



## Malaria in a Liver Transplant Recipient: A Case Report

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### ABSTRACT

Malaria is an exotic complication in liver transplant patients. It can be acquired either by transfusion of blood products or through the transplanted organ. Infections caused by *Plasmodium* spp are unusual in liver transplants; to date, only four cases have been reported in the literature. Herein we have presented a case of *Plasmodium vivax* in a liver transplant patient. This diagnosis must be excluded in febrile transplant patients in endemic areas, especially during the first 2 months. An epidemiological history relevant for malaria both in the donor and in the recipient must be routinely included with screening tests.

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As solid organ transplantation is becoming a therapeutic option for treatment of certain chronic conditions, a new trend of complications related to parasitic infectious diseases is appearing, such as those by *Trypanosoma cruzi*, *Strongyloides stercoralis*, *Leishmania* spp, and *Toxoplasma gondii*. Malaria is also a parasitic infection that can be acquired either by transfusion of blood products or through the transplanted organ. In liver transplants, infections caused by *Plasmodium* spp are unusual; to date, only four cases have been reported in the literature.<sup>1-4</sup>

We present a case of *P vivax* malaria in a liver transplant patient. This diagnosis must be excluded in febrile transplant patients living in endemic areas, particularly if the donor has a previous history of malaria.

### CASE REPORT

#### Donor

A 25-year-old Afro-Colombian man from Medellín, Colombia, had brain death caused by a cerebrovascular hemorrhagic and a medical history of no importance except for having lived in Antioquia, an area endemic for malaria localized in the northwest of the country. His serological studies for HIV, hepatitis B and C, cytomegalovirus (CMV), Epstein-Barr virus, herpes virus, and *T gondii* were negative.

#### Recipient

A 46-year-old woman from Bogotá, Colombia received a liver transplant due to sudden liver failure of unknown cause. Pretransplant serological studies were positive for CMV, herpes virus 1, Epstein-Barr virus, hepatitis A, and *T gondii*. During the procedure we transfused 6 U of red blood cells, 20 U of platelets, and 18 U of plasma. Immunosuppression was achieved with azathioprine, methylprednisolone, cyclosporine, and daclizumab. The graft evolution was adequate and the patient was extubated on the third day.

On the fifth day she experienced convulsions and pontine myelolysis was diagnosed by magnetic resonance imaging. Intravenous clonazepam was started with clinical improvement. On posttransplant day 15, she was discharged from the intensive care unit, although she displayed generalized weakness, a neurogenic bladder, and a urinary infection with *Pseudomonas aeruginosa* and *Enterobacter cloacae*. Meropenem was administered in accordance with the sensitivities. On posttransplant day 17 the hemoglobin began to decrease progressively over 5 days to 7 g/dL. Both external hemorrhage and gastrointestinal bleeding were excluded. On posttransplant day 22, she displayed a temperature of 39°C (102.2°F) associated with chills. A thoracoabdominal computed tomography scan, a lumbar puncture, blood cultures, and new urine cultures showed negative results. On posttransplant day 30 *Plasmodium vivax* parasite forms were detected in a peripheral blood smear we administered chloroquine for 3 days (1.5 g, total dose) and primaquine (15 mg/d) for 14 days (210 mg, total dose). Two days later, the febrile peaks disappeared, hemoglobin loss stopped, and the thick smear was negative. The patient recovered without any further complications and was discharged from the hospital on posttransplant day 45. At follow-up 1 year later the patient was asymptomatic with complete recovery neurological sequelae and no new febrile episodes.

