Rhabdomyolysis and acute renal failure in Plasmodium falciparum malaria

Sir,

Acute renal failure is a common complication in malaria infection. This can be the result of multiple mechanisms [1]: hypovolaemia, excessive haemolysis, disseminated intravascular coagulation or impaired microcirculation due to a high level of parasitized erythrocytes. Rhabdomyolysis is another uncommon way of inducing renal failure in malaria infection. The diagnosis is based on high serum level of muscular enzymes; Creatine Phosphokinase (CPK) and clinical symptoms like myalgias. To our knowledge, only six cases of rhabdomyolysis complicated by acute renal failure during malaria infection have been described [2,3].

Case. A 20-year-old woman was admitted in our institution with a 5 day history of fever, nausea and muscle pain. She was a Malagasy woman and had been living in France for many years. Six days before, she returned to France after a prolonged stay in Madagascar. During this stay, she did not use any chemoprophylaxis against malaria.

On the day of admission, vigilance was impaired (Glasgow coma score: 12) and central temperature was 36°C. On examination, there was a cutaneous lesion on her leg, probably induced by a mosquito bite, without any infectious symptom. Blood pressure was low (88/44 mmHg). Cardiac pulse rate was 64 beats/min. The patient was anuric. Abdominal examination revealed a palpable 1 cm hepatomegaly, but no splenomegaly. Blood samples revealed serum haemoglobin level 12.2 g/dl, total white blood cell count 14000/mm³ and platelet count 19000/mm³. Blood smear showed ring-form Plasmodium falciparum in 7% of erythrocytes. C-reactive protein level was 171 mg/l. Serum potassium concentration was 3.9 mmol/l, sodium 124 mmol/l, creatinine 724 µmol/l and blood urea nitrogen 37.8 mmol/l. Serum creatinine kinase and myoglobinemia levels were very high (71940 U/l and >20000 U/l, respectively). Her liver function tests showed hyperbilirubinaemia (41 µmol/l) and elevation of liver enzymes [TGO level: 373 U/I (normal: <35 U/I) and TGP level: 1129 U/I (normal: <30 U/I)]. Urine analysis revealed pigment on dipstick examination and the absence of red blood cells in urine. Proteinuria was low at 0.25 g/l. Because of high CPK level, viral and bacterial serologies were prescribed: Legionella, Mycoplasma, Chlamydia, Leptospira, influenzae A and B and para-influenzae viruses. Results were all negative.

The patient was treated with intravenous chloroquine (24 mg/kg/day) and intravenous hydration. Creatinine level increased initially in spite of a high daily urinary excretion, but returned to normal values after 10 days. No haemodialysis was performed. CPK level decreased, too. Rapidly, neurological status became normal. After complete recovery, the patient was lost of sight.

Comment. Ischaemic acute tubular necrosis is by far the most common cause of acute renal failure in P. falciparum malaria. It is the result of hypovolaemia, peripheral pooling of blood and blockage of microcirculation by parasitized red cells and non-specific effects of infection. In this case, none of these mechanisms may explain the renal failure. This patient had a severe rhabdomyolysis that may be the actual reason of this acute renal failure. Many mechanisms may induce these muscle damages [4]. In this case, rhabdomyolysis could not be explained by usual causes (hyperthermia, crush syndrome, metabolic abnormality, drugs or other infectious diseases). Thereafter, the responsibility of P. falciparum as the physiopathological mechanism of the rhabdomyolysis was supposed.

Only a few publications are available about rhabdomyolysis and P. falciparum infection [2,3]. The mechanism postulated to explain rhabdomyolysis is the sequestration of parasitized erythrocytes in striated muscle capillaries, inducing microcirculatory obstruction. Plasmodium falciparum may also induce myositis with myoglobinuria [5]. This mechanism may explain the muscle pain experienced by our patient and the high level of CPK.

We suggest that rhabdomyolysis has to be researched in patients with acute renal failure and P. falciparum malaria infection, especially if muscle pain is present.

Conflict of interest statement. None declared.
rhabdomyolysis. On examination, he was pale and afebrile. He had periorbital puffiness, lip swelling, diffuse goitre and generalized non-pitting oedema. He had an atrophic plaque on his abdomen.

