Case Reports

Transfusion Malaria in Sick Neonates

Ranjan Kumar Pejaver
I. Al Hifzi
F. Al Temawy*
B. Abdullah*

Malaria is an uncommon illness during the neonatal period and early infancy. Transplacental barrier, presence of acquired immunity from the mother (in endemic malarious region) and preponderance of fetal hemoglobin are some of the reasons for this observations(l). Post-transfusion malaria is a possibility not only after whole blood transfusion, but also after infusion of components such as platelet, leukocyte concentrates or cryoprecipitate. In neonates and infants who have contracted the infection this way, it can be quite severe or even fatal. This may be in part due to delayed diagnosis or it may have further complicated a serious underlying disorder, or poor general condition. Here we report three cases of malaria in infants who had received blood transfusion during the neonatal period.

Case Report

Case I: A ten-week old male infant was admitted with a history of fever for 2 days, and not feeding well for several days before admission. He was born to a 24 year old Saudi mother at 30- weeks of gestation, following a normal pregnancy until the onset of preterm labor. His birth weight was 1.2 Kg. He had hyaline membrane disease and was successfully treated in the Neonatal Intensive Care Unit (NICU), with surfactant and ventilatory support. He had also received three packed red blood cell (PRBC) transfusions at the age of 3, 15 and 27 days. He had been discharged from the NICU in a good condition at the age of 40 days.

On this admission, he had pallor and hepatosplenomegaly. The hemoglobin level was 8.2 g/dL. Liver function tests were within normal limits. The blood film revealed Plasmodium vivax parasites. He responded to treatment with chloroquine. The organomegaly had regressed by the time of first follow-up which was about a month from the date of the second admission. One PRBC transfusion was needed to perk up the low hemoglobin during the second admission. He remained well on follow-up.

Case II: This 11 week old female infant presented to the emergency room with respiratory distress and seizures. She had been unwell for 3 days prior to arrival, having had fever, vomiting and lethargy. She was born at 29 weeks of gestation and her birth weight was 1.1 Kg. She had an eventful neonatal period having had severe RDS needing prolonged ventilation, and also had necrotizing enterocolitis. She had received five PRBC transfusions between the age of 2 days and 45 days. She was discharged from the NICU at the age of 60 days in good condition.

From the Department of Pediatrics and Preventive Medicine, North West Armed Forces Hospital, Tabuk, Saudi Arabia.

Reprint requests: Dr. Ranjan Kumar Pejaver, Associate Professor, Department of Pediatrics, M.S. Ramaiah Medical Teaching Hospital, M.S. Ramaiah Nagar, Bangalore 560 054.

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The present admission was to the Intensive Care Unit. Her general condition was poor and she was semiconscious. A full septic screen was performed. The blood film showed heavy parasitemia with *Plasmodium vivax* and *Plasmodium falciparum.* Intravenous infusion of Chloroquine was commenced and after 24 hours changed to intravenous quinine as the condition deteriorated. She developed disseminated intravascular coagulation. She got into further respiratory difficulties, warranting ventilation. Her convulsions were difficult to control. She did not respond to treatment and succumbed to her illness on day 3 of admission. Cerebral complications of malaria could explain the developments leading to death.

Case III: This male infant aged eight weeks was admitted for investigation. He had been experiencing high grade (>40°C) fever for six days with no significant findings on clinical examination. He was born at term, but developed respiratory distress soon after. He was diagnosed as having diaphragmatic hernia. The child was operated on day 1, and needed ventilatory support for 3 days. He had received three PRBC transfusions during his 12 day stay in the NICU.

During the current admission, his blood film showed *Plasmodium falciparum* and *Plasmodium vivax* parasites. He was treated with chloroquine without achieving clearance of his parasitemia. He responded to quinine sulphate and has remained well on follow-up. His hemoglobin level held on and improved without needing any top-up transfusion.

All the above cases came from areas which are nationally established as free of malaria. Following these episodes, the Department of Community Medicine investigated and reconfirmed this. None of the family members, particularly the mothers, had visited endemic areas. The mothers had been repeatedly tested and were negative for malaria.