### DISCUSSION

Although malaria has been previously described in transplant patients,<sup>5-9</sup> it is an unusual complication rarely described in liver transplant patients. Only 41 cases have been

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described, most of them in patients with kidney transplants, with only four liver transplants. According to some authors, the prognosis of malaria is worse in liver transplant recipients than in kidney transplant recipients, because it is possible that the decrease in the amount of active transmitted *Plasmodium* sp directly correlates with the time course of cold preservation, which is longer for the kidney (24 to 48 hours) than for the liver (<12 hours).<sup>4</sup> Previously, in South America a case of infection by *P vivax*, had been described, but the transplanted organ was the kidney.<sup>10</sup>

The most common forms of transmission of *Plasmodium* spp are through the bite of *Anopheles* spp mosquitoes or by transfusion of blood products. In some cases parasitized red blood cells within the transplanted organ cause the infection. Additionally, *P ovale* and *P vivax* can be transmitted through the transplanted liver, due to their persistence as hypnozoites within hepatocytes for months or even years. Stress and immunosuppression associated with the transplantation can facilitate the occurrence of a relapse. In the reported malariae infections associated with transplants, it has not always been possible to describe with certainty the form of transmission.<sup>2,3</sup>

Although malaria is endemic in Colombia, transmission does not occur at altitudes beyond 1300 m above sea level. Thus, major cities like Bogotá, at an altitude of 2600 m, are malaria-free. The liver recipient patient had not lived nor traveled to a malaria-endemic area. Since there is no transmission in Bogotá where the transplant was performed, acquisition via a mosquito bite is excluded. Although it is possible that the blood transfusions during the surgical procedure may have been the source of the infection, we consider this unlikely since in our blood bank all units are routinely screened for the presence of the parasite, due to the high risk of donors having visited malaria endemic areas within the country and because the records of all donors of blood, plasma, or platelets were reviewed; None of them came from nor had visited any malaria endemic areas during the year before donation. Generally, *P vivax* infections due to infected blood cells have a longer incubation period (20 days)<sup>11</sup> because exoerythrocytic schizogony in the liver is bypassed. In this patient malaria symptoms started at the end of the third week.

Although the organ donor did not have a clinical history of malaria, he did have a record of traveling to malaria endemic areas. Unfortunately, liver biopsy or tests for the detection of *Plasmodium* spp in blood were not performed on the donor; therefore, it was not possible to determine if he had a subclinical infection or if hypnozoites were present in the grafted organ.

In this case, as in those of infections by *P vivax* previously described, the most relevant symptom was the presence of fever. In cases caused by *P falciparum*, it has been possible to find diverse clinical manifestations related to severe malaria.<sup>1-4</sup> Other laboratory findings described previously (liver function test deterioration) were not observed. Possibly because diagnosis was done at the early onset of

symptoms, neither the clinical manifestations nor the laboratory test alterations were severe.

We recommend, particularly in endemic countries, that an epidemiological history relevant for malaria both in the donor and in the recipient be routinely included, besides the search for *Plasmodium* spp in the donor, because it is not always possible to obtain a clear epidemiological history and the screening tests (thick and thin blood smears) are easy to perform, fast, and cheap. However, blood tests do not exclude the presence of hypnozoites, only of the blood forms. In nonendemic countries, one must evaluate the cost-benefit ratio of performing serological tests when the information about the donor is not clear or when there is a suspicion of exposure to the parasite.

Because of the possibility of relapses, due to *P vivax* and *P ovale*, hypnozoites, and of false-positive results with the screening tests because of the low number of parasites in subclinical infections, it is necessary to consider malaria as one of the differential diagnoses in the posttransplant febrile patient, especially during the first 2 months. Treatment is recommended at the usual dosage: chloroquine plus primaquine for *P vivax* and *P ovale*. In *P malariae* infections chloroquine should be administered, but infections by *P falciparum* must be considered as severe malaria. Quinine should be started, despite its adverse effects described elsewhere.<sup>2</sup>

In general, the prognosis is worse in infections caused by *P falciparum*, because of the known virulence of this species. Another factor associated with a poor prognosis is the nature of the transplanted organ; patients with kidney transplants have a better evolution than those with heart or liver transplants. This observation has been reported in multiple transplants from the same donor where the outcome of malaria was more severe in those receiving the liver or the heart.<sup>4</sup> In this case, given that the infection was caused by *P vivax* and that adequate treatment was prescribed, the outcome was satisfactory with complete recovery of the infectious process.

In conclusion, although transmission of malaria through organ transplantation is uncommon, screening of both donor and recipients must be considered. In endemic countries, malaria is to be suspected in patients presenting fever, especially during the first 2 months posttransplant.

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