INTRODUCTION

According to World Health Organization (WHO), approximately 40% of the world's population, mostly those living in the world's poorest countries, is at risk of malaria. The disease was once more widespread but it was successfully eliminated from many countries with temperate climates during the mid 20th century. Today malaria is found throughout the tropical and sub-tropical regions of the world and causes more than 300 million acute illnesses and at least one million deaths annually,\(^1,^2\) including Latin America.

This is in part due to the development of unacceptable levels of resistance to one drug after another in the malaria parasites, especially *Plasmodium falciparum.*\(^3\) Additionally, many insecticides are no longer useful against mosquitoes transmitting the disease.\(^4,^5\) All this represents a public health threat, even in those areas where malaria is not endemic, or where *P. falciparum* is not present; due to migration, travels and other people mobilizations, which could spread resistant strains.

We report an unusual case seen in a gold mine traveler from Irapa, Sucre state, Venezuela (where *P. vivax* is endemic, but not *P. falciparum*),\(^6\) returning from El Manteco, Bolivar state, Venezuela; initially diagnosed as *Plasmodium vivax* malaria, which after a detailed epidemiological, clinical and paraclinical evaluations was diagnosed as imported severe malaria due to *P. falciparum* with recrudescence and therapeutic failure to chloroquine, successfully treated with intravenous quinine.
CASE REPORT

In April 2003, a 24-year-old male presented with complaints of fever, chills, and malaise for 4 days. He was initially seen by a local practitioner in the Irapa District Hospital (Sucre state, northeastern Venezuela) after returning from a 2-month trip to gold mines in El Manteco (Bolivar state, southern Venezuela) (Figure 1) (a zone with high incidence of *Plasmodium falciparum* malaria); being initially diagnosed as a presumptive *Plasmodium vivax* malaria case. He was admitted and treated with chloroquine (CQ) (25 mg/kg/3 days po) and primaquine (PQ) (0.25 mg/kg/14 days po) (this is the national standard treatment policy for *P. vivax* infection). Four days after, paraclinical evaluations including thick and thin blood smears were performed. At this moment non significant additional alterations were seen at those tests, except for mild thrombocytopenia (92,000 platelets/mm$^3$). Hospital's laboratory initial blood smears evaluation indicated *P. vivax* (no stages or parasitemia were reported) (Figure 2). Patient continues with CQ and PQ. Two days later patient presented paleness (but Hb still was normal, 12.9 g/dL) moderate hepatomegaly and a lower urinary tract infection treated with ciprofloxacin. At this time thick and thin blood smears were taken by our Malariology Office revealing a monoinfection due to *P. falciparum* (showing various parasite stages and a load of 4,200 parasites/µL) (Figure 3). As part of our National Malaria Policy, all positive slides and 10% of negative, are re-assessed by a second regional reference microscopist and by a third national reference microscopist to confirm or rule-out the diagnosis. Oral quinine was recommended by us, but the patient's treatment was not changed. He was discharged by the hospital after a week with apparent clinical success and negative slides. Two weeks later patient returned to the hospital again with complaints of fever, chills, and malaise, with clinical and paraclinical evaluations revealing anemia, hypoglycemia, renal failure and moderated increase in hepatic enzymes (AST and ALT). He was admitted again and our Malariology Office was consulted to evaluate this case in detail. Blood samples for paraclinical evaluations were taken again; thick and thin blood smears revealed a significant number of gametocytes of *Plasmodium falciparum* (load of 18,600 parasites/µL) (Figure 4). His family was also evaluated by us, resulting all the members negative for *Plasmodium spp*. No vectors were identified in their peridomical area, although we found impregnated bed nets in the house. We treated the patient with quinine, initial intravenous infusion of 20 mg/kg in first 4 hours, after that continuing with 10 mg/kg (in 2 hrs) q8h 3 days. Electrocardiograms and biochemical tests were regularly done. Given clinical and paraclinical improvements, patient was switched to oral quinine (10 mg/kg q8h 7 days) and discharged at 4th day. Further slides were all negative, being followed for an additional month. Patient indicates us that in the gold mine 9 workers were febrile at the moment of his departure. No further information of those individuals was obtained. After this case occurred, the hospital's laboratory personnel was re-trained in malaria microscopy diagnosis (considering an acceptable diagnostic concordance index >85% in 100 reference slides).
DISCUSSION

Imported malaria has been an increasing problem in Venezuela, in endemic and non-endemic zones in the last 2 decades. Different possible reasons exist for this increase, first the increase in the number of travelers to tropical areas, as well as a growing number of people migrating temporarily to malaria-endemic zones, even from an endemic area for certain species to others with different ones. The risk for tourism and other type of travelers is evident and should be a concern for physicians who give pretravel advice or evaluate a returning traveler with fever.

As in this case, where a patient with malaria was seen in an endemic zone, but only for *Plasmodium vivax*, a detailed epidemiological investigation should be done, because if patient was previously in a different endemic zone, where other parasites are endemic, clinical presentations could differ, as happen in this case where patient comes back from a *P. falciparum* endemic zone; where recent studies have demonstrated chloroquine-resistance in circulating strains, even for quinine. For this reason, in 2004, national policy changed the treatment of *P. falciparum* infection to mefloquine plus artesunate as primary choice therapeutic scheme.

In the last decades, *P. falciparum* has become widely resistant to chloroquine, and resistance to pyrimethamine-sulfadoxine and mefloquine is increasing in some parts of the world and recrudescence related to this, is commonly described. In other hand, reports of deaths associated with inadequate malaria prophylaxis and therapy in US and Canadian travelers further underscore the importance of adequate use of antimalarial drugs in these individuals, which should be taken into account for the area of travel and the parasite resistance patterns.

Cases as the seen by us, increases the need for additional diagnostic tools in endemic zones, as rapid diagnostic tests, to help in the differentiation of *Plasmodium* species, and enhance the importance of antimalarial susceptibility studies in such areas. Epidemiological surveillance on all kind of travelers should be done in endemic (for domestic and imported cases) and non endemic zones where cases with suspicion of malaria should be investigated regarding travel to risky areas.

REFERENCES


Figure 1. Map of Venezuela showing Irapa, Sucre state (place where patient lives) (10°34’10.64” N, 62°34’57.78” W) and El Manteco, Bolivar state (where he acquired the *P. falciparum* infection) (7°21’06.06” N, 62°32’01.40” W).

Figure 2. First peripheral thick and thin blood smears misdiagnosed as *Plasmodium vivax* showing trophozoite stages of *Plasmodium falciparum*. (Giemsa, ×1,000).
**Figure 3.** Second peripheral blood smears also showing various stages of *Plasmodium falciparum* (load of 4,200 parasites/µL). (Giemsa, ×1,000).

**Figure 4.** Third peripheral blood smears revealing various stages of *Plasmodium falciparum* including the gametocyte stage (load 18,600 parasites/µL). (Giemsa, ×1,000).