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Case Note

Two cases of severe falciparum malaria in KMCTH

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Abstract
Malaria is the most important parasitic disease of man. It is the protozoan infection of RBCs transmitted by bite of blood feeding female anopheline mosquito. Until the 19th century malaria was found throughout Europe, North America and Russia. Since then, it has been eradicated from these areas but in tropics though initial efforts of eradication had been successful, there has been resurgence of disease[1] accompanied by increasing resistance of the anopheline vector to insecticide and of the parasite to antimalarial drugs. We report two cases of falciparum malaria in which there was co-existent vivax malarial infection. These two cases were both exposed to highly endemic zone for malaria.

Key words: Sequestration, malaria, falciparum.

These two cases highlight the possibility of severe falciparum malaria in Kathmandu although the area is not endemic. Cerebral malaria should also be suspected in stuporous comatose patient especially if they have been exposed to endemic zone.

Case No. 1
18 years boy from Assam, India on holidays in Nepal came to Kathmandu Medical College, Emergency with complaints of headache for 15 days and fever for 4 days. He was advised for admission, which he denied & went away. Two days later, again he presented in emergency with additional complaints of vomiting several episodes since that morning and altered sensorium for same duration. There was no photophobia, neck rigidity or seizures. He was also passing dark coloured urine and output was decreased. No burning micturition or frequency was present. No history of cough, chest pain.

Examination (at arrival):
General condition was poor. He was semiconscious (GCS 8/15). No neck rigidity or other signs of meningeal irritation was present. Pallor ++ , Icterus +++. Systemic examination: NAD.

Investigation
Hb. 9.2gms% (12.8 gms % two days earlier)→7.7 gm % (within 12 hrs.) →6.2 gms%
Total count: 10,900 c.c, DLC: P 83 L17
Platelet count: 31,000 / C.C →96,000 / C.C (after PRP transfusion) →46,000/C.C
BUN /S. creatinine: 149 /1.8 mg % (58/ 0.6 mg % 2 days earlier) → 205/ 3.8 mg %→ 209/ 4.8 mg %→ 237/ 5mg %
CSF analysis : TLC -2/c.c , All lymphocytes, sugar 79 mg % , protein 660 mg %
HIV, HCV, HBs Ag – Negative
Malarial Antigen Test: Positive for P.vivax & P.falciparum
LFT: Unconjugated Hyperbilirubinemia

Management
He was started on parenteral quinine with other supportive therapy. His fever and other symptoms responded from second day, however his urine output did not improve and so was his renal parameters. He underwent two cycles of haemodialysis and also was transfused with 4 units of whole blood and 4 units of platelet rich plasma. He was switched to oral quinine 72 hours after when he was able to take the medications orally & continued for 7 days. His renal parameters also improved and was discharged on primaquine for 15 days.

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Case no. 2

21 years old male, resident of Ramechhap, working in Kolkotta for 1.5 years presented in ER with c/o high grade (103F) fever associated with chills & rigors, bloody diarrhoea, headache, red coloured urine for 4 days. He had also c/o yellowish discolouration of sclera and repeated vomiting for last 2 days.

Examination

Pallor ++, Icterus ++, temperature 103F, moderate hepatosplenomegaly, no meningeal signs, no chest findings.

Investigations

Peripheral Blood Smear- Normocytic normochromic RBCs, platelets reduced, trophozoites of *P. vivax* and ring form of *P. falciparum* seen.

Hb=11.2gm%, TLC=8800/cc, DLC=P(61)L(39), Platelets= 56000/cc, Urea/Creatinine=43/0.9 mg%, SGOT = 55U/L, SGPT= 62U/L,ALP=464 U/L, Total bilirubin=8.4mg%, Direct bilirubin=5.8mg%, Stool R/M: RBCs =5-7/hpf, Pus cells=plenty/hpf, Blood c/s= sterile, Urine examination= RBCs20-22/hpf.

