Case Report

Looking beyond the obvious: diagnosis and management of malaria and human immunodeficiency virus coinfection

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ABSTRACT

An atypical presentation of malaria with an unusual complication can initially leads to an incorrect diagnosis, whose puzzling clinical features resolves once the correct diagnosis is made and the treatment is initiated. Here, we report one such unusual presentation of vivax malaria which masqueraded as an acute coronary syndrome (ACS) in a 46-year-old male. The patient had been on Tenofovir + Lamivudine+ Efavirenz for acquired immunodeficiency syndrome and presented to us with a history of chest pain, breathlessness, and pedal edema. We found him to have elevated blood pressure, diffuse abdominal tenderness, splenomegaly, and pedal edema. ACS was diagnosed based on the clinical and laboratory features, though the absence of regional wall motion abnormality on the echocardiogram was puzzling. Antiplatelet therapy and statins were started. Although the clinical picture was not typical, the combination of hepatic and renal dysfunction and thrombocytopenia prompted us to test for malaria, which turned out to be strongly positive. The patient received treatment for malaria, after which both clinical and laboratory parameters improved. We present this case to illustrate the diagnostic challenge when coexisting diseases result in atypical presentations of common illnesses.

Key words: Acute coronary syndrome, Coinfections, Malaria, Tropical infections

Acquired immunodeficiency syndrome (AIDS) is a chronic, potentially life-threatening condition caused by the human immunodeficiency virus (HIV). The prevalence of HIV AIDS in India is 0.2% [1]. There were 338494 cases of malaria reported in India in 2019 [2]. Vivax malaria is more common than falciparum in India. Malaria and vivax malaria coinfections have been reported from South India, with patients with HIV more likely to suffer from vivax malaria [3]. Although the complications of renal insufficiency, hepatic dysfunction, and thrombocytopenia are more common in falciparum malaria, these are being more frequently reported in vivax malaria as well. Although physicians are taught to consider uncommon presentations of common diseases, this lesson can sometimes be forgotten. This is more likely in the presence of a coexisting illness which could further mask the typical symptoms of a disease.

We report the case of a gentleman with an atypical presentation of vivax malaria, with an unusual complication, leading to an initially incorrect diagnosis, whose myriad clinical and laboratory abnormalities resolved once the correct diagnosis was made and treatment was initiated.

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CASE REPORT

A 46-year-old male presented to us with a complaint of chest pain of 1-day duration. There was no history of fever, cough, palpitations, or diaphoresis. Before this, he had been admitted to another hospital with a 10-day history of breathlessness and bilateral pedal edema. Pulmonary thromboembolism was suspected after ruling out other causes and he had undergone a computed tomography (CT) angiography for the confirmation of the same. Immediately after the procedure, he developed decreased urine output and was found to have impaired renal function. He was diagnosed to have radio contrast-induced nephropathy (RCIN) for which he underwent two cycles of hemodialysis. The patient had been on Tenofovir + Lamivudine+ Efavirenz regimen for the past 10 years for AIDS. He was a non-smoker and was a regular consumer of ethanol, with a weekly intake of 24 units of alcohol.

On examination, his blood pressure was elevated; he had a normal respiratory rate and 96% oxygen saturation on room air. He had diffuse abdominal tenderness, mild splenomegaly, and bilateral pitting pedal edema. Respiratory and cardiovascular systems were normal on examination and there was no third heart sound.

Laboratory investigations revealed hemoglobin – 10.3 g/dL; total count – 9900/mm^3; platelet count – 109,00/mm^3;

