

An unusual case of heart failure due to *Plasmodium vivax* infection with a favorable outcome

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ABSTRACT

Although malaria is one of the oldest types of parasitic infection, we have recently witnessed substantial changes in the outcome of malarial infections. Severe *Plasmodium vivax* infections have recently become more frequent, and are occasionally associated with fatal outcomes. Cardiac arrhythmia and myocardial failure have also been reported, typically in association with *Plasmodium falciparum* infections. We report a case of myocarditis and heart failure, due to *Plasmodium vivax* infection, along with the favorable outcome.

Keywords: Malaria. *Plasmodium vivax*. Myocarditis. Heart failure.

INTRODUCTION

With its associated morbidity and mortality, malaria has threatened human beings since time immemorial. The infection is common in tropical and sub-tropical areas, as their environment favors the survival and multiplication of the malarial parasite. According to the latest figures, released in December 2013 by the World Health Organization, there were approximately 207 million cases of malaria in 2012 (uncertainty range, 135-287 million) and an estimated 627,000 deaths (uncertainty range, 473,000-789,000)¹. Of the 5 species of the malaria parasite, *Plasmodium falciparum* (*P. falciparum*) infection is most often associated with complicated malaria. However, over the past few years there has been an increasing trend in cases of complicated malaria associated with *Plasmodium vivax* (*P. vivax*). Once considered benign, *P. vivax* malaria is becoming hostile, creating fresh challenges for clinicians and epidemiologists. Although rare, cardiovascular complications are known to be associated with *P. falciparum* malaria², while myocarditis associated with *P. vivax* is extremely rare in the literature³. We report the case of a 22-year-old male who presented with myocarditis and heart failure due to *P. vivax* malaria.

CASE REPORT

A 22-year-old male resident of India presented with high-grade fever associated with chills and rigor of 5 days duration, as well as breathlessness of 1 day duration. There was no

history of cough, chest pain, dysuria, loose stools, yellowish discoloration of the eyes or skin, bleeding, joint pain, or other symptoms that might indicate previous significant medical or surgical illness. Upon physical examination, the patient was febrile with a temperature of 101°F. His respiratory rate was 30/min, pulse was 98/minute, and systolic blood pressure was 70mmHg. Examination of the cardiovascular system revealed no signs of murmur or gallop rhythm, and his heart sounds were normal. His spleen tip was palpable during an abdominal examination, and respiratory system examination revealed crepitations in the bilateral infrascapular regions. The rest of his systemic examination was normal, and there were no clinical findings suggestive of acute rheumatic fever.

The patient's hemoglobin level was 12.3g/dL, with a total leucocyte count of $5.7 \times 10^9/L$ (68% polymorphs and 32% lymphocytes), and a platelet count of $270 \times 10^9/L$. His erythrocyte sedimentation rate was 8mm/h, his C reactive protein (CRP) level was 1mg/L, and his anti-streptolysin O (ASO) titer was 32 units. Liver and kidney function tests were normal, and his serum calcium was 8.4mg/dL. A peripheral smear detected the ring and schizont stage of *P. vivax*, and the malaria antigen test was positive for *P. vivax* only. Blood and urine cultures were sterile, and typhoid immunoglobulin G and Leptospira slide macroagglutination tests were negative. Viral serology for adenovirus, cytomegalovirus, Coxsackie virus, and enteric cytopathic human orphan virus were also negative, and the patient was non-reactive for the human immunodeficiency virus. Electrocardiography (ECG) detected sinus tachycardia with T-wave inversion in the inferior leads. Cardiac enzymes were within the normal range and the troponin-T test was negative. Chest radiography revealed cardiomegaly with bilateral lower zone infiltrates (**Figure 1A**). Echocardiogram revealed dilated cardiac chambers (**Figure 2**) with left ventricular systolic dysfunction (ejection fraction of 25-30%); no regional wall motion abnormalities were detected.

