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Transfusion-Induced Malaria in a Child after Open Heart Surgery in Korea

We had an opportunity to evaluate a child who developed fever approximately two to three weeks after the open heart surgery for tetralogy of Fallot. His peripheral blood smear showed rings and various stages of *Plasmodium vivax*. The patient had received packed red blood cells during the surgery and postoperative care, one unit of which was later proved sero-positive for malaria. The possibility of malaria should be included in the differential diagnosis of the patients with unexplained fever after multiple blood product transfusions for the open heart surgery.

Key Words : *Malaria, vivax; Blood Transfusion; Thoracic Surgery*

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INTRODUCTION

Malaria is a febrile disease usually acquired from the bites of previously infected female anopheline mosquito, which serves as a vector and host for sexual reproduction of the parasite (1). In other instances, malaria can be transmitted directly from a person to person after the transfusion of infected blood, accidentally (2). Transplacental transmission may also occur (3). Transfusion-induced malaria has been reported with increasing frequency, especially in non-endemic area (4, 5).

We report the first case of transfusion-induced malaria in a child after open heart surgery in Korea.

CASE REPORT

A 12-month-old Korean boy had a total correction of 'tetralogy of Fallot' on February 23, 2000. Three units of packed red blood cells (RBCs) were transfused during the surgery and one unit of fresh frozen plasma with 30 mLs of packed RBCs was transfused post-operatively. He was discharged on the 7th post-operative day uneventfully.

Two weeks after the discharge from the hospital, the patient was brought to the outpatient clinic of the hospital for fever and chills of 3-days duration. Physical examination did not reveal any abnormalities except for the fever of 38.9°C. Laboratory data showed: white blood cell 9,900/μL (polymorphs 24%, bands 6%, lymphocytes 62%, monocytes 6%, atypical lymphocytes 2%), Hb 11.8 g/dL, Hct 33.1%, platelet 95,000/μL, ESR 7 mm/hr, CRP 6.72 mg/dL. Urinalysis was normal. A provisional diagnosis of viral infection was made. Five days after the visit to the outpatient clinic, he was readmitted to the hospital as intermittent fever occurred at the intervals of 48 hr.

On admission, he was not in acutely ill appearance. His weight was 10.4 kg (25-50 percentile), height 74 cm (10-25 percentile), pulse rate 120/min, respiration rate 32/min, temperature 37°C, and blood pressure 90/50 mmHg. Heart sound was regular but, there was a grade 3/6 systolic ejection murmur at the left upper sternal border. The laboratory data were: white blood cell 10,500/μL (polymorphs 25%, bands 3%, lymphocytes 54%, monocytes 17%, metamyelocyte 1%), Hb 10.5 g/dL, Hct 31.8%, platelet 78,000/μL, ESR and CRP were normal. Urinalysis was normal. On the Wright stained peripheral blood smears, the Plasmodium species were seen in the RBCs, incidentally, with a count of 29,200/μL of RBC. The RBCs contained delicate ring form trophozoites, many cells showing multiple ring and applique forms, indicating various stages of *Plasmodium vivax* malaria (Fig. 1). But, he had never been traveled out of town, especially to the endemic area. The patient was treated with 13 mg/kg of hydroxychloroquine sulfate, followed by 3 doses of 6.5 mg/kg at 6, 18, and 24 hr later. And then primaquine phosphate 0.5 mg/kg/day was given for 14 days to prevent relapse. The peripheral blood smear did not reveal any malaria parasite from 10 days after the start of the treatment and on.

