Acute renal failure in Falciparum malaria—increasing prevalence in some areas of India—a need for awareness

J. Prakash¹, A. Gupta¹, O. Kumar², S. B. Rout², V. Malhotra² and P. K. Srivastava²

¹Department of Nephrology, Indira Gandhi Institute of Medical Sciences, Patna; ²Division of Nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

Abstract Twenty-six cases (4.8%) from a total of 540 patients with acute renal failure (ARF) of diverse aetiology had ARF in association with falciparum malaria. Their ages ranged from 15 to 85 years (mean 31.2). Urinary sediment abnormalities and proteinuria (less than 1 g/24 h) were observed in 15 (57.7%) cases. The probable underlying factors leading to ARF were: volume depletion 17 (65.3%), intravascular haemolysis 8 (30.8%), hyperparasitaemia 8 (30.8%), cholestatic jaundice 6 (23%), and hypotension 5 (19.2%). Dialysis therapy was required in 15 patients (57.7%) as they had severe renal failure, and the remaining 11 patients improved with supportive measures. All patients received antimalarial therapy. The clinical course of ARF was consistent with acute tubular necrosis in 20 patients. Six cases were subjected to percutaneous renal biopsy. One patient showed histological features of necrotizing glomerulonephritis along with acute tubulointerstitial nephritis. The biopsies in the other five patients showed features of acute tubular necrosis in three, and acute interstitial oedema with patchy tubular necrosis in two. The mortality rate was 30.8%. Thus falciparum malaria, which has been an important cause of ARF in certain highly endemic zones of India, is showing an increasing prevalence in other parts such as Eastern Uttar Pradesh due to an imbalance between the increasing population and inadequate sanitary facilities, which further worsen during floods.

Introduction

Falciparum malaria is one of the common parasitic diseases causing high morbidity and mortality in the tropics. The clinical spectrum of renal involvement varies widely [1]. Some authors described urinary sediment abnormalities, mild proteinuria, fluid and electrolyte changes, and acute renal failure (ARF) in association with falciparum malaria [2]. Still other authors reported the overall prevalence of ARF due to falciparum malaria to be less than 1% [3]. Malarial ARF has been reported in 1.08% of cases from certain parts of India [4]. The incidence of malarial ARF seems to be high in Eastern India, as malaria is endemic in the Indian subcontinent [5]. We studied the causes, clinical features, and outcome of ARF in patients with falciparum malaria.

Subjects and methods

A total of 540 cases of ARF of differing aetiologies were studied over a period of 10 years (1984–1994). ARF in 26 of these was considered to be induced by falciparum malaria. Of these 26 patients, 19 were males and seven were females with age ranging from 15 to 85 years. Fifteen patients were very ill at the time of admission and had a common type of clinical presentation with high temperature with chills followed by decreased urine output and development of renal failure. The referral diagnosis in these cases were viral hepatitis, septic meningitis, hepatorenal syndrome, and Gram-negative septicaemia which caused ARF. All patients had a thorough physical examination on admission. Laboratory tests (serum creatinine, serum urea, nitrogen, sodium, potassium) were done in each. The severity of ARF was assessed. Liver function and haematological tests and blood and urine cultures for bacterial infection were carried out. Detection of hepatitis B virus surface antigen was by ELISA technique. Blood films were examined for malarial parasites. All patients received antimalarial drugs. Both peritoneal, as well as haemodialysis was performed in patients requiring dialysis, along with supportive measures. Percutaneous renal biopsy was carried out in six patients due to longer duration of oliguria (> 5 weeks).

Results

In a total of 540 patients with ARF, 26 had ARF in association with falciparum malaria. The majority (92.3%) of patients had fever of varying degrees (102–106°F) continuous/irregular at initial presentation. The presenting feature of 26 patients is shown in Table 1. The diagnosis of malaria was confirmed in each case by demonstration of malaria parasite in peripheral blood film. The clinical features of patients
Acute renal failure is one of the dreaded complications of falciparum malaria. The overall prevalence of ARF is less than 1% in falciparum malaria [3] but the incidence may increase up to 60% in patients with hyperparasitaemia. The prevalence of ARF due to falciparum malaria is 4% in an area where malaria is endemic [1]. We have observed the incidence of malarial ARF to be 4.8% in our study. The onset of ARF is usually within 4–7 days after the appearance of fever. The duration of ARF ranges from a few days to several weeks, and may be oliguric or non-oliguric in form. ARF is observed, as a rule, only in patients with heavy parasitaemia, or intravascular haemolysis with or without glucose-6-phosphate dehydrogenase deficiency [2].

Two mechanisms are involved in the pathogenesis of ARF in falciparum malaria: impaired microcirculation (ischaemia) due to parasitized erythrocytes, and non-specific effects of infection. The latter include hypovolaemia, intravascular haemolysis, disseminated/intravascular coagulation, endotoxaemia, and cholestatic jaundice. Parasitized erythrocytes have decreased deformability, which results in sluggish blood flow in the microcirculation. Erythrocyte viscosity is also increased because of rigidity of the infected erythrocytes; the whole-blood viscosity thus is increased and contributes further to the slow flow in the microcirculation.

Severe jaundice (serum bilirubin 11.8–23.4 mg%) was observed in six (23%) patients. Biochemical features of cholestasis were obtained in all six patients. Falciparum malaria complicating cholestatic jaundice and ARF were reported [7]. Other authors have considered massive intravascular haemolysis as the main mechanism of malarial ARF [4,8]. Intravascular haemolysis contributed to ARF in eight (30.8%) cases in the present study. Jaundice is of haemolytic origin in falciparum malaria, and it may be severe since serum bilirubin accumulates in the presence of oligoanuria. However, very severe hyperbilirubinaemia in falciparum malaria indicates the possibility of intrahepatic cholestasis [7]. We have observed cholestatic jaundice in 23% of our patients. Both conjugated and unconjugated bilirubin and bile acid as well have shown to be involved in the pathogenesis of acute renal failure in falciparum malaria [9–11]. Endotoxin has been implicated in the pathogenesis of acute renal injury [12]. The vascular response to catecholamine is enhanced and plasma renin activity increased in the presence of hyperbilirubinaemia [13]. Furthermore, hyperuricosuria due to jaundice could further com-
promise renal function in states of low urine flow and acidic urine [14].

The prognosis of ARF is favourable in patients who have early and frequent dialysis. Approximately 60% of patients with malarial ARF require dialysis [1,15]. We dialysed 15 (57.7%) cases in our study. The mortality has decreased from 30% in the past to less than 10% at present. However, the prognosis is grave when multiple organs are involved, especially when acute respiratory failure is present. The high (30.8%) mortality in our study is due to advanced age, delay in referral, associated organ failure, and cerebral malaria.

References

5. Panda SK, Das GC, Padhiary K.K, Mohanty S, Mahakur AC. A profile of acute renal failure following falciparum malaria—
a study of 280 cases. 5th Asian Pacific Congress of Nephrology, New Delhi, India. 1992; 44