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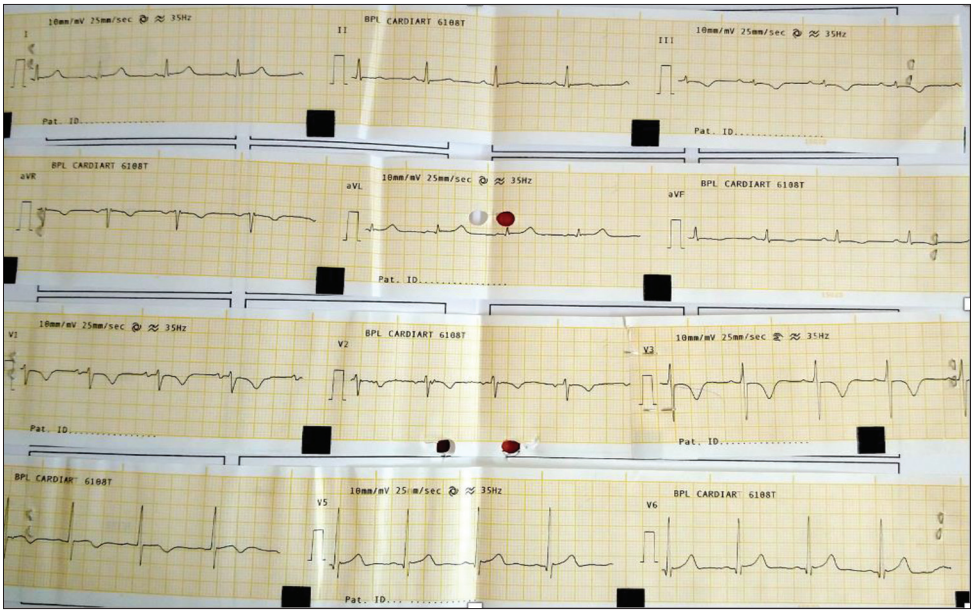

Figure 1: Electrocardiogram showing T wave inversion

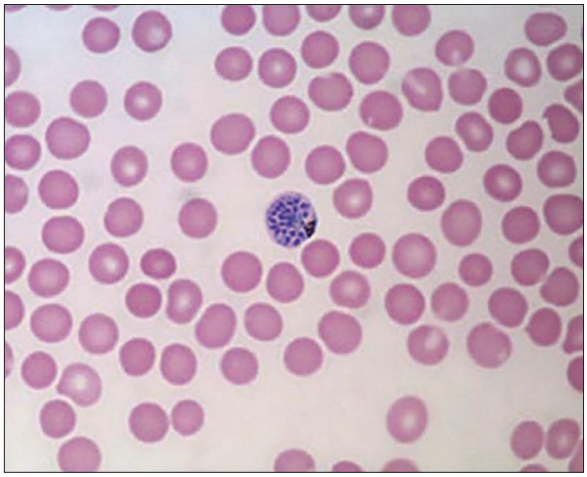

Figure 2: Malarial parasite

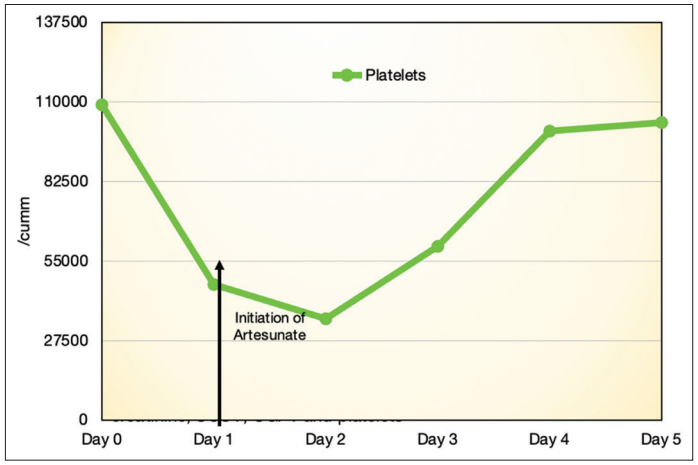

Figure 3: Platelet trends

total bilirubin – 1.62 mg/dL, direct bilirubin – 1.40 mg/dL; SGOT - 2517 IU/ml; SGPT – 1974 IU/ml; prothrombin time - 16.2s (Control – 11.2s); activated partial thromboplastin time – 34.4s (Control – 30.4s); INR – 1.45; serum creatinine – 3.44mg/dL; blood urea – 99mg/dL, and CD4 count – 519 cells/mm^3. Urine routine examination showed 5–10 pus cells/hpf.