Simultaneously, the four donors of the blood products had

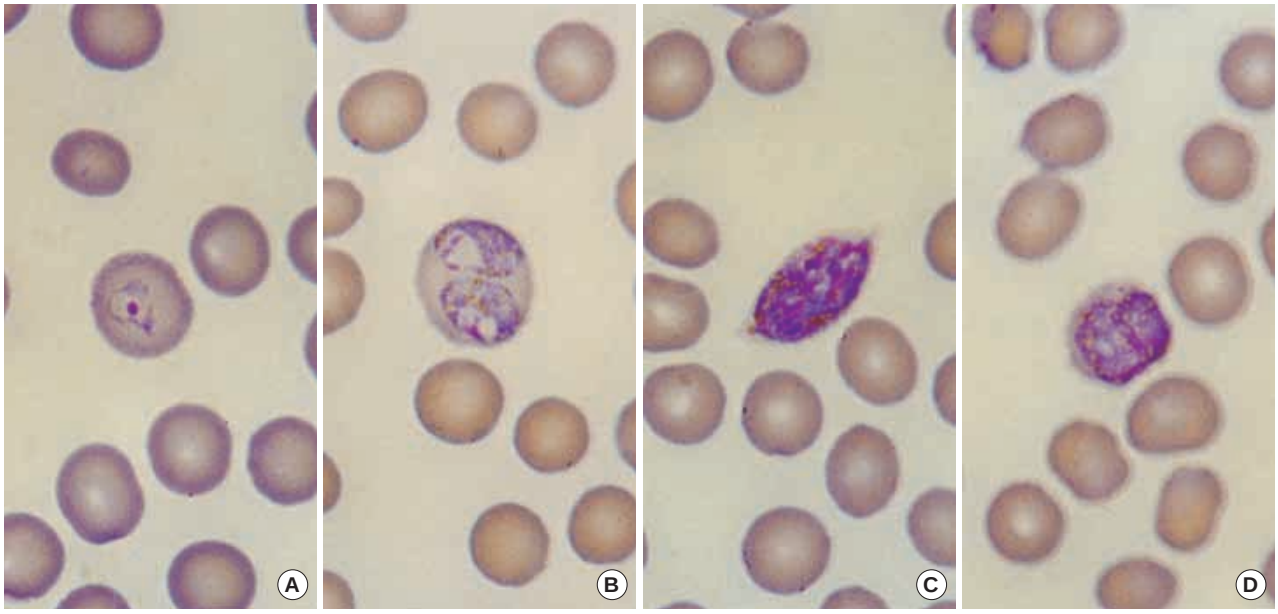

Fig. 1. The peripheral blood smear shows various stages of *Plasmodium vivax* in the enlarged red blood cells. (A) Early ring stage. (B) Trophozoite stage. (C) Schizont stage. (D) Gametocyte stage. (Wright, ×1,000).

received the test for the malaria and one was positive for the malaria with a titer of 1:256 by indirect fluorescence antibody test on March 31, 2000. This donor was a 21-yr-old healthy soldier serving in the Yeon-chon area, where 223 cases of malaria had been reported in 1999 (6). He donated his blood on February 19, 2000, which was 4 days prior to the transfusion to the patient. But, malaria parasites were not seen in his RBCs and the polymerase chain reaction for malaria was negative on March 31, 2000. He did not have any symptom of malaria later.

DISCUSSION

After the public campaigns from 1959, the malaria seemed to be completely eradicated from Korea. But the imported malaria has been diagnosed occasionally in the people after returning from travelling abroad since 1970 (7). From July 1993, the cases of indigenous malaria have been reported in increasing frequency in the area near the 38th parallel (demilitarized zone). Yeon-chon is one of the three risk areas near the 38th parallel (8). The blood transfusion-related malaria in a child has not been reported previously in Republic of Korea and this is the first case in a child after open heart surgery in Korea.

If a patient develops fever after open-heart surgery, the differential diagnoses include endocarditis, postcardiotomy syndrome, as well as transfusion induced infections, such as hepatitis, cytomegalovirus infection, etc. Additionally, transfusion-induced malaria should be included for the differential diagnosis.

The cases of transfusion-induced malaria after open heart surgery were reported by Cokkinos et al. (9) and Garvey et al. (10). These cases were diagnosed as *Plasmodium malariae* infections. Transfusion-induced malarias have been increasing in non-endemic countries (4, 5). In non-endemic countries, the frequency is less than 0.2 cases per million units of blood transfused (11). It is extremely rare in Republic of Korea: only one case was reported in 1999 (12), even though Kim et al. reported that army donated blood had high detection rates of malaria antibody and antigen (13).

There are two apparent reasons for the continued prevalence of transfusion-induced malaria. First, Plasmodium appears to survive the temperatures of refrigerator for the preservation of blood for up to 2 weeks (11). Secondly, it is quite difficult to prove the parasitemia from the blood of the donors directly under the microscope due to the very low parasite density in their blood, particularly when several donors are involved in one case.

The incubation period of transfusion-induced malaria depends on the numbers and strains of plasmodia transfused, the host, and the use of antimalarial prophylaxis (11). But generally has generally been longer than that of the mosquito-transmitted malaria; usually between 1 week and 3 months (14, 15). In this case, incubation period was 24 days.

The definitive diagnosis is made by identification of the parasites on the blood smear. Recently, indirect immunofluorescence, hemagglutination test, and DNA probes have been widely applied as the epidemiologic tools and can be used to obtain serologic evidence of malaria in the individual patients and also for tracing the donor involved in transfusion-induced malaria (16-19). But the diagnosis of trans-

fusion-induced malaria is difficult because the detection of plasmodia on the routine initial peripheral blood smear is difficult because the density of parasitemia is usually low. And also diagnosis of malaria may be obscured by the absence of the suggestive cyclic temperature curve.

Usually, chemotherapy brings an excellent outcome in *P. vivax, P. malariae*, and *P. ovale* infections. In contrast, infections with *P. falciparum* potentially follows a fatal course if not treated promptly (20).

Therefore, the possibility of malaria must be suspected in patients with unexplained fever who had received multiple blood product transfusions for the open heart surgery. In these cases peripheral blood smear examinations should be repeated, keeping in mind that the typical temperature pattern of malaria may not be seen in transfusion-induced malaria.

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