Transfusion-transmitted malaria in a kidney transplant recipient

How safe is our blood transfusion?

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ABSTRACT

مريض في الواحدة والخمسين(٥١) من العمر أجريت له عملية زراعة كلى في إيران في شهر حزيران ٢٠٠١، أصيب بمرض حمى الملاريا – بلازميديوم فالسيباروم. كان المريض يتعاطى عقاقير MMF ، Cyclosporine A و Prednisone. في شهر أغسطس٢٠٠٥ تعرض المريض إلى نزيف معوي مما أدى إلى إعطائه عدة وحدات من الدم و مشتقاته في أحد المستشفيات المحلية. بعد شهرين تم تحويله إلى مركز الظهران الصحي لما كان يعانيه من ارتفاع في درجة الحرارة، آلام في البطن، حرقان في البول و إرهاق شديد . و قد تم التعرف على جرثومة الملاريا من نوع falciparum في ٧٠٪ من الخلايا الحمراء، و عليه تم علاجه بنجاح بعقاري الـ quinidine و doxycycline إضافة إلى نقل الدم. أجريت تحريات لتحديد مصدر الإصابة بحمى الملاريا و الذي نرجح أن يكون سببه نقل الدم الذي تعرض له المريض في المستشفى السابق. تم في هذا المقال مناقشة الأساليب التي تؤدي إلى تقليص احتمال الإصابة بحمى الملاريا .

A 51-year-old male patient with living, unrelated kidney transplantation in Iran in June 2001, developed *Plasmodium falciparum (P. falciparum)* infection. He was maintained on cyclosporine A, mycophenolate mofetil, and prednisone. In August 2005, he was admitted to a medical facility in the local community with upper gastrointestinal bleeding, and received several units of blood and blood products. Two months later, he was referred to Dhahran Health Center, and admitted with fever, abdominal pain, dysuria, and severe fatigue. *Plasmodium falciparum* with a parasitemia of 70% was detected in the peripheral smear. He was treated with intravenous quinidine gluconate and oral doxycycline, in addition to blood transfusion, and he responded well to the treatment. An investigation was carried out to try to find the source of malaria infection, which is believed to be the blood or blood products that he received during his initial acute illness. Measures to minimize transfusion related malaria are discussed.

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The eastern region of the Kingdom of Saudi Arabia is believed to be free from indigenous transmission of malaria.[1-3] The majority of reported cases were imported, and linked to travel to endemic areas.[2,3] In the Kingdom, the incidence of transfusion-related malaria is not known. A few cases were described in 1992 and 1995.[4,5] In the United States, the incidence rate of transfusion-associated malaria ranged from 0-1.37 cases per million units transfused in 1965-1970; and from 0-0.18 cases per million units transfused in 1993-1998.[6] We describe a renal transplant recipient who developed transfusion malaria. Although malaria is infectious, the low immunity of the patient may have played a major role in the severe clinical presentation. Strategies to improve screening tests, and minimize transfusion related malaria are discussed.

Case Report. A 51-year-old male patient with a longstanding history of hypertension and type II diabetes mellitus, complicated by severe diabetic neuropathy and nephropathy. He developed end-stage

renal disease and underwent living, unrelated kidney transplantation in Iran in June 2001. He had been maintained on cyclosporine A, mycophenolate mofetil (MMF), and prednisone. He developed chronic allograft nephropathy and serum creatinine stabilized at 2 mg/dl. After kidney transplantation, he never traveled outside the eastern region of Saudi Arabia. There was no prior travel to Africa, southern Saudi Arabia, or any other malaria-endemic areas. Over the past several months prior to his presentation to Dhahran Health Center (DHC) he had a few episodes of *Escherichia coli* urinary tract infection requiring hospitalization. In August 2005, he was admitted to a medical facility in the local community (the referring hospital) with a bleeding duodenal ulcer for which, he received several units of blood and blood products. Three days prior to transfer to DHC, he was admitted to his local community hospital with fever, abdominal pain, dysuria, and severe fatigue. He had severe anemia, and required 3 units of blood transfusion. A gastroscopy showed no evidence of active bleeding. He was transferred to DHC in January 2006, with sepsis and severe anemia for investigation. Systemic review was significant for a 2 month history of severe fatigue, intermittent fever, sweats, poor appetite, and weight loss.

Physical examination revealed a chronically sick looking, middle aged male. He was afebrile with a blood pressure of 111/65 mm/Hg, heart rate was 82/minute, respiration 20/minute, and his weight was 70 kilograms. The head examination was significant for pallor and jaundice. The neck was supple with no lymphadenopathy. The lungs and heart exam was unremarkable. The abdomen was soft with no tenderness. There was splenomegaly of 2 fingers below the left costal margin, but no hepatomegaly. Laboratory data revealed glucose: 89 mg/dl, urea: 104 mg/dl, creatinine: 4.1 mg/dl, sodium: 136 meq/L, potassium: 5.1 meq/L, chloride: 110 meq/L, total CO_2: 12 meq/L, and an anion gap of 14. White blood cells count was 15,500/mm^3, hemoglobin: 7.1 gm/dl, and platelet count: 147,000 mm^3. The peripheral blood smear showed ring forms, trophozoites, and banana-shaped gametocytes of *Plasmodium falciparum (P. falciparum)*, with a parasitemia of 70% of all red blood cells (RBC) (**Figure 1**). He was treated with intravenous quinidine gluconate and oral doxycycline, in addition to blood transfusion. He responded well to the treatment, and his parasitemia decreased quickly to 5% 4 days after the initiation of treatment, and to 0.3% 10 days later. The malarial smear showed only gametocytes up to 5 weeks after the initiation of treatment. The MMF was temporarily withheld for 3 weeks, and his allograft function remained stable throughout hospitalization. Upon follow-up, hemoglobin remained stable at 10 gm/dl, and he had no further symptoms. An investigation was carried out to find the source of the

malaria infection. It was possibly due to the blood or the blood products that he received at the referring hospital. Apparently the patient received several units of packed RBCs and fresh frozen plasma from a total of 14 donors, the majority of whom were expatriates originating from different countries including Egypt, Sudan, India, Pakistan, and Bangladesh. Some of them were traced and screened, but several others could not be reached as they had left the country permanently.

