



**Case Report**

# A Case Report of Transfusion-Transmitted *Plasmodium malariae* in a Non-endemic Country

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**Abstract:** A 57-year-old woman with chronic hemodialysis for 16 years, who presented at the Avicenna hospital in Marrakesh with fever and hepatosplenomegaly. Three months earlier, he received 2 units of packed red blood cells. Laboratory studies indicated hemolytic anemia (hemoglobin, 9.5 mg/dl) and thrombocytopenia (platelet count, 105000/mm<sup>2</sup>). Malaria smear was consistent with *Plasmodium malariae*. The level of parasitemia was 1% (10 per 1000 erythrocytes). As a result, the patient's antimalarial therapy was continued for a total of 7 days followed by mefloquine for 7 days once the blood smear results revealed *P. malariae* infection. Evolution was favorable after antimalarial therapy with the disappearance of fever and hepatosplenomegaly. The control of parasitaemia remained negative until 28 days. This is the first case of hepatosplenomegaly secondary to blood transfusion related *Plasmodium malariae* infection in a non-endemic country in chronic hemodialysis.

**Keywords:** Chronic Hemodialysis, Malaria Transfusion, *Plasmodium malariae*

## 1. Introduction

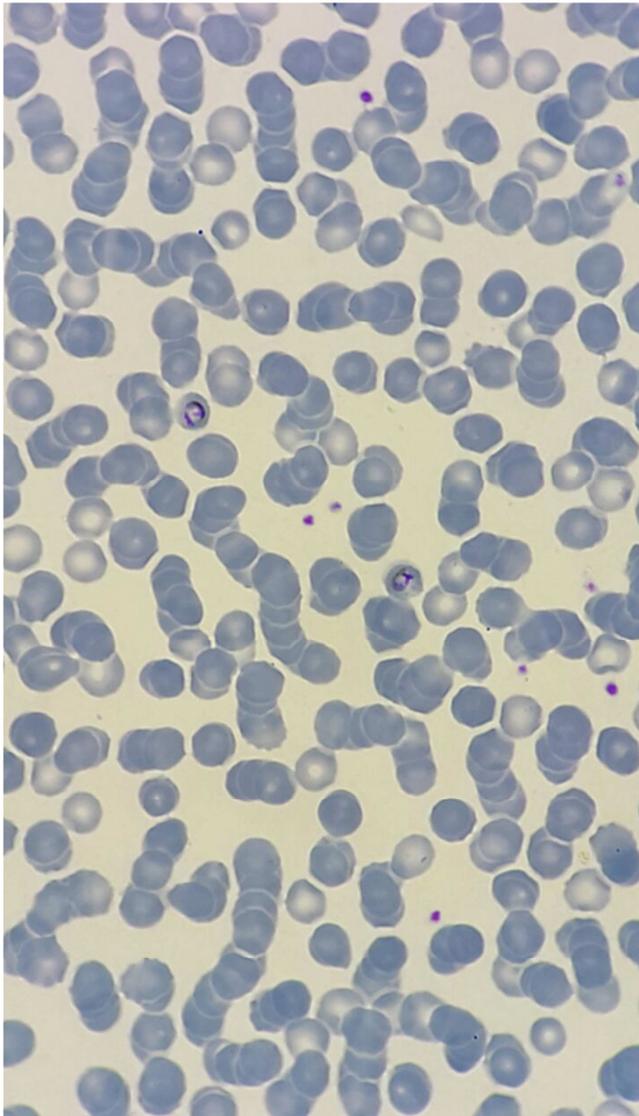
Malaria is a protozoan infection that is almost always transmitted by the bite of the female Anopheles mosquito. Currently the world's first endemic parasite, malaria remains a major public health problem. It is responsible each year for 300 to 500 million acute infections, about 90% of which occur in sub-Saharan Africa. In rare cases, the infection is acquired by the direct inoculation of infected blood such as during transfusion. The first case of transfusion-transmitted malaria (TTM) was reported in 1911 [1]. In non endemic regions, the reported incidence of transfusion-transmitted malaria ranges from 0 to 2 cases per million transfusions, most of which are caused by *Plasmodium falciparum* [2]. The authors report the case of a patient with *Plasmodium malariae* in non endemic whose condition improved after exchange transfusion. And

we discuss the efficiency of prophylactic measures.

