CASE REPORT

Acute Renal Failure in Falciparum Malaria

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Summary

We report two patients who had cerebral malaria, heavy parasitemia, hyperbilirubinemia, hypercatabolism with rapid rises of blood urea and serum creatinine and acute renal failure. There was no evidence of intravascular hemolysis. Renal biopsy was consistent with acute tubular necrosis. Both patients responded to treatment with intravenous quinine and dialysis.

Key Words: Acute renal failure, Malaria

Introduction

Falciparum malaria is one of the major causes of tropical acute renal failure. In Thailand it accounts for 38.0% of cases of renal failure due to tropical disease and 18.5% of all cases of acute renal failure[1]. Acute renal failure occurs in less than 1% of all patients with falciparum malaria. However, it occurs in 60% of patients with severe infection. In Malaysia it accounted for 1.6% of all cases of acute renal failure and 16.7% of renal failure due to tropical disease[2].

Acute renal failure in malaria is associated either with intravascular hemolysis or heavy parasitemia. Intravascular hemolysis may be related to drug administration in patients with G6PD deficiency or unrelated to drugs or G6PD deficiency as in blackwater fever.

We report here two patients who had heavy parasitemia who developed acute renal failure. Renal biopsy in both patients showed features of acute tubular necrosis.

Case Reports

Patient 1

A 35-year-old Indonesian man was admitted for fever, chills and rigors of four days duration and drowsiness and vomiting of one day duration. On examination he was drowsy, jaundiced and febrile with a temperature of 38.5°C. There was neck stiffness. Fundi were normal and there was no focal neurologic deficit. There was mild hepatosplenomegaly.

The haemoglobin was 101g/L, white cell count was 12.1 x 10^9/L, platelet count was 13 x 10^9/L, reticulocyte count was 1.8%, blood urea was 35mmol/L, sodium was 136 mmol/L, potassium was 4.0mmol/L, creatinine was 665 µmol/L, random blood sugar was 4.7mmol/L, serum albumin was 25g/L, serum globulin was 33g/L, serum bilirubin was 87µmol/L, serum alkaline phosphatase was 68µ/L and serum transaminase was 113µ/L. The prothombin time was 19.0 seconds, the activated partial

thromboplastin time was 59.5 seconds, thrombin clot time was 18.2 seconds, the fibrinogen degradation product titre was 1/20 (10μg/ml) and the serum fibrinogen was 370 mg%. The HbsAg, anti-nuclear factor, rheumatoid factor, Widal Weil Felix test, blood cultures and serology for virus and leptospirosis were negative. The G6PD test was normal. Blood film for malarial parasites indicated parasitaemia with plasmodium falciparum (200,000/cumm). Urinalysis showed 1+ protein, 10 x 10^6 leucocytes, 33 x 10^6 isomorphic red cells and 8 x 10^6 epithelial cells/L, finely granular casts, no myoglobin and no organisms on culture.

Ultrasound of the kidneys showed increased echogenecity. Renal biopsy showed features of acute tubular necrosis (Fig. 1). There was irregular foci of tubular epithelial cells necrosis. Necrotic epithelial cells and occasional casts were seen within the tubular lumen. There was no hemosiderin deposit in the tubules. There were occasional foci of neutrophil and lymphocytic infiltrate in the interstitium. The glomeruli were normal except for congestion of the capillaries. Immunofluorescence staining demonstrated IgA and IgM. Staining was negative for C3, C4 and IgG. There was nonspecific reaction for fibrin.

The blood urea and serum creatinine rose to a peak of 56.0 mmol/L and 766 μmol/L respectively four days after admission. The renal failure was nonoliguric with urine output ranging from 0.9 to 2.6L/day. The renal failure was treated with rehydration and peritoneal dialysis. The cerebral malaria was treated with intravenous quinine. Fresh frozen plasma, cryoprecipitate and platelets were also administered to the patient. Patient subsequently became afebrile, alert and the acute renal failure resolved.

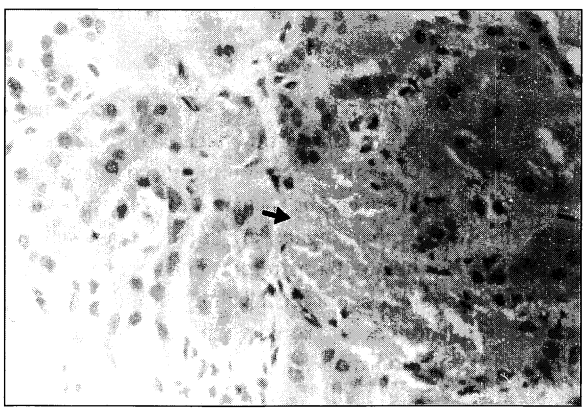

Fig. 1: Section of renal biopsy showing a focal area of tubular necrosis and edema of the interstitium (H & E. x 1000)

Patient 2

A 30-year-old Indonesian man was admitted for high grade fever chills and rigors of three days duration. On the day of admission he was found lying unconscious on the floor. On examination, he was comatose, febrile with a temperature of 39.5°C. There was neck stiffness. Fundi were normal and there was no focal neurologic deficit.