Discussion. The patient developed malaria with *P. falciparum* while residing in a non-malaria area. The eastern region of Saudi Arabia was believed to be free from indigenous transmission of malaria.[1,2] The majority of reported cases were imported, and linked to travel to endemic areas.[2,3] Since his kidney transplantation 5 years earlier, our patient never traveled outside the Eastern Province of Saudi Arabia. Although the source of infection could not be identified with certainty, we believe donated blood or blood products were the source of infection. He received a large quantity of blood and blood products from a total of 14 donors. None of the other patients who received blood from the same donors experienced malaria clinically. The immunocompromised state of the current patient may have played a major role in the development of malaria, allowing a small infective dose to cause severe disease. Most of the donors were expatriates, and originated from countries where malaria is still epidemic such as Sudan and the Indian subcontinent. The donors were traced, and the available ones were screened by doing thick and thin malarial smears at the Ministry of Health regional Laboratory in Dammam, Saudi Arabia. However, a few had left the country permanently, and therefore could not be reached for screening. In previous reports from Saudi Arabia, 12 malaria cases in Riyadh were found
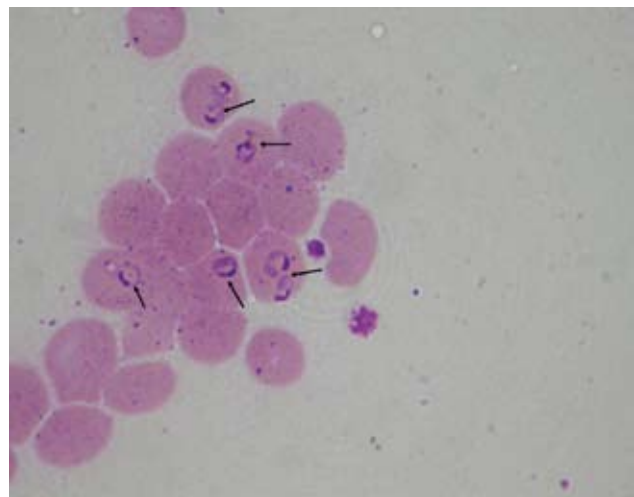
Figure 1 - Histopathological result showing 70% red blood cells infected with *Plasmodium falciparum*, and ring forms are seen.

to be post-blood transfusion from 1989 to 1992, and one patient had postoperative transfusion malaria in January 1992.[4,5]

Identification of the infective donor is not always possible, especially by using thick and thin smear. In the United States between 1963 and 1999, a total of 93 cases of transfusion-transmitted malaria from 91 presumed donors were identified and reported to the Centers for Disease Control and Prevention.[6] Among the 10 patients who died of malaria, 6 had *P. falciparum*, 2 had *P. vivax* and 2 had *P. malariae*. The infective donor could be identified in only 67 cases (74%). Most of the cases were identified by performing serological testing. Malarial smear was positive in only 17 (35%) of the 49 donors in whom it was performed, indicating that this method had poor sensitivity in screening for malaria.[6] Currently, there is no approved laboratory test in the Kingdom to screen for malaria among blood donors. Prevention depends mainly on the exclusion of potentially infected donors identified during the interview. People who have been to a malaria region within one year of donation, and those who had infection less than 3 years prior to the date of donation, are excluded. In addition, all blood units are screened by preparing thick and thin smears. Blood smears seem to be insensitive to detect low level parasitemia, therefore other methods have been suggested.[7] The poor sensitivity of the thick and thin smears as a screening tool adds to the difficulty of preventing transfusion-related transmission of malaria.[6] Many times, it is difficult to obtain an accurate travel history. In addition, clerical errors during the time of interview may occur. In a country like Saudi Arabia where there is a large expatriate population, many of whom originated from third world countries where malaria is still endemic, such as Asia and Africa, proper screening and exclusion of potentially infected persons may be difficult to accomplish. Some authors advocated the use of malaria antigen as a screening method.[8-10] Other tests such as indirect fluorescent antibody titers or polymerase chain reaction of the malaria DNA or ribonucleic acid may not necessarily implicate active infection, and/or may not be practical for mass screening.[6,11,12] According to the guidelines of the American Association of Blood Banks, and the Food and Drug Administration in the United States, immigrants and visitors from endemic areas may be accepted for blood donation 3 years after departure from the area, if they have been asymptomatic.[6] It was suggested that the blood banks in the Kingdom should use a more sensitive (such as immunochromatographic) test to detect low parasitemia.[13] Applying this guideline in our country would exclude the majority of people from endemic areas who currently live in the Kingdom. To further complicate the issue, some of the medical facilities offer financial reimbursement for donating blood. This practice encourages people, especially expatriates with low incomes, to donate blood. This, in addition to the lack of sensitive screening methods for malaria, may jeopardize the safety of blood transfusion.

In conclusion, malaria is still one of the most important transfusion-transmitted infections and should be considered in the differential diagnosis of patients with unexplained fever. Rapid diagnosis and treatment are essential in reducing morbidity and mortality, especially in immunocompromised hosts. Current exclusion criteria in Saudi Arabia may not be adequate enough to exclude potentially infected donors, and additional measures are needed.

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