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Unusual presentation of malaria as tetany: a case report

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Malaria is a major disease of public health importance with a high morbidity and mortality. Various atypical presentations of malaria have been described in literature[1]. Physicians should be aware of the different ways in which malaria can present to ensure its early diagnosis and treatment. We herein describe an unusual presentation of malaria as tetany and discuss in brief regarding calcium, phosphate and magnesium metabolism in malaria.

Case report: A 12-year old Indian boy hailing from Mumbai was admitted in Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai, India with fever for four days and painful, intermittent muscle spasm of the left foot since one day. Fever was high-grade, intermittent and associated with rigors. There was no history of loss of consciousness, altered sensorium, paresthesia, trauma, drug intake or convulsion. His past, development and family history was normal. His dietary history was normal with an adequate calcium intake. On admission, the child was febrile with a heart rate of 140/min, respiratory rate of 28/min and blood pressure of 100/78 mm Hg. There was pallor and mild icterus on examination. Chvostek sign and Trousseau sign were negative. Intermittent muscle spasm of the left foot was seen on examination. The liver was tender and palpable 4 cm below the right costal margin with a span of 7 cm. The spleen was palpable 3 cm below the left costal margin. On central nervous 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 7.8 g/dL, total leukocyte count 12,600 ml, and platelet count 70,000/ml. Peripheral blood smear showed ring-form trophozoites of *Plasmodium falciparum*. OptiMal test was positive for *P. falciparum* malaria and the parasite index was 3%. Other investigations showed: serum calcium 7.1 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 1.4 mg/dL (normal range 1.8–3 mg/dL), alkaline phosphatase 200 U/L, serum albumin 3 mg/dL (normal range 3.5–5.5 mg/dL). The corrected calcium was 7.8 mg/dL {Corrected calcium = Calcium + (normal albumin – serum albumin) x 0.8}. Serum parathormone was 9.2 pg/ml (normal range 9–65 pg/ml), urinary calcium/creatinine ratio was 0.5 (normal <0.2). Urinary phosphorous could not be done due to non-availability of this facility at our institution. 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 seven days. Intravenous calcium gluconate (10 ml of 10% solution thrice

a day) was also started in the patient.

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. The patient became afebrile on the third day of treatment. Repeat serum levels of calcium, magnesium, phosphorous, and urinary calcium/creatinine done on the seventh day were normal. Serum parathormone levels had increased on the seventh day (63 pg/ml). The child was discharged on the seventh day and was asymptomatic on follow-up after one month.

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 hypocalcemia is commonly seen in malaria regardless of the severity of infection[2]. However, in some cases hypocalcemia can be severe and symptomatic[3]. Hypocalcemia in malaria can cause prolonged Q-Tc interval which could be a risk factor for quinine cardiotoxicity and sudden death[3, 4]. It has been found that with clinical recovery and parasite clearance, the serum calcium level returns to normal. Thus, monitoring serum calcium can have prognostic value in severe malaria[3]. Various hypotheses have been put forward for the explanation of hypocalcemia 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[5]. 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 malaria[7]. 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 malaria[5]. 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 wish 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.

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