MYOCARDITIS COMPLICATING FALCIPARUM MALARIA

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INTRODUCTION

Over the last couple of years, infections with Plasmodium falciparum continue to increase worldwide due to a combination of factors including increasing resistance of malarial parasites to chemotherapy, changes in climate and increased international travel to endemic areas. About 1.5 to 2.7 million deaths each year are caused by this disease[1]. Though the major complications which may prove fatal include cerebral malaria, renal failure, pulmonary edema/ ARDS, disseminated intravascular coagulation and multi- organ dysfunction, myocarditis can also be seen rarely. We describe two cases of falciparum malaria complicated by myocarditis.

CASE REPORT

CASE NO. 1

A 38 year old male reported to Combined Military Hospital Quetta on 17 Nov 2006 with six days history of fever, nausea and epigastric discomfort. He did not have any chest pain, dyspnoea, cough, vomiting, bleeding from any part of the body or altered sensorium. He had not taken any antimalarial prophylaxis. Two days earlier, he was discharged from skin ward of the same hospital after completing 20 days course of parenteral meglumine antimoniate as a treatment for cutaneous leishmaniasis. Electro cardiograms (ECGs) performed regularly during that hospital stay did not reveal prolongation of QT interval.

Clinical examination revealed a conscious young man with fever, tachycardia and jaundice. He was normotensive with a blood pressure of 100/ 70 mmHg. Both the liver and spleen were enlarged. Lesions of cutaneous leishmaniasis were seen on right forearm, left wrist and anterior abdominal wall. Complete blood count revealed haemoglobin 13.9g/dl, TLC $3.5X10^9$/l and platelets 48 X 10^9/l. Ring forms of plasmodium falciparum were seen on giemsa stained peripheral blood film, with a parasitemia of 0.2%. Random plasma glucose, ECG and urine dipstick examination were normal.

Following initial assessment, the patient was admitted to medical ward and started on oral quinine sulphate (600mg X TDS) and doxycycline (100mg X BD). After 15 hours of admission, he suddenly developed cardiac arrest from which he could not be revived. Postmortem examination provided a histological diagnosis of myocarditis complicating falciparum malaria. There was a scattered infiltrate of lymphocytes and histiocytes, some of which were containing malarial pigment.

CASE NO. 2

A 34 year old male was admitted to Combined Military Hospital Sibbi on 14 Sep 2006 with fever for the last six days and vomiting of one day duration. Clinical examination revealed fever with jaundice and hepatosplenomegaly. Serum bilirubin was 77 µmol/l and ALT 124 U/l. Peripheral blood smears did not show malarial parasite. Complete blood counts and ECG were normal. A possibility of cerebral malaria was still kept in mind because of high endemicity; the patient was started on parentral artemether in addition to supportive care. Over the next couple of days, the jaundice deepened and the patient developed altered consciousness. Considering the limited facilities available, the patient was evacuated to Combined Military Hospital Quetta (tertiary care hospital) by helicopter on 19 Sep 2006. He developed cardiopulmonary arrest enroute and could not be revived. Autopsy revealed evidence of congestive hepatosplenomegaly, cerebral edema and myocarditis (with malarial pigments in histiocytes). Ring forms and trophozoites of plasmodium falciparum were seen on bone marrow aspirates taken at the time of postmortem exam.

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DISCUSSION

The first patient had a sudden unexpected death while he was being treated with oral quinine for uncomplicated falciparum malaria. This raises a strong possibility of a cardiac arrhythmia as the terminal event. Possible explanations include: myocarditis complicating falciparum malaria, cardiotoxicity of antimalarial drugs and effects of antimony compounds. Though quinine itself is cardiotoxic and can prolong QT interval leading to a variety of arrhythmias including torsades de pointes/ ventricular tachycardia and ventricular fibrillation[2], this was unlikely to be the case considering that the autopsy revealed histological evidence of myocarditis and that the patient had a normal QT interval before starting treatment only a couple of hours earlier. Similarly, meglumine antimoniate was stopped two days earlier and its cardiotoxicity is not likely to manifest at this stage.

The second patient had fatal cerebral malaria, with histological evidence of myocarditis on autopsy. No malarial parasites were found on peripheral blood smears. This examination is operator dependant, requires considerable expertise and adequate quality control, and even with greatest care, around 5% cases may be missed on first smear[3]. Negative results may partly be attributed to the absence of P. falciparum from the peripheral blood for a portion of its life cycle[4]. The second lesson to learn is that empirical treatment must always be started in case of strong clinical suspicion. In doubtful cases, diagnosis may be confirmed by bone marrow examination for malarial parasites.

Historically, it was believed that the heart was frequently affected in severe malaria, with up to 14% of deaths being attributed to a cardiac basis[5]. However, we now know that myocarditis is a rare complication of falciparum malaria, reported in 0.6% of patients in one series[6]. This is more common in autopsy studies, e.g. in four of 25 fatal cases of falciparum malaria[7]. Plasmodium falciparum is the causative agent in almost all reported cases of malaria complicated by myocardial damage[8]. Damage can result from mechanical blockage of capillaries by malarial parasites and parasitized cells. Toxic effects of a group of polypeptides especially tumor necrosis factor may also play a significant role in this pathophysiological process[9]. These polypeptides also increase thrombospondine secretion, which in turn enhances the sequestration of knob-bearing parasitized red cells. Cardiac troponins are useful for diagnosis of myocarditis[10]. However, troponin T or creatinine kinase (total and MB fraction) were not done in either case because myocarditis was not being suspected at all (high threshold for suspicion because of rare occurrence). ECG monitoring is not required in patients with otherwise uncomplicated falciparum malaria and lack of evidence of an underlying cardiac condition[6].

In view of the increased burden of malaria in Pakistan, especially in Balochistan and Sind, all cases of severe falciparum malaria should be managed in intensive care unit (ICU) with regular monitoring for complications. Myocarditis rarely complicates falciparum malaria but should be looked for in all cases so as to prevent sudden death by prompt treatment of cardiac arrhythmias.

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