The haemoglobin was 136g/L, white cell count was 9 x 10^9/L, platelet count was 89 x 10^9/L, blood urea was 9.5 mmol/L, sodium was 133 mmol/L, potassium was 3.9 mmol/L, creatinine was 200 μmol/L, random blood sugar was 7.8 mmol/L, serum albumin was 38g/L, serum globulin was 30 g/L, serum bi lirubin was 39 μmol/L, serum alkaline phosphatase was 130 U/L and serum transaminase was 49 U/L. The HbsAg, anti-nuclear factor, rheumatoid factor, Widal Weil Felix test, blood cultures and serology for virus and leptospirosis were negative. The G6PD test was normal. Blood film for malarial parasites indicated parasitaemia with plasmodium falciparum (150,000/cumm). Urinalysis showed 1+ protein, 12 x 10^6 leucocytes and 70 x 10^6 isomorphic red cells/L, hyaline and granular casts, no epithelial cells, myoglobin and no organisms on culture. Computed tomography of the brain was normal. Lumbar puncture was performed and the cerebrospinal fluid was clear. The CSF glucose was 4.2 mmol/L, protein was 0.6g/L and chloride was 117 mmol/L. Globulins were present. There were 15 cells (mainly lymphocytes)/hpf. Microscopic examination revealed no acid fast bacillic, organisms and cryptococci and culture showed no organisms in the CSF. Ultrasound of the kidneys showed increased echogenecity. Renal biopsy showed features of acute tubular necrosis. The tubules showed focal areas of tubular necrosis. The lumen showed presence of reddish and brownish granular material. There was no hemosiderin deposit in the tubules. There was edema around the necrotic tubules. The glomeruli were normal.

Immunofluorescence staining demonstrated segmental distribution of C3 in one glomerulus. Staining was negative for C4, IgG, IgA and IgM. There was non-specific reaction for fibrin.

The blood urea and serum creatinine rose to a peak of 53.6 mmol/L and 756 μmol/L respectively five days after admission. The renal failure was nonoliguric with urine output ranging from 0.8 to 3.4L/day and was treated with haemodialysis. The cerebral malaria was treated with intravenous quinine. Patient subsequently recovered.

Discussion

Renal involvement in malaria varies from mild proteinuria to acute renal failure. Mild proteinuria of less than 1g/24 hours and an abnormal urinary sediment consisting of a few red blood cells or leucocytes with occasional granular casts are commonly seen in patients with falciparum malaria. Proteinuria is both glomerular and tubular in origin and is noted in 20 to 70% of patients[3]. It is transient. Renal function is usually normal. Electrolyte abnormalities such as hyponatremia, hypokalemia, hyperkalemia, hypocalcemia and hypophosphatemia can also occur[3].

Acute renal failure is associated with acute intravascular hemolysis or heavy parasitemia. Intravascular hemolysis may be caused by malarial infection or by antimalarial drugs such as quinine, chloroquine and pyrimethamine in a patient with or without G6PD deficiency. Blackwater fever is diagnosed when drug-induced hemolysis is excluded. It need not be associated with quinine or G6PD deficiency[3]. In renal failure associated with heavy parasitemia, the patient is ill with high fever. The renal failure is catabolic in type. There is jaundice which is usually cholestatic. Disseminated intravascular coagulation can also occur. Renal histology indicates acute tubular necrosis[3]. Pathogenetic factors for renal failure include catecholamine release, hypovolemia, hyperviscosity of blood, hyperbilirubinemia and endotoxemia[3].

Quinine is the drug of choice and should be administered intravenously in severe cases. The dose is 8.4 mg/kg every eight hours for seven days in patients with serum creatinine up to 300 μmol/L. In patients whose serum creatinine exceeds 300 μmol/L, the standard dose can be given for the first 24 to 48 hours to reduce the parasitemia. Thereafter, the dose can be reduced to 8.4 mg/kg every 12 to 24 hours for seven days. When indicated dialysis should be performed frequently because of hypercatabolism. Hemodialysis is preferred to peritoneal dialysis as vasoconstriction and impaired paeritoneal microcirculation due to parasitized erythrocytes makes peritoneal dialysis less effective. In patients with heavy parasitemia and or severe hyperbilirubinemia, exchange blood transfusion can be used.

Renal failure can be prevented by prompt antimalarial therapy, maintenance of fluid and electrolyte balance and good urine flow and alkalinising the urine when hemoglobinuria occurs. Dopamine (1μg/kg/min intravenously) and furosemide (200 mg 6 hourly, intravenously) have been shown to be useful in maintaining renal blood flow and urinary output[3].

The prognosis of acute renal failure is good in patients who have early and frequent dialysis. The prognosis is grave when multiple organs are involved especially when acute respiratory failure is present.

The two patients in our case reports had cerebral malaria, heavy parasitemia, hyperbilirubinemia, hypercatabolism with rapid rises of blood urea and serum creatinine and acute renal failure. There was no evidence of intravascular hemolysis. Disseminated intravascular coagulation was noted in patient 1. Renal biopsy was consistent with acute tubular necrosis. Both patients responded to treatment with quinine and dialysis.

Although the number of reported cases of acute renal failure resulting from falciparum malaria in Malaysia is small[2], it is important to recognize the condition and to treat it aggressively as it can lead to mortality especially when other organs are involved as well. In patients with heavy parasitemia and or hemolysis, measures to prevent acute renal failure as outlined above should be instituted. In patients with established acute renal failure, hemodialysis should be instituted early and frequently. Where facilities for hemodialysis are not available, peritoneal dialysis can be performed although it is less effective than hemodialysis. Quinine should be administered intravenously in doses outlined earlier.

Acknowledgement

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