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Case Reports

Multiple-organ dysfunction in a case of *Plasmodium vivax* malaria

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Malaria is a major public health problem in India. Previously considered benign, *Plasmodium vivax* malaria infection is now increasingly being recognised as a cause of severe and complicated malaria[1]. We present a case of an 11-yr-old male child, who developed multiple organ dysfunction in the form of oliguric acute renal failure, hepatitis, gastrointestinal bleeding with shock, bacterial peritonitis along with severe anaemia and thrombo cytopenia. The patient required multiple sessions of haemodialysis and blood product transfusions. The patient responded to standard antimalarial treatment and recovered without any sequel.

Case Report

An 11-yr-old male child presented with high grade fever with chills and rigors for 5 days along with progressive swelling all over body and decreased urine output. A yellowish discoloration of sclera for past 1 day was also noticed. Past history was unremarkable and he had no prior history of renal disease. On examination, he was febrile (Temperature 102 °F) with pulse rate 110/min, respiratory rate 28/min, and BP = 116/70 mm Hg. He had mild pallor, icterus and bilateral pitting oedema along with facial puffiness. A petechial rash was noticed all over the body. Abdominal examination revealed splenohepatomegaly with free fluid in the abdomen. His neurological status was normal. Investigations revealed an Hb 6.4 g/dl; TLC 9200/mm^3; and platelet count 27,000/mm^3. Peripheral smear revealed schizonts of *P. vivax.* Blood urea 174 mg/dl, serum creatinine 4.5 mg/dl; and there was metabolic acidosis on blood gas analysis. His urine output was 0.8 ml/kg/h. Ascitic fluid analysis revealed 45 cells with 80% polymorphs and protein level of 2 g/dl. A chest X-ray revealed bilateral parahilar infiltrates. Serum electrolytes showed hyperkalemia. Liver function tests showed total bilirubin 4.0 mg/ dl; direct bilirubin 2.4 mg/dl; SGOT was 177 IU/L; SGPT was 303 IU/L; and ALP was 149 IU/L. Test for malaria antigen was positive for *P. vivax* and negative for *P. falciparum.* Blood culture showed no growth and WIDAL test was negative. Viral markers for hepatitis (Anti HAV Ig M, HBs Ag, Anti HB_C) and HIV were non-reactive. He was started on injectable Artesunate therapy along with blood product transfusions in view of severe anaemia and thrombocytopenia. However, his condition deteriorated with a further rise in blood urea and serum creatinine levels. Urine output declined to 0.6 ml/kg/h. He was treated with supportive measures and repeated sessions of haemodialysis. He developed severe gastrointestinal bleeding leading to shock and cardiopulmonary arrest. He responded to cardiopulmonary resuscitation and required mechanical ventilation. Haemodialysis was repeated and inotropes were gradually tapered off. His urine output improved (1.1 to 1.7 ml/kg/h) and renal functions started improving. Slowly his oedema and icterus subsided. Repeat levels of liver enzymes showed a declining trend. He recovered completely and was discharged after 31 days of stay in the hospital. All the biochemical parameters six months later were normal.

DISCUSSION

Malaria is a significant public health problem not only in India but in other countries also. *Plasmodium vivax* and *P. falciparum* infections account for majority of cases in our country[2, 3]. However, *P. falciparum* had been associated with severe manifestations and increased mortality. However current literature suggests that *P. vivax* malaria infections are also severe and present with unusual manifestations and complications. Some of these manifestations reported are cerebral malaria, severe anaemia, thrombocytopenia, glomerulonephritis, ARDS, hepatic involvement, disseminated intravascular coagulation; etc[1–10]. Untreated, severe malaria has a high rate of mortality. Our case had primarily acute renal failure with hepatic involvement along with other multiple

severe manifestations like severe anaemia, thrombocytopenia and peritonitis.

Anaemia is a frequent co-existent morbidity in malaria but severe thrombocytopenia is an uncommon feature of *P. vivax* malaria. It may be due to direct lysis of the platelets, reduced platelet survival and IgG mediated destruction[10, 11]. *Plasmodium vivax* infection may also cause destruction of uninfected RBC's which may be related to the host immune response. The mechanisms proposed for acute kidney injury in *P. vivax* infection are heavy parasitaemia, acute tubular necrosis, volume depletion, intravascular haemolysis, renal ischemia and microvascular sequestration[6, 9, 12, 13]. Hepatic dysfunction associated with *P. vivax* malaria in children has also been reported[1, 2]. Severe manifestations of *P. vivax* malaria have been attributed to both sequestration related and non-sequestration related complications.

It is essential to understand the basic difference in the pathophysiology of *P. falciparum* and *P. vivax* malaria. It has been reported that RBCs infected with *P. vivax* are more deformable than those infected with *P. falciparum*. These less rigid RBCls are less likely to be sequestered in the spleen and are also less likely to block capillary beds in the vital organs. Thus, exact host parasite interactions, pathogenesis and reasons of multiple organ dysfunction in *P. vivax* infection are unclear[11, 14, 15]. *Plasmodium vivax* invades young red blood cells and requires duffy antigen as a single host cell receptor. Moreover, *P. vivax* is capable of inducing fever at lower levels of parasitaemia than *P. falciparum*. The host inflammatory response in these patients at a similar level of parasitaemia is more intense with higher levels of fever inducing cytokines like TNF-α[16, 17]. In a recent clinic-epidemiological study, which included 303 children admitted with malaria, it was found that there was a greater risk of severe disease in those infected with *P. vivax* than those infected with *P. falciparum* (OR = 2.3)[18]. The reasons for the changing epidemiological profile and spectrum of variable severe manifestations associated with *P. vivax* malaria could be the rampant and indiscriminate use of antimalarial drugs and increasing immunity. The National Vector Borne Disease Control Programme recommends that cases of severe *P. vivax* should be treated like severe *P. falciparum* malaria with artemisinin derivatives or quinine[19]. Despite having multiple organ dysfunction, our patient survived with definitive antimalarial treatment and intensive supportive therapy.

In view of available evidence, *P. vivax* malaria infection should not be considered benign anymore and may present with a wide variety of severe manifestations and complications[1, 18, 20]. Multiple organ dysfunction and shock are associated with a greater risk for mortality in malaria infection[21]. The use of rapid diagnostic tests helps in prompt diagnosis. Intensive care and supportive measures along with standard protocols of management are required to treat these cases[4]. Clinicians must be aware of unusual manifestations and prompt presentation of malaria infection. Early diagnosis and treatment can prevent associated morbidity and mortality. Due to a change in epidemiology, recognition of severe manifestations of *P. vivax* malaria and emerging drug resistance, emphasis must be on strict preventive measures to curb the burden of this disease.

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