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ACUTE HEPATITIS E: CASE REPORT

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SUMMARY

Hepatitis E viral infection has been reported in North Africa, Western Africa and some outbreaks in refugee camps in Somalia and Sudan. We present the rare case of a Kenyan health care worker with documented acute viral Hepatitis E infection.

INTRODUCTION

The Hepatitis E virus was discovered in the early 1980's by scientists who were testing the stored blood samples drawn from patients during an acute hepatitis epidemic which swept through New Delhi, India in 1955. It was originally designated as an Enteric non-A-non-B. Hepatitis virus and was later renamed Hepatitis E due to its enteric nature but also because made alphabetical sense because Hepatitis viruses A to D had been discovered up until then (1). We believe this is the first documented case of acute viral Hepatitis E infection in Kenya.

CASE REPORT

The patient is a 43 year old African male who presented to our hospital with a nine day history of nausea, vomiting and generalised pruritus. He is a nurse and had been working in Sudan at a refugee camp run by a non-governmental organisation.

The symptoms started nine days prior to his presentation and he had been started on Ciprofloxacin based on a positive widal test for Salmonella Typhi. Two malaria slides done. There reported negative. There was no improvement in symptoms after three days of taking Ciprofloxacin so he travelled to Kenya for treatment.

He presented to our casualty with complaints of persistent nausea and vomiting. The vomiting was

non-projectile, bilious and sometimes blood stained. He denied any abdominal pain or diarrhoea. He also had generalised pruritus with no associated rash and on further enquiry he reported pale stools and deeply yellow urine.

His past medical history was significant for admission five years prior with a diagnosis of Acute Stress Reaction. On a routine outpatient visit six months prior to the current presentation, his liver function tests were normal. He reported being allergic to Sulphur drugs. He was married with three children and did not smoke or take any alcohol. He reported no family history of liver disease or malignancy and no use of herbal preparations.

On examination we found a young man with normal vital signs. Scleral jaundice was noted but he had no stigmata of chronic liver disease and no hepatic flap. He was mildly tender in the right upper quadrant with a negative Murphy's sign. Liver span was 10 centimetre. The rest of the systemic examination was normal.

His initial investigations showed elevated liver enzymes with negative screens for Hepatitis A, B and C. However Hepatitis E IgM and IgG antibodies were found to be positive. Haemogram, Renal function tests, Amylase, Lipase, CA 19-9, Ferritin and Ceruloplasmin levels were normal. HIV Elisa was negative.

A hepatobiliary ultrasound revealed a normal liver with a thickened gall bladder but no gall stones and no pericholecystic fluid and this was confirmed on a computed tomography scan of the abdomen.

Test	Normal Values	5 th Jan 2010	7 th Jan 2010	21 st Jan 2010
Total Bilirubin	0-2µmol/l	364	286	52
Direct bilirubin	0-3.4µmol/l	185	148	19
SGOT	30.5U/L	257	1,800	38
SGPT	10.8U/L	137	2,450	80
ALP	72U/L	206	163	92
Gamma GT	29U/L	81	81	42
Serum Protein	82.7U/L	66		
Serum Albumin	47.0U/L	34		

He was started on supportive management with intravenous fluids and multivitamin supplements and was allowed home after four days.

Two weeks later, his repeat liver function tests were markedly improved. He reported complete resolution

symptoms and was able to report back to work.

DISCUSSION

The Hepatitis E virus is a single stranded RNA virus

with an icosahedral structure which belongs to the genus *Hepevirus* and family *Hepeviridae*. The HEV genome contains three open reading frames (ORFs). ORF-1 codes for the non-structural proteins responsible for final replication. ORF-2 contains genes encoding the capsid. The function of ORF-3 is not very clear, but antibodies directed against ORF-3 epitopes have been identified (1).

There are four documented genotypes of Hepatitis E virus with different geographical distribution and differing levels of virulence. Genotype 2 includes isolates from Asia, the Middle East and North Africa. Genotype 2 has been found in Mexico and Nigeria. Genotype 3 was recovered from swine in North America, Europe, Egypt, Asia and New Iceland and from humans in North and South America, Europe, Japan and China. Genotype 4 was found in humans and swine in Asia. Genotype 1 is the most virulent which may explain the severity of disease in India where it is the most common subtype found whereas genotypes 3 and 4 are less pathogenic and may explain subclinical disease seen in the North America and Europe.

Hepatitis E is endemic to Asia, Africa, Central America and the Middle East. There have been some sporadic outbreaks in other parts of the world with the largest outbreak occurring in China between 1986 and 1988 where more than 100,000 cases were documented. Outbreaks have also been reported in refugee camps in Somalia and Sudan. It occurs mainly in young adults aged between 15 to 40 years and is usually subclinical when it occurs in children. Severe hepatitis can occur in adults and mortality is between 1 to 2%.

Transmission is mainly by faecal-oral route following contamination of sources of drinking water. Zoonotic transmission from animal reservoirs has been suggested by the presence of high levels of anti-HEV antibodies in people in close contact with animals like veterinarians and farmers. Rodents have also been suggested as reservoirs causing zoonotic transmission (2).

Parenteral transmission by transfusion of blood and blood products also occurs and mother to child transmission has also been documented. However there is no evidence of transmission via breast milk.

Person to person spread of Hepatitis E has not been documented clearly in the past but a recent study carried out during an outbreak in Uganda suggests that person to person transmission was occurring among household members (3).

Once the contaminated water is ingested the incubation period lasts between three to nine weeks during which time the virus replicates mainly in the liver. There is a prodromal phase during which the patient experiences myalgia, arthralgia, low grade fevers, anorexia, nausea and vomiting. This is followed by the icteric phase characterised by symptoms of acute viral hepatitis. These include jaundice, pruritus, dark urine and pale coloured stools. The main findings on physical exam are jaundice and sometimes hepatomegaly. Subclinical disease with no symptoms occurs mainly in children.

Liver transaminases and bilirubin levels are elevated and they usually resolve along with the clinical symptoms in about eight weeks. Coagulopathy is rare except in cases of liver failure but there have been three documented cases of thrombocytopenia associated with Hepatitis E infection (4). The exact mechanism was unclear but the process was thought to be immune mediated.

Hepatitis E does not run a chronic course and similar to Hepatitis A a presence of antibodies seems to confer immunity from re-infection.

Liver histology shows a cholestatic picture with stasis of canalicular bile and marked proliferation of intralobular bile ductules and inflammatory infiltrate of mononuclear cells.

Pregnant women have more severe hepatitis usually leading to fulminant liver failure with high mortality rates of 15-25%. This is thought to be due to the presence of high level of steroid hormones that cause immunosuppression thus promoting viral replication and also inhibit liver regeneration by inactivation of Nuclear Factor kappa B (NF- κ B) which plays a major role in both immunity and liver regeneration (5).

Diagnosis of Hepatitis E virus is based on detection of anti-Hepatitis E Viral Antibodies in blood as well as detection of Hepatitis E RNA copies in serum, liver, and stool samples in the early stages of infection. Immunoglobulin M is present in early infection and remains detectable for up to six months. Immunoglobulin G is also detectable from the second week of infection and both can remain positive for more than six months.

Hepatitis E Viral RNA copies become undetectable between one to six weeks from symptom onset. Management of Hepatitis E is mainly supportive since the disease is self-limiting in most cases. In severe cases with fulminant liver failure, liver transplantation is required. Good sanitation and complete separation of sewage from water sources to prevent contamination can prevent transmission of Hepatitis E vaccine to prevent infection with Hepatitis E is currently being developed and has shown promising results (6).

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