A diagnosis of *P. vivax* myocarditis was made and patient was placed on inotropic support with dobutamine injection for 48h.

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Antimalarial treatment was provided as a combination of artemether and lumefantrine. Supportive care was administered in the form of oxygen, intravenous fluids, furosemide, and antipyretics. The patient's blood pressure normalized and he became afebrile in 3 days. Glucose-6-phosphate dehydrogenase levels also returned to the normal range, and the patient was treated with primaquine for 2 weeks to prevent relapse. Seven days later, follow-up ECG, radiography (**Figure 1B**), and echocardiography detected no cardiac abnormalities.

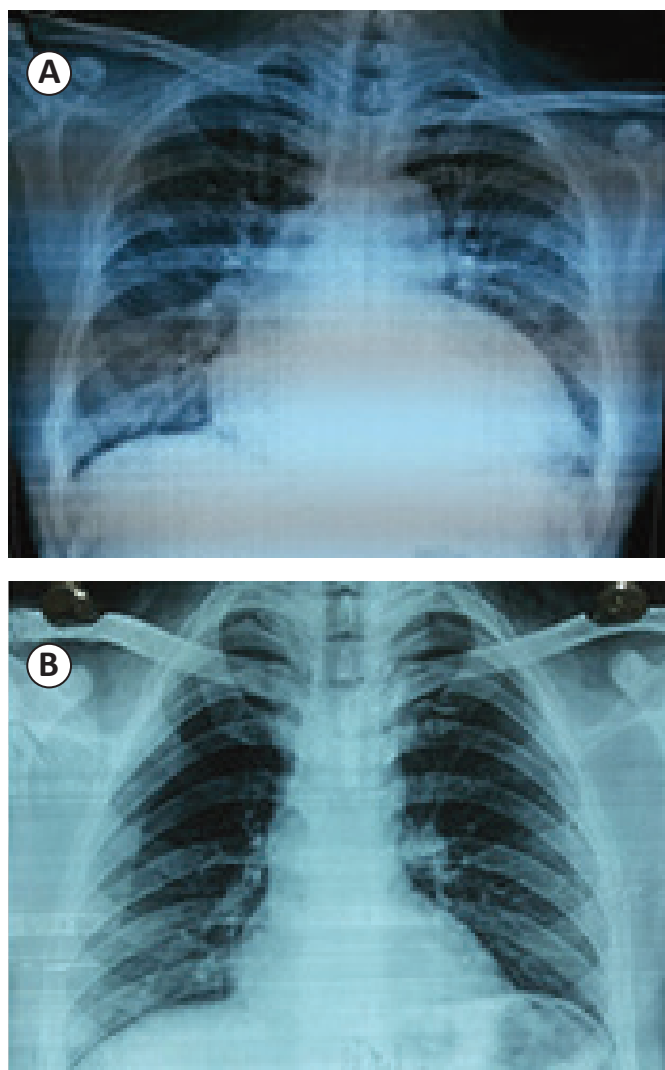


FIGURE 1 - A: Chest radiography image obtained at admission. **B:** Chest radiography obtained at discharge.

DISCUSSION

The clinical course of *P. vivax* malaria, traditionally called benign tertian malaria, appears to be changing, given the recent reports of *P. vivax*-associated serious complications^{3,4}. Cardiovascular complications, such as bundle branch block, pericardial effusion, and cardiomyopathy, are more frequently