## 2. Case Report

A 57-year-old Moroccan woman presented with 3 days of fever and hepatosplenomegaly. This is a patient with chronic renal failure treated by dialysis for 16 years. Known hypertensive depuis 6 years as a calcium channel blocker and beta-blocker 10 mg 50 mg. Known carrier of a goiter with hypothyroidism treated with levothyroxine sodium 75 mcg for a year. She was stuporous with a temperature of 101.5°F. Three months earlier, he received 2 units of packed red blood cells. Laboratory studies indicated hemolytic anemia (hemoglobin, 9.5 mg/dl) and thrombocytopenia (platelet count, 105000/mm<sup>2</sup>). Malaria smear was consistent with *Plasmodium malariae* (figure 1). The level of parasitemia was

1% (10 per 1000 erythrocytes). As a result, the patient's antimalarial therapy was continued for a total of 7 days followed by mefloquine for 7 days once the blood smear results revealed *P. malariae* infection. The patient had never traveled to malaria-endemic areas. Further investigation revealed that patient's blood donors was an 37-year-old man from Morocco who claimed he had visited Equatorial Guinea 4 years before donating blood, but the time was actually 9 months. Evolution was favorable after antimalarial therapy with the disappearance of fever and hepatosplenomegaly. The control of parasitaemia remained negative until 28 days.



**Figure 1.** Two young trophozoites of *Plasmodium malariae* detected on the peripheral smear

### 3. Discussion

Malaria is a real threat to blood transfusion. Plasmodium species can survive for at least 3 weeks in refrigerated blood. Depending on the number of parasites in the inoculum, symptoms may appear days or weeks after transfusion. The index of malaria infection following a blood transfusion varies

greatly from region to region. In non-endemic countries, it varies from 0 to 2 cases per million donations. In a recent and complete review of transfusion malaria in the United States, the incidence during the period 1993-1998 varied from 0 to 0.18 cases per million units transfused [2]. A similar impact can be deduced for Australia with the last case in 1991 [3]. On the other hand, the incidence in endemic countries is likely to exceed 50 cases per million units of blood. 4 recent US TTM reports, 5 in Canada, 6 Switzerland, 7 and the United Kingdom (Dr A. Cuisine, written communication, 23 January 2004) confirm a continuing threat of transfusion in non-endemic countries as a consequence of import malaria [1].

Although asymptomatic malaria is relatively common in endemic countries, *P. malariae* infections in nonimmune travelers are very rare [3]. In the United States (US), travelers in endemic areas are excluded as blood donors for 1 year and those who live in endemic areas are excluded from 3 years [4]. Transmitted malaria remains rare in the United States. The occurrence rate is estimated at 0.25 per million units of blood collected and the incidence reported by the Centers for Disease Control and Prevention (CDC) is one to three cases per year [4, 5]. Unlike in European countries, legislation in the United States is based solely on the exclusion of potentially infected donors identified during the medical interview in accordance with guidelines established by the American Association of Blood Banks and FDA (Food and Drug Administration) [6, 7]. There are no FDA-approved laboratory tests for malaria [8]. In France, donors are postponed for 4 months after returning from endemic areas. Between 4 months and 3 years, the donor is accepted if the serological test for anti-plasmodium antibodies by indirect immunofluorescence is negative [9]. Otherwise, the donor is definitely excluded from the donation of blood [10, 11]. In the present case, the donor should have been dismissed, since he visited Equatorial Guinea two years before the donation of blood.

There is no universal blood test used in blood donors for the detection of asymptomatic forms of malaria. The current strategy used in most countries, including Morocco, is based on the exclusion of potentially exposed donors after a thorough history [12, 13].

