CASE REPORT: AN UNUSUAL LATE RELAPSE OF *Plasmodium vivax* MALARIA

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Abstract. We observed an unusual case of *Plasmodium vivax* malaria who presented with an initial relapse four years after the primary infection. This occurred in Cameroon, where the patient, a 56-year-old priest, acquired a mild form of malaria and was treated with only chloroquine. Since he returned to Italy, he had not experienced any malaria-like symptoms, had not visited any other areas endemic for malaria, and had not received a blood transfusion. Blood smear microscopy confirmed the presence of *Plasmodium spp.* parasites, but unclear morphologic characteristics did not allow discrimination between *P. vivax* and *P. ovale*. A nested polymerase chain reaction–based molecular analysis identified *P. vivax* as the plasmodial species responsible. This case emphasizes the importance of taking into account the possibility of a very late initial relapse of *P. vivax* malaria and the relevant issues in terms of infection control.

INTRODUCTION

The current burden of *Plasmodium vivax* malaria is increasing worldwide and causing great concerns in public health systems. The clinical picture of *P. vivax* malaria may be characterized by an acute and debilitating illness, with occasional reports of severe and fatal cases. These are usually associated with lung injury and respiratory distress.

Late forms of *P. vivax* malaria rarely exceed two years. Few reports of a longer period of relapse have been published in the last 10 years. With the aim of further enriching the knowledge on *P. vivax* malaria and drawing the attention of clinicians and epidemiologists to such a peculiar phenomenon, we report an unusual case of *P. vivax* malaria who presented with an initial relapse of the disease four years after the primary infection.

CASE REPORT

A 56-year-old Catholic priest was admitted to the Division of Internal Medicine of the Second University of Naples (Naples, Italy) in March 2001 because of a fever (up to 40°C) that had begun 12 days earlier and persisted despite treatment with oral antibiotics and anti-inflammatory drugs. Fever episodes occurred every 48 hours, with high peaks followed by abrupt resolution. The patient was asymptomatic between the episodes. From January to March 1997, he had been in Cameroon, where he acquired a mild form of malaria that was treated by local doctors with only chloroquine. He had not received any anti-malarial prophylaxis before going to Africa. After he returned to Italy, he had not experienced any malaria-like symptoms, had not visited any other areas endemic for malaria, and had not received any blood transfusions. His previous clinical history was otherwise unremarkable.

On presentation, he was afebrile and pale, and had tachycardia and hepatosplenomegaly. Laboratory tests showed a low platelet count, high levels of triglycerides, and mild hepatomegaly. Significant liver steatosis was found by abdominal ultrasound.

The parasitologic picture was unclear. Microscopy of peripheral blood smears showed trophozoites in dysmorphic, granulated erythrocytes, with a parasitemia of 1.5%. Some enlarged, infected erythrocytes, typical of *P. vivax* parasites, were observed, but other red blood cells showed typical *P. ovale* characteristics, such as oval shape, slightly fimbriated aspects, and coarse Schuffner’s stipplings. Such a late initial relapse was also suggestive of a *P. ovale* infection. The geographic origin of the case was compatible with the presence of both species. Thus, we decided to pursue molecular diagnosis of the parasite species.

Plasmodial DNA was extracted from the patient’s blood smears. Blood from slides (thin film) was rehydrated and scraped off with a sterile razor blade. The DNA was extracted (QIAamp DNA Blood Kit; Qiagen, Valencia, CA), purified, and concentrated (Millipore Corp., Bedford, MA). The variable regions V-7 and V-8 of the small subunit 18S rRNA were amplified by a semi-nested polymerase chain reaction (PCR) using the genus-conserved primer pairs 841 and 844. An aliquot from the product of the first PCR was used as a template in each species-specific primer reaction. Amplification products were analyzed by electrophoresis on a 3% agarose gel and staining the gel with ethidium bromide (Figure 1).

The patient was treated with chloroquine (1,200 mg base) followed by primaquine (15 mg base for 14 days). His fever resolved promptly and he remains asymptomatic after nine months of follow-up.

DISCUSSION

We observed an unusual case of *P. vivax* malaria who presented with an initial relapse four years after the primary infection. The patient recovered completely after the first episode in Cameroon, but had not been treated with primaquine. The possibility of a *de novo* infection acquired after he left Cameroon can be ruled out, since he did not subsequently visit other areas endemic for malaria, and he reported no proximity to potentially gametocyteic hosts. Furthermore, he did not take any antibiotics with anti-malarial activity (such as chloramphenicol, rifampin, and tetracyclines), pyrimethamine-sulfadoxine and co-trimoxazole, and had not received any blood transfusions. Molecular analysis identified the *Plasmodium* species responsible for this relapse.

This case provides further information on latency and relapse pattern in a *P. vivax* infection, showing a relatively short incubation period and a very long-term relapse period. The mechanisms controlling this variability remain an area of great interest, and molecular studies on specific strains of *P.*
vivax seem to be successfully addressing the problem of the presence of genetically distinct subpopulation.\(^9,10\)

Individuals returning from areas endemic for malaria to their non-endemic countries should be warned about the possibility of a late relapse of the disease. Physicians working in blood transfusion services should be aware that blood donors with asymptomatic parasitemia may be a risk of post-transfusion, blood-borne malaria,\(^11\) and that current guidelines may fail to identify potentially infected donors.\(^12\) Finally, efforts should be made to improve diagnostic efficiency and provide adequate treatment to malaria patients in endemic areas.

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References