Electrocardiogram (ECG) revealed T wave inversions in limb lead III and the precordial chest leads V1-V4 (Fig. 1). Troponin I – 0.48 ng/mL (< 0.05 ng/mL) and Creatinine Kinas Myocardial Band – 62 IU/L (5 -25 IU/L) were found to be elevated. Echocardiography showed dilated right atrium, right ventricle, mild tricuspid regurgitation, pulmonary hypertension, and a normal left ventricular ejection fraction of 55% with no regional wall motion abnormalities (RWMA). We considered that the elevated creatinine was possibly due to RCIN after the CT angiogram in the previous center.

Acute coronary syndrome (ACS) was diagnosed based on the clinical and laboratory features though the absence of RWMA was difficult to explain. Antiplatelet therapy (aspirin 150 mg) and statins (atorvastatin 40 mg) were started. We considered the possibility of beriberi as well, and thus thiamine supplementation was commenced. In addition, injectable ceftriaxone was started for the urinary tract infection.

Although the patient improved initially, laboratory investigation repeated on the 2nd day showed further deterioration in renal and liver function as well as worsening thrombocytopenia (35,000/mm^3). At this point, the worsening thrombocytopenia, hepatic and renal function was thought to be either an adverse drug reaction or a consequence of sepsis and consumption coagulopathy. Cultures were repeated and serum procalcitonin was tested. However, cultures were sterile and procalcitonin was negative. Although the clinical picture was not typical (no history of fever), the combination of hepatic and renal dysfunction and thrombocytopenia prompted us to test for malaria. Smear showed the presence of *Plasmodium vivax* (Fig. 2). The patient received three doses of injection artesunate, each given 12 h apart. The platelet count increased to 60,000/mm^3 by the 3rd day. He was changed over to a combination of artesunate, pyrimethamine, and sulfadoxine on the 3rd day, and the antibiotic was stopped as

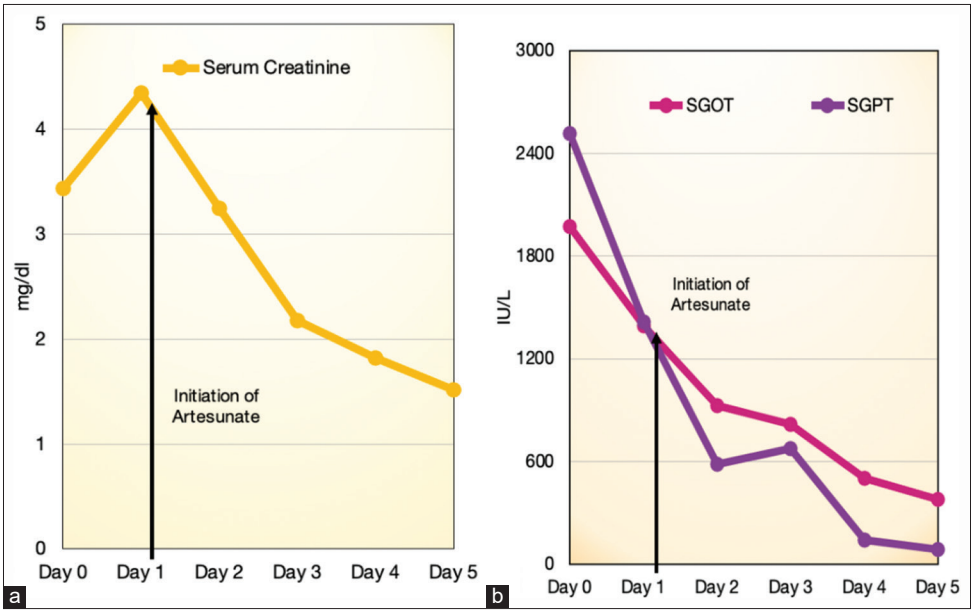

Figure 4: (a) Creatinine trends; (b) transaminase trends

the urine cultures remained sterile. With antimalarial, the platelet count, creatinine, and transaminases improved (Figs. 3 and 4).