His laboratory findings were as follows: serum urea 32 mg/dl, creatinine 1.9 mg/dl, aspartate aminotransferase (AST) 122 IU/l, alanine aminotransferase (ALT) 66 IU/l, creatine kinase 2291 IU/l (normal <397), lactate dehydrogenase (LDH) 476 IU/l (normal 98–192), free T3 0.41 pg/ml (normal 1.8–4.6), free T4 0.06 ng/dl (normal 0.7–2), thyroid-stimulating hormone (TSH) >100 mIU/ml (normal 0.26–4.2), anti-microsomal antibody >600 IU/ml (normal <34) and anti-thyroglobulin antibody >4000 IU/ml (normal <115). His creatinine clearance was 58%. Other laboratory tests were normal. Ultrasonography and needle biopsy of the thyroid were concordant with thyroiditis. The biopsy made from the atrophic lesion was concordant with morphea.

Findings were compatible with autoimmune thyroid disorder, primary hypothyroidism and rhabdomyolysis. He received thyroxine replacement. His symptoms and laboratory values were normalized after 4 weeks of thyroxine replacement. However, his creatinine was still high. For this reason, we performed needle biopsy of the kidney. Examination of kidney biopsy specimens revealed oedematous renal medullary tissue.

Discussion. Hypothyroidism, though rare, should be considered a definite and authentic cause of rhabdomyolysis. The exact cause of rhabdomyolysis in hypothyroidism remains unclear. Usually an aggravating factor such as use of lipid-lowering drugs, alcohol, exercise or chronic renal failure has been identified [2,3]. Rhabdomyolysis manifests with muscular symptoms (e.g. myalgia and weakness) and severely elevated serum levels of muscle enzymes. It can become a life-threatening disorder when complicated by acute renal failure [2]. Thyroid hormone replacement therapy improves thyroid and renal functions and reverses rhabdomyolysis.

Only a few cases of rhabdomyolysis due to hypothyroidism have been reported [4-6]. The present case describes a patient suffering from rhabdomyolysis due to hypothyroidism, with no additional precipitating factor.

As a result, hypothyroidism must be considered in patients presenting with acute renal failure and elevated muscle enzymes. As soon as the diagnosis is made, levothyroxin should be started.

Conflict of interest statement. None declared.

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doi:10.1093/ndt/gfh745

Advance Access publication 16 February 2005

Recurrent rhabdomyolysis and mild acute renal failure associated with acute Brucella infection

Sir,

Various infectious agents have been reported to cause rhabdomyolysis [1–5]. We present a case of acute Brucella infection, complicated with recurrent rhabdomyolysis and mild renal failure.

A 39-year old man was admitted to hospital because of muscular pain and dark urine. Ciprofloxacine was begun 1 day before his referral with the possible diagnosis of urinary infection. He reported consumption of unpasteurized milk products 1 month before his admission. Physical examination was normal except for high fever (38.2°C). Abnormal laboratory results were as follows: erythrocyte sedimentation rate 70 mm/h, C-reactive protein 14.0 mg/dl (normal: 0.0–8.0 mg/dl), creatine phosphokinase (CK) 2365 U/l, CK-MB 60 U/l, aspartate aminotransferase (AST) 383 U/l and alanine aminotransferase (ALT) 549 U/l. The standard tube agglutination (STA) test for brucellosis, other serological tests for infectious agents and cultures were negative. Urinalysis revealed dark brown urine with a positive dipstick reaction for blood. Renal ultrasonography was normal. The estimated glomerular filtration rate by the Cockcroft–Gault formula was 90 ml/min and it decreased to 65 ml/min on the second day. On the third day, temperature and most of the biochemical tests returned to normal, and on the fifth day the patient was discharged. Ciprofloxacine was continued for 2 weeks. Twenty days after his discharge, the patient was re-admitted with high fever (39.2°C) and muscular pain (Figure 1). Reconsumption of unpasteurized milk products or other risk factors for brucellosis were not found. Laboratory tests were as follows: CK 1545 U/l, AST 48 U/l, ALT 65 U/l, urea 23 mg/dl and creatinine 1.01 mg/dl. Urinalysis revealed dark brown urine with a positive dipstick reaction for blood. The Brucella

Fig. 1. Time course of serum creatine phosphokinase (CK) and axillary temperature levels.