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Malarial hepatitis and renal failure: a study of two cases

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Abstract

We report two cases of severe malaria who presented with non-specific clinical features. One of the cases is a 50 year old female who was brought to our hospital with high grade fever and severe abdominal pain, whereas the other case was a 20 year old male presented with high grade fever and headache. Both the cases presented with abnormal liver and renal function tests. *P.malariae* and *P.falciparum* are responsible for clinically important renal disease the former causes chronic progressive syndrome and the latter causes acute renal disease. Severe malaria may present with non specific clinical features making it difficult to distinguish from other febrile illness.

Key words: Plasmodium falciparum malaria, acute renal failure, fulminant hepatic failure

Introduction

Malaria is a protozoal disease transmitted by the bite of an infected female *Anopheles* mosquito. The parasite belongs to the genus *Plasmodium*. *Plasmodium falciparum, Plasmodium Vivax, Plasmodium ovale* and *Plasmodium malariae* are responsible for most of the human infections. *Plasmodium knowlesi* infection has been reported to cause life threatening human infection in Malaysia [1]. In 2008, 109 countries were endemic for malaria. There were an estimated 247 million malaria cases among 3.3 billion people at risk in 2006, causing nearly a million deaths, mostly of children under 5 years [2]. Malaria is one of the major public health problems in India. Around 1.5 million confirmed cases are reported annually by the National Vector Borne Disease Control Programme (NVBDCP) of India, of which 40–50% are due to *falciparum* [3]. Serious complications like cerebral malaria, acute renal failure (ARF), severe anaemia, jaundice, acidosis, acute respiratory distress syndrome (ARDS) etc are seen usually associated with *falciparum* malaria. The clinical features of severe malaria may be non-specific and can occur in other severe febrile diseases such as meningitis, encephalitis, septicaemia, typhoid fever, leptospirosis and viral infections that are commonly seen in areas subject to malaria. In view of its non-specific presentation, it is difficult to recommend a standard clinical case definition for the disease [4]. Hence, we report two such cases who showed non-specific symptoms on presentation to our Hospital.

Case report 1

A 50 year old female arrived at KLE'S Dr Prabhakar Kore Charitable Hospital with high grade fever with chills and rigors in the previous ten days, severe abdominal pain, nausea and vomiting. On examination she was febrile, pale and jaundiced. Her blood pressure was 80/48 mm of Hg which was stabilized with treatment. Her pulse was 98 beats per minute. Abdominal examination revealed diffuse tenderness and hepatosplenomegaly with no free fluid. Cardiovascular System, Respiratory System and Central Nervous System examinations were normal. A Blood analysis was carried out and showed the following values: Serum Creatinine 2.5 mg/dL, Blood Urea 111 mg/dL, Serum Potassium 5.4 mEq/L, Serum Sodium 144mEq/L, Total Bilirubin 17.1 mg/dL (Conjugated 14.7 mg/dL and Unconjugated 2.4 mg/dL), Serum Aspartate aminotransferase 62 IU/L, Alanine aminotransferase 28 IU/L, Alkaline Phosphatase 65 IU/L, Total Protein 6 g/dL, Albumin 2.4 g/dL and A:G ratio 0.7. Haematological report showed: Haemoglobin 9.5 g/dL, ESR 48 mm/hr, WBC total count 5.9 x 10^3/mm3, Differential count: Neutrophils 60%, Lymphocytes 38%, Eosinophils 2% and Basophils 0%, Platelet count 188 x 10^3/mm3, Reticulocyte count 0.6%, Coagulation parameters such as bleeding time, clotting time and prothrombin time were normal. Peripheral smear revealed normocytic hypochromic anaemia. Malaria parasite identification using quantitative buffy

coat was positive and parasite index was 10%. Microscopy was positive for *Plasmodium falciparum* in the peripheral blood sample. The Ultrasonography confirmed the clinical findings of hepatosplenomegaly with no free fluid. Both chest x-ray and abdomen x-ray were normal. A diagnosis of severe *falciparum* malaria with renal and hepatic involvement was made. Patient received IV Ceftriaxone 2 gm BID, IV Artesunate 60 mg BID, IV Metranidazole 0.5gm TID, IV Pantoprazole 40 mg BID, IV Vitamin K 20 mg OD, Cap Doxycycline 100 mg BID and a Tablet of Primaquine 15 mg OD. The patient's condition improved and was subsequently discharged and advised to have a follow up investigation for all parameters within a week.

