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CASO CLÍNICO

Parasitemia with *plasmodium falciparum* in a patient after cardiac surgery in a non-endemic country

Summary

We present a case-report of a febrile patient after cardiac surgery; the patient had no history of travel to areas where malaria is endemic. After several studies and due to the background of blood transfusion, blood smear, serology and PCR were done and revealed the presence of *P. falciparum*; 14 donors were associated with the transfusions; none had travelled to malaria areas; serology, PCR and chromatography were negative in 13 (1 refused testing); no cases of post-transfusion malaria were reported in the region. Transmission of malaria infection in the reported case remains unknown but might be linked to blood transfusion, although malaria due to establishment of *Plasmodium sp.* in indigenous or aircraft-travelling mosquito remains a possibility. Increases in international exchanges from endemic areas enhance the possibility that blood donors might have been in contact with malaria. Accurate histories of potential exposure to blood transfusions are necessary in the work-up of febrile patients.
Key words: Blood transfusion. Fever. Malaria. *Plasmodium*.

Resumen

Se presenta el caso de un paciente sin antecedente de viajes internacionales recientes que presentó fiebre tras cirugía cardiaca. Tras varias pruebas complementarias y dado el antecedente transfusional se realizaron una tinción de Giemsa de sangre periférica, serología y PCR que fueron positivas para *P. falciparum*. La investigación de los 14 donantes fue negativa (no antecedente de estancia en zona endémica para malaria; serología, PCR y cromatografía negativas en 13 –un donante se negó a más estudios); no se comunicaron otros casos de malaria post-transfusional en la región. Aunque no se pudo confirmar el origen de la infección podría estar relacionada con la transfusión, sin poder descartar transmisión local en zona no endémica por mosquitos autóctonos o "malaria de los aeropuertos". Los movimientos migratorios aumentan el riesgo de exposición a *Plasmodium spp.* entre donantes de sangre. En el estudio de un paciente con fiebre se debe valorar el antecedente de transfusión e incluir la malaria en el diagnóstico diferencial.
Palabras clave: Fiebre. Malaria. *Plasmodium*. Transfusión sanguínea.

Introduction

Malaria is one of the most important infectious diseases in the world, causing hundreds of millions of illnesses and an estimated 1 million deaths each year[1]. It is widely distributed in tropical and subtropical zones and it is transmitted by the bite of an infected female anopheline mosquito; the infecting agent is the sporozoite, which is in the mosquito's saliva[2]. Infection may also be acquired transplacentally and by blood transfusion or inoculation, via the blood stages of the parasite (trophozoites and schizontes)[3-5]. We describe the case of a patient who developed fever 15 days after coronary artery bypass surgery; he had no history of travel to areas where malaria is endemic, he had not recently visited an airport and he had not had close contact with a person with malaria.

Case report

A 69-year old Argentinean man presented in December 2006 to our hospital (Hospital Universitario Virgen de la Arrixaca, in Murcia) 15 days after cardiac revascularisation surgery. He was from Mendoza (Andes Region). He never travelled to other areas in Argentina or South America. He flied to Spain one year before admission (from Mendoza to Chile, then to Rio de Janeiro (Brazil) and finally to Madrid and Murcia). He did not travel to any other country and he did not go to any airport. His past medical history was unremarkable. One month before being admitted a diagnosis of acute coronary syndrome was made and coronary artery bypass surgery (CABS) was required; plasma, platelets and red cells transfusion were needed (2, 10 and 2 units respectively). Fifteen days later, he complained of fever, shivering and malaise. Physical examination revealed a mildly-ill-appearing man with a temperature of 39ºC but otherwise not remarkable findings. Laboratory data revealed mild pancytopenia. Blood and urine cultures, hepatitis B, C and HIV viral load and serology for these viruses were negative. Light microscopic examination of Giemsa-stained blood smears (Figure 1) detected *Plasmodium falciparum* gametocytes. The rapid malaria diagnostic test (NOW® ITC Malaria Test; Binax, INC., Portland, ME) was strongly positive detecting HRPII antigen (*P. falciparum* specific) and mild-positive for the common *Plasmodium* sp. antigen (Figure 2). Serology (IFAT) and polymerase chain reaction (PCR) were also positive for *P. falciparum.* The patient was treated with quinine sulphate and doxycycline. Fever and malaise disappeared and pancytopenia improved after 2 days. At follow-up, two months later, the patient was fully recovered and another microscopic examination and PCR were negative. An investigation of all 14 blood donors was done within 2-3 months after blood donation; they had no history of travel to areas where malaria is endemic, they were not born in a malaria endemic country, they had not recently visited an airport and they had not had close contact with a person with malaria; *Plasmodium* sp. serology PCR and chromatography were negative in 13 donors; one donor refused to be tested. An investigation of all patients operated at the same surgery-room the day that our patient was operated was also negative for malaria. Another patient received red-cells from the donor who refused to be tested but no other case of post-transfusion malaria was reported in the region.

Discussion

Four parasite species cause human malaria. The important difference of *P. falciparum* is its capacity to cause severe or complicated malaria, thus the importance of suspecting malaria in patients with fever and epidemiological background of visiting countries with epidemic or endemic malaria and also in cases of fever after blood transfusion.

