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Case Report

Dengue Fever with Hepatitis E and Hepatitis A infection
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Abstract

Infection with dengue viruses produces a spectrum of clinical illness ranging from a nonspecific viral syndrome to severe and fatal haemorrhagic disease. Important risk factors include the strain and serotype of the infecting virus, as well as the age, immune status, and genetic predisposition of the patient. The teaching point in this case study was Dengue fever which occurred concomitantly with Hepatitis A and Hepatitis E virus infection.

Introduction

Jaundice follows due to a variety of causes including hepatitis A, B, C, D, and E viral infections, alcohol abuse, medications and toxins. Hepatitis E virus (HEV) and hepatitis A virus (HAV) are endemic in South Asia.1 Dengue fever (DF) is a mosquito-borne virus infection, caused by four distinct viruses (serotypes 1 to 4) that are closely related antigenically. Dengue virus serotype 3 is responsible for most of the DF cases in Karachi, Pakistan.2 There is no treatment of Dengue fever (DF). However, dengue fever shock syndrome requires a supportive treatment.3

Case Report

A 17 year old girl was admitted in September 2007 with jaundice for one month associated with fever for ten days and altered consciousness since one day. There was no significant past history. Patient had paracetamol and antimalarials for the last ten days. On examination, she was jaundiced and drowsy; Glasgow coma scale (GCS) was 8/15 with a pulse 108/min, blood pressure 109/73 mm Hg and temperature of 102ºF. Systemic examination was normal, besides a palpable spleen. The labs on admission demonstrated a haemoglobin of 10 (range 11.1-14.5) gm/dl, haematocrit 34.3% (range 35.4-42.0), white cell count 3.2 (range 2.0-10.0) with neutrophil 84% (range 40-75), platelet 183 x10^9/L (range 150-400); malarial parasite was not seen on film; prothrombin time (PT) 23 (range 10-15 seconds), activated plasma thrombin time (APTT) 38.4 sec (range 25-35 seconds), bilirubin 22 (range 0.25-1.0) mg/dl, alanine transaminase (ALT) 330 (range 3-33) IU/L, aspartate transaminase (AST) 220 (range 18-32) IU/L; alkaline phosphatase (ALP) 518 (range 31-141) IU/L, gamma glutamate transaminase (GGT) 33 (range 1-37) IU/L, sodium 127 (range 136-148) mmol/L, potassium 2.5 mg (range 3.6-5.0) mmol/L, albumin 1.9 g/dl, serum amylase 125 (range 25-125) U/L, lactate dehydrogenase (LDH) 705 mg, magnesium 1.8 (range 1.9-2.5) mg/dl. Plasmodium falciparum and Plasmodium Viva were negative by immunochromatographic test (ICT) detecting malaria antigen. She was admitted in intensive care unit for grade III Hepatic encephalopathy and treated with IV fluid and lactulose. She stabilized haemodynamically over next two days and her WBC count reduced to 15.3, PT 27, ALT 59, K 3.0 mmol/L. Patient recovered from Hepatic encephalopathy after 4 days. Serology was positive for HEV and HAV IgM antibodies. Hepatitis B virus s Antigen (HBsAg), Hepatitis B core IgM, Hepatitis C virus antibody and HEV virus IgG were negative. Her chest x-ray and abdominal ultrasound were normal. Blood cultures were negative. Antinuclear antibody, anti-smooth muscle antibody and anti-mitochondrial antibody screen were negative but Coomb's test was positive. Serum ceruloplasmin and Urinary copper were in the normal range. She was discharged home after two days after being stabilized, on steroids, proton pump inhibitor and folic acid for haemolytic anemia. Patient’s serology for DF IgM was positive.

Discussion

In this case, the dengue infection occurred concurrently while the patient was also suffering from HEV and HAV. Anti-dengue IgM detectable by IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) appears in half of the patients with a primary infection while they are still febrile; in the other half, it appears within 2-3 days of defervescence.4 Anti-dengue IgM levels are detectable in about 30% of patients 2 months after the onset of symptoms.5 In this case, also, dengue fever was positive on repeating the test. This is a common observation by physicians actively involved in the management of patients with dengue fever.5 Symptoms and signs of dengue...
infection, especially during the acute phase of illness, are difficult to distinguish from other diseases such as malaria and typhoid, which were negative in this case. This patient also had a positive Coomb's test which is known to be associated with acute HEV, HAV and DV infection.

Dengue fever is one of the serious emerging infection in several cities of Pakistan. There are previous case reports of DF occurring concomitantly with other viral, bacterial and parasitic infections. The cases of DF occur in the months immediately following rainy seasons. It is known that detectable levels of anti-dengue antibodies appear after several days of fever. Persons never previously infected with a flavivirus, nor immunized with a flavivirus vaccine, show a primary antibody response when infected with a dengue virus. Once detectable, IgM levels rise quickly and appear to peak about 2 weeks after the onset of symptoms, anti-dengue IgG appears afterwards. Anti-dengue IgM is conclusive for a recent dengue infection.

The cells of macrophage-lineage, interstitial dendritic cells (DC) and Langerhan cell (LC) constitute the first line of the innate host defense against invading DV in skin where it replicates after the initial bite by infected mosquito. Macrophages are the principal cells to replicate DV which impairs their function and increases severity of the damage to the body. The impact of DV infection on innate immunity is the determining factor. Early activation of natural killer (NK) cells and type-I interferon dependent immunity may limit viral replication at the early stages of DV infection. A successful challenge to virus infection requires that a balance between the induction of efficient anti-viral effector mechanisms and the avoidance of detrimental tissue damage. The increased level of progesterone and estrogens in women are also known to directly influence viral replication and viral gene expression through their effects on viral regulatory elements. The potential risk factor for enhanced viral replication/expression in women, include malnutrition and folate deficiency which increases the incidence of the multiple viral infection and/or increased viral load. A selective high susceptibility could be associated with the genes of the major histocompatibility complex (MHC), which has a strong effect on immune response to viral antigens. It is possible that a specific HLA allele(s) or haplotype(s) prevalent in women might influence the persistence infection. Dendritic cells play a central role in promoting cell-mediated immunity. Infected DCs fail to respond to tumour necrosis factor alpha as an additional maturation stimulus and were found to be apoptotic.

Conclusion

Any patient with prolonged fever should alert the physician of other serious infections such as dengue fever, which may be potentially fatal if not promptly recognized and treated. From the epidemiology point of view, family members often manage DF symptomatically, and consequently the diagnosis of dengue infection will be overlooked, remaining unreported. The case shows that concurrent infections with HEV, HAV and DV can possibly change the clinical spectrum of the disease. This combination is rare but for good outcome, careful overall assessment is required to help avoid unnecessary delay in the diagnosis of illness.

Competing Interests

The authors have no competing interests.

Consent

Written consent was obtained from the patient for publication of this short report.

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