CASE REPORT

FALCIPARUM MALARIA PRESENTING WITH TETANY: ENDOCRINOPATHIES ASSOCIATED WITH FALCIPARUM MALARIA

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Malaria is a common public health problem which may have high morbidity and mortality. Physicians should be aware of the unusual presentations of this disease so that it can be timely diagnosed and treated. Herein we are presenting a case of falciparum malaria who presented to the hospital with carpopedal spasm and tetany. We will subsequently discuss mineral homeostasis and the mechanisms of hypocalcaemia in falciparum malaria and the dysregulation of calcium, phosphorus and magnesium metabolism.

Keywords: Falciparum malaria; Hypocalcaemia; Tetany

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INTRODUCTION

Malaria can present in an atypical manner.[1] Mild asymptomatic hypocalcaemia is common in malaria and it has no relation to the severity of infection.[2] Davis *et al* reported that at presentation one-third of patients with falciparum malaria will have calcium levels below 2.12 mmol/l and a larger number of patients will have hypocalcaemia in the first few days following treatment.[3] In most cases, it is seen that the calcium levels will normalize after clinical recovery and clearance of parasitaemia.[3] However very few patients may present with severe and symptomatic hypocalcaemia which may cause ECG changes like prolonged Q-Tc interval.[2] This could be a risk factor for cardio toxicity and sudden death especially when medications like Quinine are used for its treatment.

CASE REPORT

49-year-old Pakistani gentleman with the history of hypertension, presented to the hospital with 3 days history of fever with rigors. This was accompanied with mild diarrhoea and poor oral intake. He was a transit passenger from Umrah flight from Saudi Arabia.

At admission, he was febrile and tachycardiac and dehydrated, with a blood pressure of 107/46 mmHG, pulse 100/min, Temperature 39 ºC. The patient was conscious and alert, there was no neck stiffness, mild pallor was present.

Initial laboratory investigations revealed, mild leukocytosis with mild neutrophilia, thrombocytopenia and high procalcitonin level: WBC 11,400/ul (3600–11,000/ul), (neutrophils 64.5%), haemoglobulin 10.7 gm/dl (13–18 gm/dl), platelets 128,000/ul (150,000-400,000/ul).

Procalcitonin: high risk, c reactive protein 58.5 mg/l (<5 mg/. l), serum lactic acid 1.3 mmol/l (0.5–2.2 mmol/l), creatinine 6.3 mg/dl (0.7–1.2 mg/dl), urea 319mg/dl (12–40 mg/dl) sodium 115 mmol/l (136–145 mmol/l), potassium 4.2 mmol/l (3.3 mmol/l - 4.8mmol/l), chloride 76 mmol/l (98–108 mmol/l), Bicarbonate 18.3 mmol/l (20–28 mmol/l).

Liver function test normal, albumin 2.8g/dl (3.4–4.8 g/dl), Urine routine: unremarkable, Blood and urine culture: negative.

Shortly after admission, the patient became hypotensive, requiring frequent boluses of fluids to maintain blood pressure and urine output. He also developed perioral paraesthesia, severe muscle cramps. Then he developed carpopedal spasm and tetany. Chvostek sign was positive. Serum calcium was checked urgently. Calcium 6.9 mg/dl (8.9–10.2 mg/dl), corrected calcium level 7.4 mg/dl ionized calcium (in ABG) 0.81mmol/l (1.15–1.29 mmol/l) rest of parameters in arterial blood gases were normal, serum phosphorus levels normal.

Parathyroid 130 pg/ml (6.2–29 pg/ml), magnesium (2.51 mg/dl) (1.7–2.55 mg/dl). Chest x-ray and ECG were unremarkable. Urinary phosphate and 25 (OH) vitamin D levels were not checked. Peripheral smear: falciparum malaria (ring forms). Parasitaemia index (3%) (3 in 100 infected Red blood cells)

He was started on Quinine and doxycycline. He was given intravenous fluids and calcium gluconate three times a day. 72 hours after admission renal functions normalized and patient became afebrile and was maintaining hemodynamic and having adequate urine output.

DISCUSSION

Search of literature reveals that numerous endocrinopathies are associated with plasmodium falciparum infections. Many studies have suggested that there may be disturbance in calcium homeostasis, depression of pituitary thyroid and adrenocortical axis.

