Fulminant hepatic failure due to combined infection with Plasmodium falciparum and hepatitis A virus

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ABSTRACT

Acute viral hepatitis due to hepatitis A and malaria are very common diseases in India. Both malaria and acute hepatitis A virus infection can each present with fulminant hepatic failure. Literature on concurrent infections leading to fulminant hepatic failure is scanty. Forty nine years old male, coal mine worker, presented with history of fever followed by yellowish discoloration of eye and urine and irrelevant talk, drowsiness. Patient had Ig M anti HAV antibody positivity. Patient was treated with standard measure for fulminant hepatic failure. Patient did not improve. Patient had disproportionate anemia, mild elevation of transaminases and mild derangement of prothrombin time. Rapid malarial antigen test was positive for plasmodium falciparum though peripheral blood smear was non-contributory. Antimalarial treatment was started and patient improved. FHF related to malaria and hepatitis A virus infection has similar clinical presentation. Patient with malaria simulating FHF may have significant anemia, mild derangement of prothrombin time compared to viral FHF. This case teaches us that co-infections with two hepatotropic pathogens require immediate attention with early intervention which may lead to survival of patient.

Keyword: Falciparum malaria, Fulminent Hepatic Failure (FHF), Hepatitis A virus

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INTRODUCTION: Malaria and hepatitis A infections are major health problem in India, accounting for sizeable morbidity, mortality.[1, 2] Previous study showed Falciparum malaria occasionally presents with encephalopathy, jaundice and fever mimicking fulminant hepatic failure (FHF).[3]

So both acute hepatitis A and falciparum malaria can each present with fulminant

hepatic failure. Early detection and treatment of malaria in these categories of patient may lead to complete recovery. Although concurrent infections of these two highly prevalent infections are likely to occur, knowledge about their prevalence and potential significance is poor.

CASE:

Forty nine years old male, coal mine worker, presented with history of yellowish discoloration of eye and urine for 6 days and irrelevant talk for 2 days followed by drowsiness. Patient had history of fever for four days initially before appearance of jaundice. Fever was moderate to high grade, intermittent in type, associated with chill, & rigor, No history of burning micturation and, cough. Then patient developed progressive jaundice. Patients were treated as acute viral hepatitis related to hepatitis A virus infection based on Ig M anti HAV antibody positivity.

There was no history of black stool, vomiting, bleeding from any site, jaundice in past, blood transfusion in past, intravenous drug abuse, alcohol intake, reddish coloured urine.

On examination, patient was drowsy but arousable. At admission his pulse was 90 per minute, respiratory rate 26 per minute, and blood pressure 116/68mm of mercury. There was no neck rigidity, no focal neurological sign. Patient has grade 3 hepatic encephalopathy. There were icterus and mild pallor. Lymph nodes were not palpable. On abdominal examination liver and spleen was not palpable below costal margin with liver span of 6 cm. Her respiratory, cardiovascular examination was unremarkable.

On investigation haemoglobin was 9.2 g/dL, total leucocyte count 2.6×10^3 per μL with polymorphs 54%, lymphocytes 42%, monocyte 4%, platelet count 11×10^3 per μL. Blood sugar was 64 mg/dL. Total serum bilirubin was 7.3mg/dL, direct fraction of 5.3mg/dL. SGOT was 109 and SGPT 210. Serum total protein was 5.3 gram (gm) and albumin 2.9 gm per 100mL of blood. Blood urea nitrogen was 71 mg/dL, creatinine 2.26mg/dL, sodium 117 meq/L, potassium 4.1meq/L. Prothrombin time was 18/11 with INR of 1.61. Arterial blood gas analysis showed pH7.46, partial pressure (PP) of oxygen 114, PP of carbon dioxide 34, and standard bicarbonate 24meq/L. Arterial ammonia was 104. Viral markers (HBsAg, IgM hepatitis C and E) were negative. Chest X-ray was normal

and ultrasonography abdomen showed mild hepatosplenomegaly and minimal ascites. Next day serum Bilirubin was increased to 11.5gm/dl with direct fraction of 7.2gm/dl but prothrombin time was not increased significantly. Patient was treated conservatively with standard anticoma measure for acute liver failure. Patient did not improve. Rapid malarial antigen test was positive for plasmodium falciparum though peripheral blood smear was non-contributory. Leptospira and dengue serology were negative.