Management

The patient was started on oral Quinine and continued for 7 days .Fever subsided from 2nd day and his hospital stay was uneventful. He was discharged on Primaquine for 15 days.

Discussion

Severe disease is unusual with three benign malarial parasites; *P. vivax, P. ovale, P.malarie,* although occasional patients die of ruptured spleen. Almost all deaths are caused by P. falciparum that causes potentially lethal infection with rapid progression to severe disease. Severe falciparum malaria may present as cerebral malaria characterized by unarousable coma, severe anaemia, renal failure, pulmonary oedema or ARDS, hypoglycaemia, circulatory collapse, spontaneous bleeding/ DIC, acidemia, jaundice, hyperpyrexia, hyperparasitemia. In severe falciparum malaria there is multiple vital organs dysfunction & more than one of the above mentioned conditions may be present.

The process whereby RBCs containing mature forms of P.falciparum adhere to microvasculature endothelium is called cytoadherence and thus disappear from circulation is known as sequestration. There is a related phenomenon of rosetting[2] whereby uninfected RBCs adhere to RBCs containing mature parasites. These two phenomena are mediated by strain specific adhesion proteins and vascular ligands, an area of intensive scientific studies in recent times. Sequestration is thought to be the centre of patho-physiology of falciparum malaria[3] that occurs predominantly in the venules of vital organs, being greatest in brain. There is also an emerging concept of toxicity cytokines in the pathogenesis of malaria. During meront rupture that produce characteristics signs and symptoms of paroxysms[4] namely shivering, cool extremities, headache, chills, spike of fever and sometimes rigors followed by sweating, vasodilatation & defeveresence, the malarial parasite induce release of cytokines in the same way as bacterial endotoxins[5]. Plasma concentration of cytokines- particularly TNF, IL-1, IL-6 are found to be elevated in both acute vivax and falciparum malaria[6].

The pathogenesis of anaemia in malaria is multifactorial with obligatory destruction of red cells containing parasites and also accelerated destruction of non-parasitized cells. This haemolytic anaemia is compounded by bone marrow dysfunction. Micro-vascular insufficiency explains part of coma in cerebral malaria but more importance is being given to NO, a cytokine which is a potent inhibitor of neurotransmission.

Micro-vascular obstruction explains renal failure that may be compounded by massive haemolysis and also gut mal-absorption. There is also accelerated coagulation cascade activity and thrombocytopenia. Passage of coca-cola coloured urine due to massive intravascular haemolysis occurs especially in patients with G6PD deficiency who may be receiving oxidant drugs or not (black water fever). There is considerable splenic enlargement and increased capacity to clear red cells. Jaundice is common with evidence of hepatic dysfunction contributing to hypoglycaemia, lactic acidosis, and reduced clotting factor synthesis. Jaundice in malaria appears to have haemolytic, hepatic and cholestatic components. In severe malaria there is hyperlactatemia mainly due to tissue anaerobic glycolysis. Hypoglycemia is associated with hyperlactatemia and shares some pathophysiological aetiology. Hypoglycemia also contributes to CNS dysfunction. Placental dysfunction leads to low birth weight and increased chance of still birth[7]. Patients with severe malaria are vulnerable to bacterial infection particularly of lungs and urinary tract.

Diagnosis of falciparum malaria involves demonstration of parasites in blood smears by conventional microscopy or Quebec method. Rapid antigen/antibody detection is also very useful investigation for the multiple organ dysfunction- aids

in assessment as well as management and has prognostic implication. Severe malaria is a medical emergency. Parenteral anti-malarial treatment should be started as soon as possible and switched on to oral form as the patient is able to take orally. Supportive care includes care of unconscious patient, prevention and treatment of convulsions, treatment of hyperpyrexia and early detection and treatment of other manifestations or complications of severe malaria.

Conclusions

1. Although mostly, Encephalitis, is the first diagnosis of fever with neurological deficits, Malaria should also be suspected in similar clinical presentation.
2. Prompt initiation of therapy with Quinine saves life in severe malaria.

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