All three infants had received PRBC transfusions during the neonatal period. The relevant donor was traced by the blood bank, all three cases had a common donor! He had donated blood on three occasions spread over a period of sixteen weeks. The donor involved had been checked with single blood films prior to donation and was found to be normal. Repeat checks, following detection of these cases, were also negative for malaria. Acridine orange staining method was unavailable. However this donor had visited malaria endemic areas several times during the months preceding blood donation. He had suffered twice from malaria during the two years prior to donation and had received treatment. On the first occasion *Plasmodium falciparum* and on the second *Plasmodium vivax* had been detected in his blood film. He was positive for antimalarial antibodies tested by ELISA method, when investigated after these events had occurred.

Discussion

The most likely way that the three infants reported got the malarial infection is via the transfusions they received earlier. Congenital malaria was ruled out by checking the mothers, and acquiring it from the community was not possible as they lived in confirmed malaria free zones. The mothers were even negative for malarial antibodies when they were tested later on. There had been no travel to or visitors from endemic areas.

The incubation period of post-transfusion malaria may vary between 12 days *{P. falciparum)* and 3-4 weeks *(P. vivax),* and may be even longer *(P. malariae).* Partially immune, symptomless carriers of malaria constitute the major risk for the recipients of their blood(2).

One way of avoiding the incidence of transfusion malaria is to defer donors with a history of malaria, and those born, living or travelled in endemic regions. This will result in the loss of a large number of potential donors. We cannot afford to do this at the present time when the demand for blood is high, especially in the countries where malaria is prevalent and donors are rare. Examination of thicks films from those at risk is unreliable, as was the case with our donors. A method using acridine orange staining in the quantitative buffy coat system has been found to be more sensitive and specific(3). However, levels of parasitemia in infected donors may be so low so as to be undetectable in peripheral blood. Moreover, the whole exercise is labor-intensive and not cost effective.

Testing for antibodies either by indirect immunofluorescence or by enzyme-linked immunosorbent assay (ELBA) has been found to be useful in some centers(4). However, this evidence is indirect. The antigen used is of P. *falciparum* which cross reacts with P. *vivax,* and hence may give unreliable results(5). It may take anywhere from 7 to 28 days, depending on the species of parasite involved, for antibody response to develop following infection. This period may be prolonged for up to 4 months when antimalarial chemotherapy has been taken(6). Conventional ELISA takes at least 5 hours. An enhanced chemiluminescent enzyme immunoassay, which does not use sophisticated equipment and can be completed in *VA* hours, has been tried(4,7). Malarial serology may be a useful way to detect donors in non-endemic countries, but in endemic areas, where antibody is present in almost the whole of the population, it has little value.

Use of monoclonal antibodies to detect even low levels of parasitemia, in a speedy and accurate manner, has been reported(8). The use of DNA probe to detect a degree of parasitemia as low as 1 in 10000 red cells has been described(9). But these are complicated immunological tests which are costly and tedious.

In some of the centers where malaria is prevalent, measures such as treatment of all donors with chloroquine have been utilized(l). This is not a fool proof method. Resistance to standard treatment, uncertainty as to whether parasites are totally cleared, need for sustained prophylaxis, side effects of drugs, are some of the limiting factors. Prophylactic treatment of all recipients has been practiced in some institution(l0). Previously mentioned factors and the danger of hemolysis, if glucose-6-phosphate dehydrogenase deficiency is also present, should be borne in mind. Addition of substances to donated blood units, with a view to purge malaria infected red cells would present considerable organizational difficulties(11).

Transfusional malaria during neonatal period and early infancy is an iatrogenic hazard resulting from improving standards of neonatal care. It is extremely difficult to screen donors and no cost effective, satisfactory manner is currently available to provide complete protection to the recipients. Even after following the recommended standards(12) for selection of blood donors, transfusion malaria has occurred(13). Early clinical suspicion, reinforced by past history of transfusion should alert the pediatrician to investigate and confirm diagnosis. When recognized and treated, transfusion malaria resolves rapidly and does not relapse because parasites do not settle in the liver(14,15).

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