He was given injection of Artesunate along with cefotaxime, vitamin K and other conservative treatment. During course of treatment, patient developed generalized tonic clonic seizure for which he was put on injection leviteracetum. His hemoglobin dropped down to 7gm/dl. Two packed red cell were transfused. His consciousness improved rapidly after antimalarial treatment. Doxycyclin (100 mg twice daily orally) was added after gaining consciousness for 7 days. Patient was discharged after 8 days.

After 3 months of discharge, patient again developed fever with chill and rigor for 3 days. Complete blood count, liver function test, prothrombin time, serum creatinine were within normal limit. Rapid malarial antigen test was positive for plasmodium vivax. Again peripheral blood smear was non-contributory. Patient was treated with chloroquine followed by primaquine, 15 mg once daily for 14 days. Patient is doing well over next six months follow up.

DISCUSSION

Malaria is a major health problem in many of the developing and tropical countries. Although rare, severe malaria may present with encephalopathy, jaundice mimicking fulminate hepatic failure (FHF) and must be distinguished from viral FHF. Early detection and treatment in this category of patients has profound implication on ultimate patient outcome. Delay in treatment may lead to serious consequences including death. The mortality of untreated severe malaria (particularly cerebral malaria) is thought to approach 100%. With prompt, effective antimalarial treatment and supportive care the mortality falls to 15–20% overall.[4]

Presence of jaundice in falciparum malaria indicates a more severe illness with higher incidence of complications and higher mortality.[1, 5]

Hazra et al. found an association of jaundice in 40% and 9.09% of cases with *P. Falciparum* and *P. vivax*, respectively, from Calcutta. This study has also noted convulsion or coma in 8.33%.[6] In another study, in patients with severe malarial infestation, the incidence of jaundice is reported to be 2.58% only.[7] According to WHO, presence of jaundice indicate severe disease.

Jaundice in severe malaria is multi-factorial and can result from haemolysis of parasitized and non-parasitized red blood cells, hepatic dysfunction and microangiopathic haemolysis associated with disseminated intravascular coagulation (DIC).[8]

Hepatitis A virus infection mostly occurs in children in developing countries, particularly in poor socioeconomic condition. HAV infection in adults is infrequent, [9] but has more severe course than in children.[10] Recent studies showed decreased seroprevalence of anti-HAV antibodies among younger age groups (16-35 years),[11, 12] possibly related to improved sanitation and urbanization.

Since, both pathogens involve hepatocytes for their intracellular replication; they could potentially escalate or inhibit progression of both infections.

Previous study showed no significant difference in duration of jaundice, interval between onset of jaundice and encephalopathy between severe malaria simulating FHF and viral FHF.[13] It is very difficult to differentiate between these two groups based on clinical presentation.

So it is important to have high degree of suspicion of severe malaria infection in patient of fever, hepatic dysfunction and encephalopathy. Others infections like leptospirosis and enteric fever should also be considered in the differential diagnosis, as prompt treatment of these conditions lead to favourable outcome. Severe anemia, mild elevation transaminases, mild derangement of prothrombin time disproportionate to serum bilirubin and encephalopathy might be clue to above infections even if patient has positive serology for viral hepatitis.

There was single case report of fulminant hepatic failure due to plasmodium falciparum and hepatitis E virus co-infection. That patient died. Falciparum co infection might play

significant role in severe liver injury in that patient.[14]

To the best of our knowledge this is the first case of co-infection that survived with timed intervention with antimalarial treatment.

In our case patient has disproportionate anemia, mild elevation of transaminases and mild derangement of prothrombin time.

Single peripheral smear examination was negative in our case. Rapid malarial antigen for plasmodium falciparum was positive.

CONCLUSION: Plasmodium falciparum and hepatitis A virus co-infection leading to FHF is rare. So Malaria co-infection may be considered in patient of viral hepatitis related FHF having disproportionate anemia, mild elevation of transaminases and mildly deranged prothrombin time. Single peripheral smear examination may not be sufficient, so rapid malarial antigen is required to diagnose.

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