusion**

Many cases of glomerulonephritis result in a mild, asymptomatic illness that remains undiagnosed.

Because hepatitis E virus has now been pathogenetically linked to glomerulonephritis in this patient, testing for this virus should be considered in the serologic work-up of patients with glomerulonephritis, particularly in countries with a high prevalence of hepatitis E virus, or patients with resent travel history to hepatitis E virus endemic countries.

References:


