CASE REPORT

Transfusion Transmitted Malaria in a Thalassaemia Major Patient

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ABSTRACT

Blood safety is a major global issue. Transfusion transmitted parasitic infections (TTPI) like malaria are rare and possibly under-reported, a situation which could be attributed to lack of awareness of the mosquito-borne transmission of infection. Such infections are still considered potential health hazards, as they can pose a significant threat especially in immunocompromised patients, where they have proven to be fatal. Prevention of the transmission depends solely on the donor's questionnaire which addresses previous or current infection with aetiologic agents. Donor deferral is effective however clear guidelines are needed. This case report features the transfusion-transmitted of *Plasmodium Falciparum* in a 15-year-old splenectomised patient with underlying beta thalassaemia major.

Keywords: Transfusion transmitted malaria, Transfusion-dependent beta thalassaemia major

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INTRODUCTION

Blood transfusion is not without risk. In tropical countries, the most well-known TTPI are *Plasmodium* species. Apart from malaria, other parasitic organisms implicated in transfusion-transmitted infections are the *Trypanosoma cruzi, Babesia microti, Toxoplasma gondii* and *Leishmania* species. The first case of transfusion-transmitted malaria (TTM) was reported way in 1911 following direct blood transfusion from an artery to a vein. TTM that occurred following the use of stored blood was reported in 1941.

In non-endemic areas, the incidence of TTM infection varies from zero to 2 cases over a million donations and is mainly caused by *P.Malariae* (1). Even though the reported incidence is low, there is still a need for definite guidelines on the blood donation screening process to prevent this transmission. There are few strategies for TTM prevention that incorporate blood donor deferral and screening, blood film malaria parasite (BFMP), serology testing, rapid diagnostic test (RDT) for malaria antigen, prophylaxis and presumptive anti-malarial treatment to the blood recipients as well as pathogen reduction treatment.

CASE REPORT

A 15-year-old Malay girl presented to Hospital Tuanku Ja'afar, Seremban with fever, lethargy and loss of appetite of two days' duration. She had underlying beta thalassaemia major and had been splenectomised and required regular blood transfusions. She received iron chelation and her last blood transfusion was two weeks prior to admission. She denied a history of jungle trekking, swimming and did not stay in a dengue-prone area.

On examination, her vital signs were stable, and she was pale with no jaundice. Her peripheral blood count showed pancytopenia with haemoglobin of 10.9 g/dL, platelets count of 73 x 10^9/l and total white blood cells of 2.6 x 10^9/L. The coagulation profile was normal. She was treated with a provisional diagnosis of dengue in the defervescence phase. However, she did not respond to the fluid challenge and remained febrile despite antibiotic coverage for atypical infection. Her serial blood counts showed persistent pancytopenia (Table 1). Her blood culture and dengue NS1 antigen were negative. Further investigations showed worsening liver function, especially increasing in liver transaminases.

Since she had a recent history of blood transfusion, TTPI was a possibility. On day eight of admission, BFMP showed positive for *P.falciparum* with a parasite count of 6080 trophozoites per µl blood (Figure 1).

The blood donation records were retrieved from the blood bank. She received a blood transfusion from one Myanmarese and two Malaysian blood donors. The blood donors were informed, and their blood was sent for BFMP. The BFMP was positive for *P.falciparum* for the Myanmarese donor with a parasite count of 8020 trophozoites per µl blood, whereas the Malaysian blood donors were negative for malaria. The polymerase chain reaction was done at the Institute of Medical Research, Malaysia for confirmation. It was confirmed that both the patient and the Myanmarese blood donor were infected with *P.falciparum*.

The infected blood donor was a 35-year-old Myanmarese male, who lived in Sagaing Division, Myanmar, a malaria-endemic village. He had been in Malaysia for three years, employed as a factory worker in Senawang, Negeri Sembilan and had never returned to Myanmar. He had donated blood twice while he was in Malaysia and the most recent time was one week prior to the patients' blood transfusion. He never had any symptoms of malarial infection and was in good health at the time of the blood donation. He was treated as an uncomplicated malaria case and was put on oral artesunate and mefloquine (Artequin®). He was discharged well four days after admission.

The patient was commenced on oral artemether-lumefantrine (Riamet®) for six doses and one dose of primaquine. Her temperature settled after administration of Riamet. Upon discharge, the patient was well, afebrile and her BFMP was negative for malaria parasites.

DISCUSSION

In this patient, the clinical symptoms were non-specific, mimicking other common infections like dengue which is more common in our community. This had caused a delay of the diagnosis which could result in fatal illness, particularly in vulnerable individuals. Patients with a splenectomy have an increased risk of malarial infections and usually develop severe malaria following a *P.falciparum* infection (2). The spleen is an important organ due to its protective role and its ability to eliminate parasites, therefore a splenectomy will ultimately affect the kinetics clearance of parasites. However, this patient who had been splenectomised, only experienced low parasitaemia levels and was treated as an uncomplicated case. The spleen is not solely responsible for protection as other organs can take over the parasite load, although they do so less efficiently than the spleen.

