

Case Report

Mixed *Plasmodium falciparum* and *Plasmodium vivax* infection with acute viral hepatitis in two brothers: A rare occurrence

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Two brothers aged 14 and 17 years presented in our emergency department with complaints of fever and yellowish discoloration of eyes and urine for 6 and 10 days, respectively. They had similar clinical presentation, examination findings, laboratory biochemical derangements and positive results for rapid tests of *Plasmodium falciparum* and *vivax* species along with IgM Enzyme-linked immunosorbent assay (ELISA) test for hepatitis A virus. They also showed similar response to therapy and improved simultaneously within two to three days. This suggests the role of immunogenetics in modifying the natural course of disease. Moreover, triple infection by these hepatotropic pathogens lead to a presentation that is much more severe than that caused by either of them alone. This could only be explained by a synergistic interaction between these pathogens. This case foretells that co-infections with two or more hepatotropic pathogens require immediate attention with an aggressive management and role of immunogenetics along with co-infections in altering the phenotypic expression of a disease.

Key words: *Plasmodium falciparum*, *Plasmodium vivax*, hepatitis A, co-infection, immunogenetics.

INTRODUCTION

Acute viral hepatitis due to hepatitis A and malaria are very common diseases in the developing world. Many factors alter the outcome in co-infection with *Plasmodium falciparum* and *Plasmodium vivax* when concomitant viral hepatitis is also associated. Among the less studied factors are co-infections (agent factors) and immunogenetics (host factors) and their role in modifying the natural history of the disease. Our case sheds some light in this direction and may also provide stimuli for further large prospective studies so that such life threatening illness could be effectively managed. As in this case, triple infection with hepatitis A, *P. falciparum*

and *P. vivax*, also presenting simultaneously among brothers, is yet to be reported to the best of our knowledge.

CASE PRESENTATION

On September 14th 2011, two brothers, 17 and 14 years old, resident of Rohtas district of Bihar, presented simultaneously in the emergency department of Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, with fever and yellowish discoloration of eyes and urine. Fever had a similar pattern in the siblings and was continuous, associated with chills and rigors and relieved incompletely with antipyretics. The elder brother had these complaints for 6 days. On examination, he had

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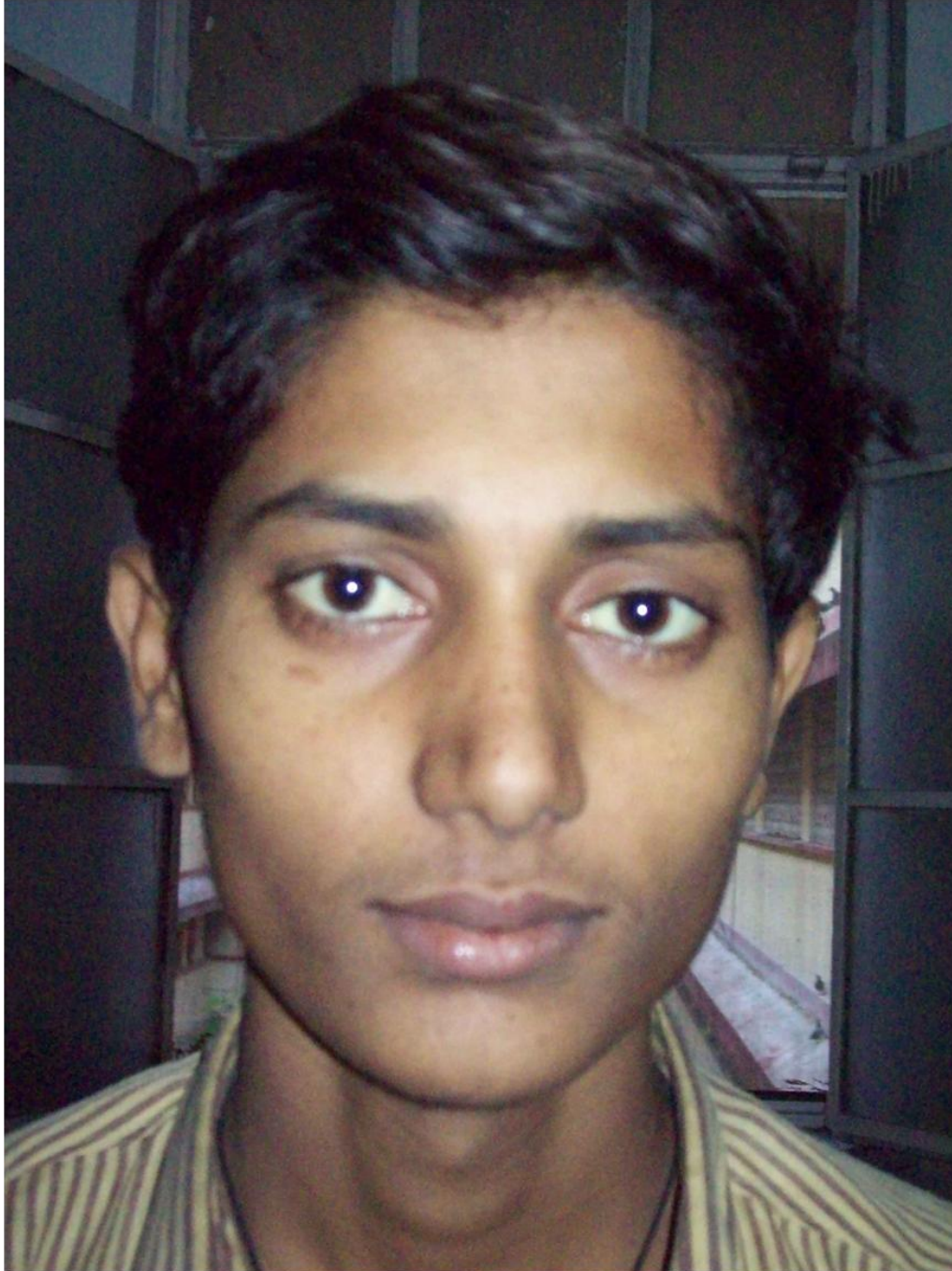