For the prevention of transfusion malaria, some authors proposed combining screening of malaria antibodies with antigen detection as a means of increasing the sensitivity of any control performed to better manage the transfusion risk [8, 14, 15]. To this extent, we have Elisa tests for both antibody and antigen research, it would be desirable to combine the two tests (Elisa Malaria Antibody test and Elisa Malaria Antigen test) with a sensitivity of 98.8% [16, 17]

Only expensive methods, such as immunofluorescence (IFA) serology and real-time PCR analysis, can detect asymptomatic *P. malariae* infection in the donor [18]. Post-transfusion malaria cases may continue to occur in non-endemic areas, regardless of the safety measures currently being taken by the blood transfusion centers [19, 20, 21]. Laboratory screening by immunological and molecular techniques (indirect immunofluorescence, PCR) remains a

possible option to reduce it [22].

Photochemical treatments of inactivation of pathogens by amotosalen hydrochloride + UVA or riboflavin + UV are active on plasma as well as on platelet products contributing to the drastic reduction of the parasitic risk associated with malaria. These techniques use a photosensitive molecule and electromagnetic radiation. Under the action of radiation, the molecule is transformed, by a photochemical reaction, into a photo-product which acts irreversibly on the nucleic acids [13].

Amotosalen-HCl (S59) is a synthetic molecule of the psoralen family. These photoactivable compounds of vegetable origin form covalent bonds with the pyrimidine bases of the nucleic acids when exposed to UVA (320-400 nm) and thus block the replication of pathogens. Because of the activation of amotosalen-HCl by UVA radiation, which is absorbed by hemoglobin, this technique can not be applied to red blood cell concentrates (RBCs). Riboflavin (Vitamin B2) is a molecule that binds to nucleic acids by intercalation. Ultraviolet radiation generates photolysis of the macromolecular complex by electron transfer and guanine oxidation reaction, nucleic acid strand breakage, and covalent bridge formation between the broken nucleic acids [19].

A number of laboratories are currently working on the subject of inactivation of pathogens in RBCs. The difficulties encountered are mainly due to the absorption spectrum of hemoglobin and the viscosity of the red blood cells. Currently, most teams have abandoned techniques using light and are moving towards targeted treatments on the alteration of nucleic acids. FRALE (S 303) or inactin (PEN 110) substances have been tested to inactivate pathogens in RBCs. The PEN 110 requires no light to be activated. After treatment, this process is followed by washing the red blood cells to remove the residual components. The FRALE (Frangible anchor linker effectors) is activated by a pH change [19].

Another alternative is to destroy malaria in the blood bag. The introduction of sulfadoxine-pyrimethamine into the blood bag is a means of prevention recommended by some authors. The effectiveness of this method was evaluated in 2005 on 90 donations of blood under the usual conditions of collection, analysis and conservation. The 180 mg / L dose, usually well tolerated in patients, was highly lethal to parasites (99% destruction within 24 hours of storage), without altering the blood components. In another study, quinine showed similar efficacy [13, 19, 21].

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The risk of malaria remains the most important and it is difficult to hope that it will be reduced in an era of

multiplication of international and intercontinental exchanges, multiplication of parasite resistances and geographical extension of vectors with global warming.

Blood transfusion centers will continue to be faced with a dilemma: eliminating the risk of transfusion malaria while ensuring a high-quality blood donation, but the current regulatory measures are a compromise and can not totally eliminate a risk of malaria transfusion [8]. At present, concomitant detection antibodies and malarial antigens by techniques adapted to blood transfusion centers should increase blood transfusion safety.

## 4. Conclusion

The risk of malaria remains the most important and it is difficult to hope that it will be reduced in an era of multiplication of international and intercontinental exchanges, multiplication of parasite resistances and geographical extension of vectors with global warming. Transfusion malaria constitutes a preventive pathogen-inactivation strategy for RBCs and whole blood in the future, which would render a priori unnecessary malaria screening and malaria chemoprophylaxis in the recipient.

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