Normally post-splenectomy, a patient will have leukocytosis and thrombocytosis. In this patient, before her last blood transfusion, she had a normal white blood cell count and the platelet count ranged from normal to mild thrombocytosis. Her normal range of white cell count could be attributed to her immunocompromised state. Her serial full blood count (Table 1) showed pancytopaenia which was clearly due to the infection. Immune-mediated destruction of circulating platelets and white blood cells has been postulated in malaria infections. In malaria, the destruction of platelets causing thrombocytopaenia is accompanied by simultaneous suppression of thrombopoiesis. Her peripheral blood

Table I : Serial peripheral blood count

Parameter (reference ranges)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
WBC(4.0-11.0 x10^9/L)	2.6	2.1	2.1	1.2	1.5	3.9	2.1	1.7
Hb (12.0 – 14.0 g/dl)	10.9	9.7	9.4	8.3	8.4	8.4	6.4	7.0
Platelet (150-450 x10^9/L)	62	73	87	52	62	103	95	78
RBC (3.80 - 5.00 x10^{12}/L)	4.11	3.73	3.60	3.20	3.18	3.18	2.42	2.51
Haematocrit (36 - 45 %)	31.5	28.7	25.1	24.1	24.1	24.5	18.5	19.6
MCV (81 - 98 fl)	76.7	77.1	76.9	75.5	77.0	77.3	76.5	78.2
MCH (27.3 - 33.6 pg)	26.6	26.1	26.1	26.1	26.5	26.2	26.5	27.9

picture displayed *P.falciparum* ring forms with one small chromatin dot and the infected red cells were not enlarged (Figure 1).

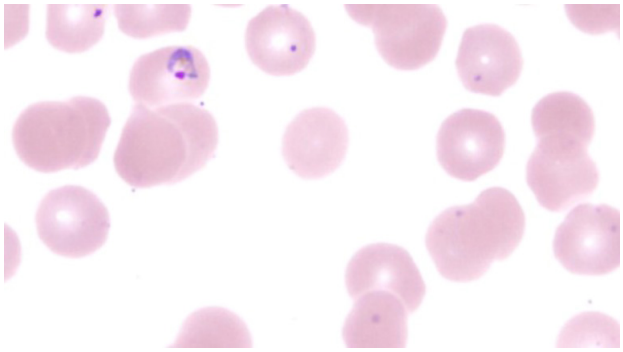

Figure 1 : P.falciparum seen in peripheral blood film (x40 magnification)

This is the second case reported in Malaysia in which the blood donor originated from Sagaing, Myanmar. The first case reported TTM caused by *P.vivax* from a blood donor who was also from Sagaing, Myanmar(3). Sagaing is located in a region of malaria-endemic villages in Myanmar and *P.falciparum* is still the dominant species(4). Even when there is good control of malaria incidence like Malaysia, sporadic outbreaks have been reported in the past because of the influx of foreign workers. In fact, our health screening program for foreign workers does not include screening for malaria(5).

Symptomless malaria carriers and partially immune donors present a major risk for recipients of their blood. Once infected with *P.falciparum*, the infectivity remains for one to three years. TTM has also been reported to be associated with blood donations from more than five years previously in the case of *P.falciparum* and several decades for *P.malariae*. The malaria parasites resist the processing steps of the blood, survive preservation and freezing conditions and retain their state of infectivity.

Screening asymptomatic blood donors alone is virtually impossible for TTM prevention. It must be combined with other strategies. Mostly in non-endemic countries, infected donors will be deferred for three years and pre-donation questionnaire is relied on as a screening method. However, there were TTM cases associated with blood donations of more than five years previously. Donor-deferral guidelines that are suitable for the respective countries need to be established. For example, countries that are malaria-endemic need to be identified. Blood donors from those countries need to undergo more stringent qualification or screening tests to donate their blood.

Some countries use malaria serology tests, but these tests do not detect current infections, in fact, they only measure past exposure. Sabah has incorporated the BFMP examination in conjunction with a pre-donation questionnaire (2). BFMP is labour intensive and time-consuming which makes it unsuitable as a screening method for use in a blood bank.

Rapid and accurate screening tools are important. Quality assurance is mandatory for sensitivity and specificity of tests used to diagnose malaria. It must be highly sensitive to ensure all clinically significant malaria infections can be detected and highly specific to pick up low parasite density. RDT for malaria which detects the circulating parasite antigens, can provide accurate diagnosis and improve the safety of blood donations. There has been vast growth of RDT available in the market with marked improvement in sensitivity and specificity. It is simple, easy to use and the results can be obtained within a few minutes, making it suitable for use in blood banks. Both BFMP and RDT have a sensitivity of 10 -100 parasites/ul, therefore they can only identify parasitaemia above their detection limits. However, even if both methods of implementation are used, total elimination of TTM is impossible. Therefore, clinicians should be mindful of the possibility of TTM in patients who have received a blood transfusion and develop a febrile illness. These are among the sensible approaches which can help to reduce the risk of TTM and increase the safety of blood donations.

Prophylaxis malaria treatment might lead to the development of drug-resistant malaria. It also conflicts with the malaria treatment guide which requires confirmation of a malaria infection.
Pathogen inactivation for blood components should not compromise the blood products' efficacy or cause any side effects. This approach might be useful where malaria is endemic.

CONCLUSION

TTM prevention that depends solely on the exclusion of potentially infected blood donors is insufficient. A more pragmatic approach is needed to ensure blood safety. In Malaysia, most malaria cases are imported, therefore donors from malaria-endemic regions need to be identified. This pool of blood donors needs to go through a screening test, such as rapid antigen testing for malaria. The risk of acquiring TTM can be lessened with effective and sensitive screening methods together with the improved implementation of blood donor selection and deferral. Rapid antigen testing for malaria provides a tool for blood donor selection.

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