At the time of discharge, serum creatinine was 1.52 mg/dL and SGOT and SGPT were 83 and 374 IU/ mL, respectively. The patient was started on primaquine and was advised to follow-up a week later for restarting his antiretroviral therapy (ART). At the follow-up visit, the patient had no symptoms of chest pain or breathlessness and his pedal edema had disappeared. Repeated blood smear showed no parasites; serum creatinine was 1.2mg/dL; platelet count was 478,000/mm^3; SGOT and SGPT values were 34 and 72 IU/L, respectively, and ECG was normal. He was restarted on his ART and was also advised to continue primaquine for 1 more week. Thiamine supplementation was also continued, and he was counseled regarding the need for strict abstinence from alcohol.

DISCUSSION

According to the world malaria report 2018, India accounted for 18% of all global cases of *P. vivax* [4]. Although benign, *P. vivax* infection may sometimes cause complications with fatal outcomes. The exact prevalence of complicated vivax malaria is not known as there are no criteria defining the severity. Progressive renal impairment, metabolic acidosis, hypoglycemia, respiratory distress, retinal hemorrhage, splenic infarction, cardiac complications, and even rare instances of facial palsy have been reported in vivax malaria [5]. Here, we report one such unusual presentation of vivax malaria which masqueraded as an ACS.

The initial diagnosis of ACS was based on the clinical presentation – chest pain, ECG changes, and elevated cardiac enzymes. However, echocardiography did not reveal RWMA. Hence, a second diagnosis of wet beriberi was considered; however, this would not explain the increasing hepato-renal dysfunction and the drastic drop in the platelet count. Cardiac complications such as myocarditis, pericardial effusion, bundle branch block, and cardiomyopathy have often been reported with falciparum malaria but there have been only few cases reported in vivax malaria. Malaria may itself be a risk factor for acute myocardial infarction [6]. In our case, we found evidence of myocarditis and elevated cardiac enzymes. According to the current literature available, the elevation of cardiac enzymes is not a common finding in malaria-associated myocarditis and this makes our case unique.

Various mechanisms such as mechanical blockage of capillaries by the malarial parasite and parasitized RBC's, direct damage of the myocardium by pigment laden macrophages, toxic effects of tumor necrosis factor (TNF), hypoglycemia and acidosis impairing the myocardial integrity, and increased thrombospondin secretion are found to be responsible for myocardial damage [7]. While cytoadherence is mainly seen in falciparum infection, cardiac complications in vivax malaria may be explained by the toxic effects of TNF-α and interleukin-10 [8].

The concurrent HIV infection could possibly explain the stormy nature of vivax malaria in our patient. While malaria itself can cause a transitory increase of the viral load in HIV, higher parasitemia, higher treatment failure, and more severe symptoms of malaria are seen among patients with HIV [9].

ART can cause hepatic dysfunction and we initially were faced with a dilemma regarding its continuation in our patient. However, interestingly, the transaminitis resolved rapidly on the commencement of antimalarial. Drug-drug interactions (DDIs) between antimalarial and ART are also a conundrum. Artesunate which was used in our patient is known to have DDIs with nevirapine and protease inhibitors. Primaquine is a relatively safe drug with no possible DDIs with any of the ART [10]. Hence, therapeutic options for treatment of malaria in HIV are limited.

The lessons we learned from this case are that the absence of fever and the presence of the typical signs and symptoms of an ACS served as a red herring and we almost missed the diagnosis of malaria in our patient. Thus, irrespective of the clinical

presentation, it is advisable to always ask for a malaria smear in an endemic area. Concurrent HIV infection tends to confound the situation further. Vivax malaria can be more hazardous than we usually consider it to be. Myocarditis in malaria may have elevated cardiac markers contrary to the usual case reports.

CONCLUSION

Diagnosing malaria in our patient was challenging in the absence of typical clinical features. Our patient not only had an atypical presentation of the disease itself but he also had a rather unusual complication, namely, myocarditis. Malaria and HIV occurring simultaneously may rightly be considered "the nightmare of the tropics" due to the myriad drug interactions resulting in limited therapeutic options. A high index of suspicion is required for timely diagnosis and treatment.

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