Figure 1. Elder brother showing icterus.

hypotension (blood pressure 80/50 mmHg), pallor, and icterus (Figures 1 and 3). Fundus examination revealed no abnormality. Systemic examination revealed hepatosplenomegaly. The other general and systemic examination was unremarkable. Haematological profile revealed anemia (haemoglobin 85 g/L), thrombocytopenia (platelet count $18 \times 10^9/L$), raised total and direct bilirubin (263.5 and 137.7 $\mu\text{mol/L}$ respectively)

and total leukocyte count being normal ($4.5 \times 10^9/L$). Serum aminotransferases (alanine aminotransferase and aspartate aminotransferase were 0.6 and 0.7 $\mu\text{kat/L}$ respectively) were within normal range and alkaline phosphatase (336 U/L) was mildly raised. Renal function tests were normal. Plasmodium lactate dehydrogenase (LDH) card test (SD Bio Standard Diagnostics Pvt. Ltd.) revealed concomitant *P. falciparum* and *P. vivax* infection



Figure 2. Younger brother showing icterus.

which was confirmed on microscopic evidence of malarial trophozoites. IgM ELISA for leptospirosis was negative. Viral marker studies revealed high titres of IgM against hepatitis A on enzyme immunoassay (DSI srl, Italy).

The younger sibling presented with similar complaints for the past 10 days. On examination, he had pallor and icterus with stable vital signs (Figures 2 and 3). Further examination findings were exactly similar to the elder brother. Haematological investigations depicted anemia (haemoglobin 69 g/L), thrombocytopenia (platelet count $23 \times 10^9/L$) and raised total and direct bilirubin (489.6 and 226.1 $\mu\text{mol/L}$ respectively). Serum aminotransferases (alanine aminotransferase and aspartate aminotransferase were 0.62 and 1 $\mu\text{kat/L}$ respectively) were in range and alkaline phosphatase (423 U/L) was mildly raised. Renal function tests were normal. All other

specific investigations, including plasmodium LDH card test, and viral marker studies were also exactly similar to those of his elder brother.

Following treatment with injectable artemesinin-based combination therapy (ACT) and initial fluid resuscitation, there was a dramatic improvement in their clinical and haematological parameters. Within two to three days of starting the therapy, the brothers became afebrile and the platelet count rose rapidly and bilirubin levels dropped close to normal levels, with improvement in anemia.

DISCUSSION

Malaria is a vector borne disease transmitted by females of the anopheline mosquito. Similarly, hepatitis A is water



Figure 3. The two brothers

borne viral disease. In India, total malaria cases reported in 2010 were 1.49 million, of which 52% were attributed to *P. falciparum* infection and a total of 767 deaths were reported (Internet, 2011). Incidence of hepatitis A virus in India is not exactly known with numerous reports of sporadic and epidemic occurrence in various cities (Indian Council of Medical Research, 1980). The concomitant infection of the two disease (in fact three different players, *P. vivax*, *P. falciparum* and Hep A virus) in two members of a family indicate that the area is highly endemic to both vector and water borne diseases. Aggressive vector control and effective hygiene practices are required to limit the epidemic of the disease. Until now, many studies done in the past has shown an association between viral diseases like hepatitis B and *P. falciparum* co-infection (Thursz et al., 1995; Barcus et al., 2002). Natural course of *P. falciparum* has also been shown to be modified by Epstein Barr Virus (EBV) co-infection (Chene et al., 2007; Moormann et al., 2005). Also, the progression of *P. falciparum* infection has been reported earlier in patients infected with human immunodeficiency virus (HIV) (Abu-Raddad et al., 2006). Few other studies like Snow et al. (2005) and Jacobsen et al. (2004) studied the role of environmental factors in predisposing the population to *Plasmodium* and hepatitis A virus infections, more so in children in developing nations (Snow et al., 2005; Jacobsen and Koopman 2004). Concomitant infections with these hepatotropic

organisms could escalate or inhibit the progression of either or both of them, suggesting a direct or immunological interaction between the two. Promotion of replication or facilitation of survival of one pathogen can occur in the presence of the other one. Either of these could lead to increased number of infective particles/bodies leading to increased likelihood of subsequent infections. This could be a possible explanation for the synergistic interaction between the two pathogens. To the best of our knowledge, it is the first case reported of such kind. Moreover, in our case, the three infections were present simultaneously in two siblings with almost similar clinical presentation, biochemical derangements and therapeutic response. This further substantiates the role of immunogenetics and co infection in modifying the natural history of a disease.

Conclusion

As we are already aware of multi-factorial nature of non-communicable diseases responsible for their varied presentations, the similar analogy could explain the vast spectrum of communicable disease presentations and response to treatments offered despite similar biochemical abnormalities. In developing countries with high burden of communicable diseases, this paradigm approach could play a substantial role in the

management of such diseases. But much work is needed in this regard and larger prospective studies are required to further elucidate the epidemiological interactions between these important human pathogens, if any.

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