Tetany with *Plasmodium falciparum* Infection

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**Abstract**

Plasmodium Falciparum is a malarial infection with high morbidity and wide spectrum of atypical presentation. Here we report an unusual presentation of malaria as tetany with alteration in calcium, phosphate and magnesium metabolism. Hypocalcaemia in malaria can cause prolonged Q-Tc interval which could be a risk factor for quinine cardiotoxicity and sudden death. Hence monitoring of serum calcium in severe malarial infection and cautious use of quinine in such patients is very important in management.

**Introduction**

Malaria is an infectious disease with a high morbidity and mortality. Wide spectrum of atypical presentations of malaria has been described in literature.1 We herein describe an unusual presentation of malaria as tetany and discuss in brief calcium, phosphate and magnesium metabolism in malaria.

**Case Report**

A 37 years old male hailing from Western UP (India) was admitted in UP Rural Institute of Medical Sciences and Research Saifai, India with fever for six days and painful, intermittent muscle spasm of the right leg since two days. Fever was high-grade, intermittent and associated with rigors. There was no history of altered sensorium, paraesthesiae, trauma, drug intake or convulsion. His past, personal and family history was unremarkable. Dietary history was normal with an adequate calcium intake. On admission, he was febrile with a heart rate of 150/min, respiratory rate of 30/min and blood pressure of 102/78 mm Hg. There was pallor and mild icterus. Chvostek sign and Trouseau sign were negative. Intermittent muscle spasm of the right leg calf was seen on examination. The liver was tender and palpable 5 cm below the right costal margin with a span of 18 cm. The spleen was palpable 4 cm below the left costal margin. On central nervous system examination, he was conscious and well-oriented in time, place and person. His motor and sensory examination was normal. Superficial reflexes were normal with bilateral brisk knee and ankle reflexes. There were no cerebellar or meningeal signs. Other systems were normal.

Investigations done on the day of admission revealed: hemoglobin 8 g/dL, total leucocyte count 12,000, and platelet count 80,000. Peripheral blood smear showed ring-form trophozoites of *Plasmodium falciparum*. Malarial parasite index was 3%. Other investigations showed: serum calcium 7.0 mg/dL (normal range 8.8-10.5 mg/dL), serum phosphorous 3 mg/dL (normal range 3.4-4.5 mg/dL), serum magnesium 1.2 mg/dL (normal range 1.8-3 mg/dL), alkaline phosphatase 180 U/L, serum albumin 2 gm/dL (normal range 3.5-5.5 gm/dL), serum parathormone was 9.2 pg/ml (normal range 9-65 pg/ml). Electrocardiography and arterial blood gas analysis were normal. The total serum bilirubin was 1.8 mg/dL with a conjugated fraction of 0.7 mg/dL. The serum concentrations of aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase were 160 U/L, 225 U/L and 598 IU/L respectively. Serum sodium, serum potassium, renal function tests, coagulation profile and random blood sugar were normal. Serological tests for dengue and leptospirosis were negative. Intravenous artesunate was started at a dose of 2.4 mg/kg at 0, 12 and 24 h followed by once a day for total five days. Intravenous calcium gluconate (10 ml of 10% solution thrice a day) was also started.

**Discussion**

Tetany is a clinical neurologic syndrome characterized by twichings, cramps, convulsions of muscles and sharp flexion of wrist and ankle joints called carpopedal spasm due to hyperexcitability of nerves and muscles caused by decreased extracellular calcium from various causes. These include parathyroid hypofunction, vitamin D deficiency, alkalosis, low magnesium level and hypoalbuminaemia. Reduced ionised calcium may cause increased excitability of peripheral nerves and tetany. Hypoalbuminaemia can occur in advance stages of Plasmodium falciparum infection with hepatic dysfunction leading to significant hypocalcaemia despite adequate dietary calcium.

As the muscle spasm did not respond to calcium supplements, intravenous magnesium (0.2 cc/kg of a 50% solution) was started resulting in symptomatic improvement within four days of admission. The patient became afebrile on the third day of treatment. Repeat serum levels of calcium, magnesium and phosphorous done on the tenth day were normal. Serum parathormone levels had increased on the tenth day (63 pg/ml). The patient was discharged on the tenth day and was asymptomatic on follow-up after four weeks.

The maintenance of plasma concentration of calcium, phosphate and magnesium within a narrow physiological range is vital to the integrity of a variety of cellular metabolic processes. Mild asymptomatic hypocalcaemia is commonly seen in malaria regardless of the severity of infection. However, in some cases hypocalcaemia can be severe and symptomatic. Hypocalcaemia in malaria can cause prolonged Q-Tc interval which could be a risk factor for quinine cardiotoxicity and sudden death. It has been found that with clinical recovery and parasite clearance, the serum calcium level returns to normal. Thus, monitoring serum calcium may have prognostic value in severe malaria. Various hypothesis have been put forward to explain hypocalcaemia in malaria. The main reason cited is the ‘sick euparathyroid
syndrome’ which describes a state in which the parathyroid response to hypocalcemia is depressed during active infection, with recovery of the glandular function as the parasitaemia gets cleared.5

Another hypothesis for malaria-associated hypocalcemia relates to the changes in phosphate metabolism. A lowered renal threshold for phosphate appears to be a major contributing factor for hypophosphatemia in malaria.6 Hypophosphatemia is associated with hypercalciuria as seen in our patient.6 Hypophosphatemia can cause encephalopathy, depressed leucocyte function, increased susceptibility to gram-negative infections, platelet dysfunction, coagulation abnormalities and haemolytic anaemia.5 These abnormalities are also seen in severe and complicated malaria7. Reduced erythrocyte concentration of 2,3 diphosphoglycerate in hypophosphatemia can further impair the tissue oxygen delivery and vital organ function in severe malaria.8 Thus, hypophosphatemia contributes to and in some cases may even aggravate a variety of clinical and laboratory abnormalities associated with severe malaria. However, routine administration of phosphate is not recommended in view of the potential risk of hyperphosphatemia and the fact that normal serum concentrations are restored within days of initiation of treatment.2 Mild asymptomatic hypomagnesemia is also known to occur in malaria9. It can cause secondary hypocalcemia by impairing the release of parathormone by the parathyroid gland and through blunting the tissue response to parathormone.9

In conclusion, we want to highlight that alteration in calcium, phosphate and magnesium metabolism can occur in patients with malaria. Also, quinine should be used cautiously in patients with severe malaria associated with hypocalcemia and prolonged Q-Tc interval.

References