Case report 2

A 20 year old male arrived at KLES Dr Prabhakar Kore Charitable Hospital with high grade fever with chills, rigors and headache for the previous six days. On examination he was pale and jaundiced. Abdominal examination revealed splenomegaly. The following parameters were investigated and were as follows: Serum Creatinine 1.6 mg/dL, Blood Urea 75 mg/dL, Serum Sodium 133 mEq/L, Serum Potassium 4.6 mEq/L, Serum Total Bilirubin 10 mg/dL (Conjugated 8.3 mg/dL and Unconjugated 1.7 mg/dL), Serum Aspartate aminotransferase 138 IU/L, Alanine aminotransferase 97 IU/L, Total Protein 6 g/dL, Albumin 2.6 g/dL and A:G ratio 0.8. The Haematological report showed: Haemoglobin 6g/dL, ESR 92 mm/hr, WBC total count 5.4 x 10^3/mm3, Differential count: Neutrophils 62%, Lymphocytes 38%, Eosinophils 2% and Basophils 0%, and a Platelet count of 152 x 10^3/mm3. Peripheral smear revealed normocytic hypochromic anaemia. Malaria parasite identification using quantitative buffy coat was positive. Microscopy was positive for *Plasmodium falciparum* in peripheral blood sample. A diagnosis of *falciparum* malaria with renal and hepatic complication was made. The Patient received IV Ceftriaxone 2 gm BID, IV Artesunate 60 mg BID, IV Metranidazole 0.5 gm TID, IV Ranitidine 50mg TID, Cap Doxycycline 100 mg BID and a Tablet of Primaquine 15 mg OD. Two pints of whole human blood was transfused to correct anaemia. The patient's condition improved and was discharged subsequently and advised to have a follow up investigation for all parameters within a week.

Discussion

P.malariae and *P.falciparum* are responsible for clinically important renal disease. The former causes a chronic progressive syndrome and the latter cause an acute renal disease. The Incidence of Acute Renal Failure (ARF) is 1% - 4% and may be as high as 60% in high risk individuals [5]. ARF is one of the most common causes of death in severe malaria and a male preponderance has been observed in the literature [6,7]. Malarial ARF (MARF) is commonly found in non-immune adults and older children with *falciparum* malaria. It is quite common in Southeast Asia and in the Indian subcontinent where the intensity of malarial transmission is usually low, with occasional micro foci of intense transmission [8]. The pathogenesis of renal failure is uncertain. It may be related to red blood cell sequestration interfering with renal microcirculatory flow and metabolism. Clinically and pathologically, ARF manifests itself as an acute tubular necrosis [9]. MARF is most commonly associated with jaundice, seen in more than 75% of the cases [10]. Jaundice by itself is not considered as severe malaria. When serum bilirubin >3mg/dl is found, in association with other vital organ dysfunction, it indicates severe disease [4]. Jaundice is described as "biphasic" with a conjugated component resulting from cholestasis and an un-conjugated component due to haemolysis [10].

Hepatitis in malaria occurs in around 20% of cases and it is characterised by elevated serum transaminases, particularly alanine aminotransferase [10]. Jaundice secondary to malarial hepatitis affects 5% to 20% of patients with severe *Plasmodium falciparum* malaria. Severe malaria due to *P.falciparum* may appear as fulminant hepatic failure (FHF), hepatomegaly with normal prothrombin time helps us to make the distinction between FHF due to malaria and viral FHF [11].

The description of the above 2 cases who presented non- specific clinical features had both renal and hepatic complications. It is thus difficult to distinguish between various febrile illnesses in a country like India where the burden of infectious disease is enormous. Severe *falciparum* malaria can mimic any of these febrile illnesses. Over the past 10-15 years, clinical presentation of severe malaria in India has slowly shifted from single to multiple complications. The Incidence of ARF and jaundice are on the rise, and development of multiple organ dysfunction results in increased mortality [8]. The measures most likely to decrease the mortality rate due to severe malaria are prevention and early diagnosis.

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