The specific diagnosis of malaria is made by examining the blood by making a film (Giemsa stained smears), which has been the reference standard for more than a century. However, it requires a sufficient level of expertise in microscopic diagnosis, which can be challenging parti-

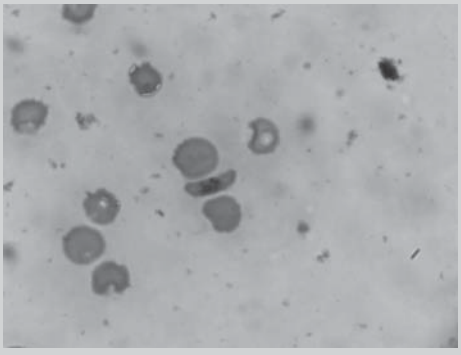

Figure 1.

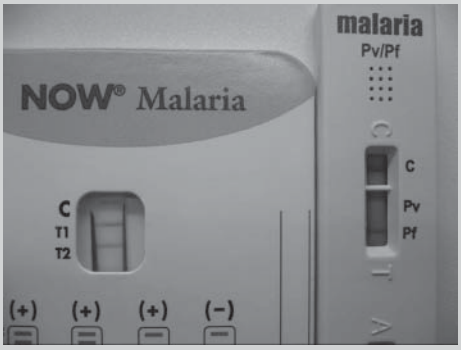

Figure 2.

cularly in non-endemic countries and non-reference laboratories. Many new rapid techniques for identifying malaria parasites are being developed[6]. NOW® ITC Malaria Test compared with PCR, shows a sensitivity of 95% for the detection of *P. falciparum* malaria and 84% for non-*P. falciparum,* with a specificity of 99%, representing a very useful technique for the diagnosis of malaria in febrile patients. Serodiagnosis of malaria is of no use for diagnosis of the acute attack. The most frequently used technique is the indirect fluorescent antibody test (IFAT). Its main use is in surveys as an approximate measure of exposure of a population to malaria but antibody detection is also been used in blood bank screening[7].

Our patient had been previously treated with several antibiotics. Many antibacterial drugs inhibit growth of malaria parasites. He had received ciprofloxacin and clindamycin and both antibiotics had shown effects on *P. falciparum.* This might be the reason for a blood smear only revealing gametocytes[8].

All *Plasmodium* species have existed in the Mediterranean area since the prehistoric times[9]. They were still widely prevalent until the beginning of the fifties, but since that time all of malaria cases are either imported or post transfusional, except in certain areas of Greece and Turkey, where *P. vivax* continues to cause sporadic epidemics[10].

Transfusion-transmitted malaria was first reported in 1911[11]. Although malaria is still a blood transmissible disease, its frequency is very low in non endemic countries[12]. But in relation to international travel and immigration from tropical areas to western countries, cases of imported malaria are increasing[1,13] and a higher number of blood donors are at risk of exposure to malaria. In regard to prevention, regulations aiming at excluding potentially contaminated donors have been implemented all along Europe[14] and North America as inhabitants of malaria endemic areas can withstand a low number of parasites without any symptoms and thus there is a risk that potential donors coming from these areas carry a significant amount of parasites that can be transmitted through transfusion. Besides, all plasmodia species can survive for at least 3 weeks in refrigerated blood and any blood component containing red cells can harbour viable parasites[15]. The real incidence of transfusion-transmitted malaria is unknown, especially in endemic areas, where the rate is likely to be more than 50 cases per million donations whereas in non-endemic countries the incidence ranges between 0-2 cases per million donations.

In non-endemic countries there are several aspects to be assessed concerning regulation of blood donors. In Spain, as in other non-endemic countries, the malaria screening mechanism is a questionnaire that should be completed by the potential blood donor and all risk cases should be excluded as donors[16]. Questions are aimed at identifying the geographical location, the length of time in any malaria area, the time elapsed since last being in an endemic area and any previous history of the disease[17]. Donors who disclose a risk of malaria are excluded but the increase of visitors to malaria areas and the increasing immigration in a time when blood products requirements continually increase bring a main drawback to this strategy: the unnecessary wastage of blood donors. For this reason, western countries have begun to elaborate new strategies to assist in identifying infective donors[10-11]. The question might be under which circumstances serological test for malaria should be requested, the policy employed in case of seropositivity and the cost of screening. The usual microbiological method for screening of donors is the detection of *Plasmodium* antibodies by IFAT or by EIA assays[18]. In France, donors are deferred for 4 months if they have returned from a malaria endemic area and then tested by an immunofluorescence assay and re-entered as eligible blood donors if negative. Similar approaches have been implemented in other European countries in an aim to elaborate policies addressed both to blood availability and blood safety[9-11,19].

In conclusion, increases in international exchanges and migration from endemic areas enhance the possibility that blood donors might have been in contact with malaria parasites. Revision of transfusion policies in non-endemic areas is mandatory[10-13] as the goal of avoiding blood transmitted malaria can be achieved only by a combination of efforts: donor education, donor selection and testing of selected blood donations[20]. Notification of cases of malaria to Public Health Authorities is also important. To many clinicians the concern about transfusion-transmitted hepatitis and HIV has overshadowed the fact that other diseases spread by transfusion of blood components[21]. Accurate histories of potential exposure to blood transfusions are necessary in the work-up of patients with fever. Although in our case a direct relation of malaria to transfusion could not be established, there was not other epidemiological explanation for the infection. Although malaria due to the establishment of *Plasmodium* sp. in an indigenous or aircraft-travelling mosquito remains a possibility, this explanation seems quite improbable and no other cases of malaria of "unknown-origin" transmission have been reported in our region.

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