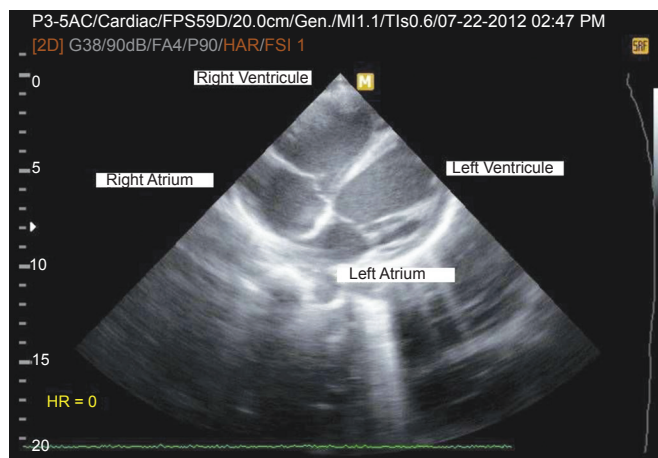


FIGURE 2 - Echocardiograph showing dilated cardiac chambers.

reported as complications of *P. falciparum* malaria, compared to *P. vivax* and experimental malaria⁵. In the present case, we found evidence of myocarditis with heart failure, which improved following symptomatic treatment. In a study of 22 adult cases of *P. falciparum* malaria, ECG abnormalities were observed in 23% of cases, while pericardial effusion and global hypokinesia were observed in 9% and 4.5% of cases, respectively⁶. Myocarditis has also been reported as a complication of *P. falciparum* malaria², although it is rarely reported following *P. vivax* malaria^{7,8}.

Unfortunately, the mechanism of cardiac complications associated with malaria is not well understood. Various case reports and pathological studies have indicated that malaria might be a cause of toxic and ischemic myocarditis. As well, ischemic cardiomyopathy can develop following the blockage of capillaries by parasites and parasitized red blood cells, as shown by various autopsy studies⁹. Interestingly, the phenomenon of cytoadherence, where red blood cells adhere to the walls of capillaries and are sequestered to the brain and heart, is typically caused by *P. falciparum*. However, as the parasite density in *P. vivax* malaria is low, these cases do not typically develop cytoadherence. Therefore, it appears that the toxic effects of cytokines, such as tumor necrosis factor alpha, interleukin-10, or other unknown factors, might play a role in cases of *P. vivax* malaria. Cytokine-mediated endothelial activation has been found to be associated with disease severity in both *P. falciparum* and complicated *P. vivax* malaria. In a case-control study from Pakistan, the authors compared 82 complicated cases and 100 uncomplicated cases, and observed that tumor necrosis factor alpha, interleukin-10, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1 were individual predictors of complicated *P. vivax* malaria¹⁰.

For patients with malaria, a detailed medical history and clinical examination, along with pertinent laboratory tests, may help establish the etiology of myocarditis. For example, in the present case, the lack of cardiac risk factors and the patient's age allowed us to exclude ischemic cardiomyopathy. Moreover, the patient's cardiac enzyme levels were not elevated and his

troponin-T test was negative. Although they may not be specific to ischemic cardiomyopathy, their absence also supported our exclusion of this condition. As well, echocardiography did not reveal any regional wall motion abnormalities, which are generally helpful in differentiating cardiac diseases and defining the nature of the myocardial dysfunction. Myocarditis is typically characterized by a decreased left ventricular ejection fraction and hypokinesia of the ventricular walls, and may be associated with pericardial effusion and valvular regurgitation¹¹. Regarding other diagnoses, we excluded acute viral myocarditis, as the serology results were negative for commonly implicated viruses. Acute rheumatic fever was also unlikely, as the ASO titer and CRP levels were normal, and there were no other significant clinical findings.

Treatment for myocarditis is mainly supportive, and involves the management of shock, arrhythmia, and heart failure. Recovery is typically complete, pending resolution of the underlying cause. Few patients exhibit evidence of residual cardiac dysfunction on follow-up¹², and in the present case, the patient's recovery was complete, with full resolution of all clinical and echocardiographical findings at the time discharge.

Myocarditis is an unusual complication of *P. vivax* malaria, although the presence of heart failure and shock during admission should arouse suspicion regarding underlying myocarditis. Echocardiography may help prove the diagnosis, and guide subsequent management of such cases.

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