It is seen that hypocalcaemia in falciparum malaria, increases the risk of tetany, convulsions and hypotension. It also further increases the risk of hypoglycaemia and lactic acidosis.[4]

Some possible mechanisms of hypocalcaemia, in these patients are as follows:

a) Due to "sick eu parathyroid", During acute infection, the parathyroid response to hypocalcaemia is blunted. However, after clearance of parasitaemia there is full recovery of the glandular function.[3]

b) The ionized calcium "set point for basal PTH secretion is decreased.[4]

How ever since our patient had an adequate Parathyroid response to hypocalcaemia as seen by the parathyroid level of 130 pg/ml (normal 6.2–29 pg/ml), this cannot be the mechanism in our patient. There are other mechanisms which may be responsible.

c) Plasmodium falciparum uses calcium-based signalling pathways. This causes reduced intracellular calcium. Hence there is disturbance in the environment of the host cell cytoplasm.[5]

d) Plasmodium Falciparum infected red blood cells have an increased permeability to calcium. Calcium influx may occur at a rate of 1mmol/l which is much more than the normal values.[6] This pathway which is responsible for the enhanced influx of calcium is expressed at approximately 30 hrs after invasion by the parasite.[6]

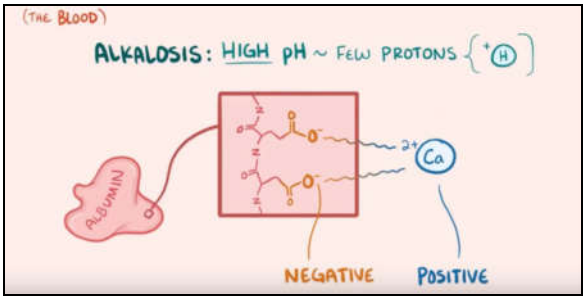


Figure-1: There is influx of calcium into plasmodium falciparum infected red blood cell. Hypo albuminemia is also a contributory factor

e) There is an increase in calcium dependent Transglutaminase activity in the cells of the parasite. This might be responsible for a decrease level of calcium. This decrease is found simultaneous with maturation of the parasite. This effect is maximum in the trophozoites which are 48 hours old. Most of the calcium was found with in the parasite.[7]

f) Studies have shown that serum calcium is utilized by the parasite and this intracellular utilization is responsible for Chloroquine resistance. However, it is seen that when these calcium channels are blocked with medications like verapamil and Fantofarone, then there is complete reversal of Chloroquine resistance. Verapamil is more potent than Fantofarone in reversing drug resistance.[5]

g) Other contributory, factor (as in our patient) may be the acute renal insufficiency which causes hypophosphatemia and it resulted in hypercalciuria. Hypomagnesaemia by itself causes hypocalcaemia because of impaired release of parathyroid hormone.[2]

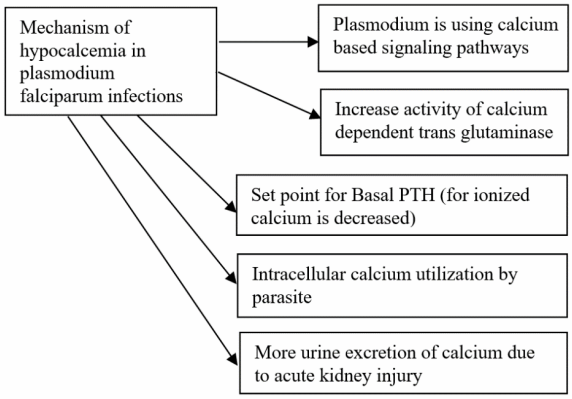
h) Decreased level of ionized calcium, (as in our patient) will cause increase excitability of peripheral nerves and tetany. Hypo albuminemia may occur due to hepatic impairment which occurs in the late stages of plasmodium falciparum infections and this can also cause hypocalcaemia.[8]

Some case reports have mentioned treating symptomatic hypocalcaemia in malaria falciparum with intravenous calcium gluconate (10 ml of 10% solution three times daily).[8]

Since our patient alkaline phosphate was in normal range so 25 OH VIT D was not checked. Ultrasound kidneys, for renal size was not done because renal functions became normal after hydration and treatment of infection. One reason for hypotension in our patient could be because of dehydration and other reason because of hypocalcaemia.[5]

It is seen that ionic Calcium plays a role in the tonic contraction of cardiac muscles and helps in maintaining blood pressure within normal range.

Hypocalcemia caused prolong. Q-T interval, it can also lead to heart failure.[5] In our patient the hypotension and the hyponatremia can also be explained by the depressed adreno cortical axis. Both primary and secondary adrenal insufficiency has been observed in severe falciparum malaria.[9] In acute uncomplicated malaria there is an altered 'set point' for cortisol inhibition of ACTH secretion by corticotrophins.[9]



Other endocrinopathies include involvement of the pituitary thyroid axis. This can be depressed in severe malaria. Literature review has revealed that thyrotropes and thyroid gland function are also depressed in acute severe malaria. These patients can have central hypothyroidism (with depressed TSH

and T4) and thyroid functions usually return to normal after the fever settles and parasitemia clears. These changes may be an adaptation to accelerated catabolism, However the role of thyroid replacement in such patients is uncertain.[10]

In conclusion Hypocalcemia is an important prognostic marker in the management of falciparum malaria.[11] The normalization of calcium correlates with parasite reduction, clinical recovery and normalization of the QT interval.

Conflict of Interest: None

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