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A Case Study of Possible Relationship between Post Transfusion Malaria and Thalassaemia

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Abstract : Cases of transfusion transmitted malaria have increased in incidence over the past few decades. Patients requiring regular transfusions are more prone to it. In the present study, the hematological parameters in a Thalassaemic patient who developed malaria and the parasite type and morphology in such a patient were studied. The results indicated that Thalassaemic patients are more prone to transfusion transmitted malaria.

Key words : Thalassaemia, Transfusion transmitted malaria, Hematological parameters.

Introduction

Transfusion transmitted malaria is common in endemic areas. Following an attack of malaria, the donor may remain infective for years - *i.e*. 1-3 years in *P. falciparum*, 3-4 years in *P. vivax*, and 15-50 years in *P. malariae*. During transfusion transmitted malaria, the inoculation of blood from an infected person to a healthy person occurs due to the transfusion of infected blood. In this type of malaria, asexual forms are directly inoculated into the blood and pre-erythrocytic development of the parasite in the liver does not occur. Therefore, this type of malaria has a shorter incubation period and relapses do not occur. The clinical features of transfusion malaria occur earlier and any patient who has received a transfusion three months prior to the febrile illness should be suspected to have malaria.

Transfusion induced malaria may be a serious threat to the life of a group of special patients; those who require many transfusions, those who have been treated with immunosuppressants, and those who have undergone splenectomy.

The incubation period of post-transfusion malaria may vary between 12 days (*P. falciparum*) and 3-4 weeks (*P. vivax*) and may even be longer (*P. malariae*) (Pejaver *et al*., 1997). Partially immune, symptomless carriers of malaria constitute the major risk for the recipients of their blood.

The infection rate in thalassaemia is affected mainly by the duration of the disease and is increased by splenectomy and in the long term, by treatment with deferoxamine (Rahav *et al*., 2006).

Several studies have indicated that infection is common in thalassaemia patients, and that more than 10% of these infections are severe. The main causes of infection are directly linked to blood transfusions, e.g. hepatitis B virus, hepatitis C virus, hepatitis G virus, human T-cell lymphotropic virus, human immuno deficiency virus and malaria.

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The present study was undertaken to study the hematological parameters in a Thalassaemic patient who developed malaria and to study the parasite type and morphology in such a patient. Literature on thalassaemia cases on transfusions that developed malaria was also reviewed.

Case Study

The Hemoglobin values, the total leucocyte counts, the parasitic type and index were evaluated in one 11 years old thalassaemic patient who was on regular transfusions and had developed malaria. The records of the treatment, the transfusions and the recovery were also noted.

11 year old male child, a known case of Thalassaemia Major, on monthly blood transfusions had chief complaints of fever with chills for 3 days. He also had right side upper abdominal pain for 3 days. His weight was 25.8 kg. He was on regular transfusions every month and was also receiving iron chelation therapy. He was splenectomised 7 years ago, *i.e*. at his age of 4 years. His hemoglobin was 9.2 gm/dl and had reduced to 5.9 gm/dl after three days of onset of the fever, suggesting a very rapid fall of hemoglobin. The total leucocyte count was 18,700/cmm and after the three days had risen to 21,000/ cmm.The peripheral smear showed *P. falciparum* rings with the parasitic index of 3/100 RBCs. He was treated with Quinine. His fever spikes reduced in severity and the parasite index also reduced with the treatment.

Discussion

A high incidence of post transfusion malaria in thalassaemic patients appears to be due to the use of fresh blood and the high frequency of blood transfusion required by these patients (Choudhary *et al*., 1990). However, on the other hand, studies have shown that heterozygous α^+- thalassaemia protects from severe malaria in African children. (Mockenhaupt *et al*., 2004) .The mechanism of protection in α^+- thalassaemia remains obscure. α^+- thalassaemia does not influence susceptibility to infection per se. Rather, the heterozygous trait ameliorates disease manifestation, that is, it influences progression from parasitemia to severe malaria. However, the fatality remains unchanged, indicating an abrogation of protection once a critical stage of disease is reached. *P. falciparum*-infected α^+- thalassaemic red cells show a decreased capacity to form rosettes, a pathogenic marker of severe malaria, but in vitro results on inhibited parasite multiplication are conflicting. Increased antibody binding to parasitized thalassaemic red cells suggests raised neoantigen expression, which would result in enhanced immune recognition and increased parasite clearance. The protective effect of heterozygous α^+- thalassaemia was strongest in the youngest children, which is during a time when malaria associated mortality is highest. Similarly, protective effects of the sickle cell trait against severe and uncomplicated malaria in Kenyan and Nigerian children, respectively, have been reported to be restricted to young age groups. These observations agree with the notion that innate resistance acts mainly before specific immunity has developed.

Irrespective of its underlying causes, protection in young heterozygous children improves the chance of survival and thus of reaching an age at which the physical capacity to cope with the infection is higher. Most infections occur in cases of transfusion of blood stored for less than 5 days and it is

rare in transfusions of blood stored for more than 2 weeks. Frozen plasma is not known to transmit malaria. In transfusion malaria, pre-erythrocytic schizogony does not occur and hence relapses due to dormant hepatic forms also do not occur. Therefore, treatment with primaquine for 5 (or 14) days is not indicated.

Chronic *falciparum* malaria may occur in people who have lived in endemic areas and have developed partial immunity to the malaria parasite, resulting in low-grade parasitaemia (Howden *et al*., 2005). A recent study (in Sudan) showed that *P. falciparum* can survive for months in human hosts during the 9-month dry season, when no transmission occurs.

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. It may take anywhere from 7 to 28 days, depending on the species of parasite involve, for antibody response to develop following infection. This period may be prolonged for up to 4 months when antimalarial chemotherapy has been taken. 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. In some of the centers where malaria is prevalent, measures such as treatment of all donors with chloroquine have been utilized. 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 institutions. It is extremely difficult to screen donors and no cost effective, satisfactory manner is currently availably to provide complete protection to the recipients. Even after following the recommended standards for selection of blood donors, transfusion malaria has occurred. 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. Infections continue to be among the major causes of mortality among patients with thalassaemia (12-46%), along with cardiovascular diseases and liver failure. The mechanisms underlying this increased susceptibility to infections in thalassaemia are not fully understood. Many of the factors that are probably accountable are associated with either the disease (e.g. anemia, reticuloendothelial system dysfunction because of iron and haemolysed erythroblasts, iron overload and altered immune response) or the treatment (splenectomy, transfusion-related infections and iron chelation). Transfusion transmitted malaria poses significant problem in regions of world where malaria is endemic. (Elhence *et al*., 2005)This may result in significant morbidity and mortality in transfusion recipients. In India though it is mandatory by drug and cosmetic act to screen donated blood for malaria, there are no definite guidelines on the choice of the test. Donors who are implicated as the source of transfusion transmitted malaria cases typically have very low level of parasitemia undetectable even on several thick films. Moreover, traditional blood film microscopy involving large number of blood donor samples is labor intensive and requires high

technical skill. Malaria antibody screening is not indicative of active infection and result in unnecessary high discarding of collected units as the antibody may persist up to several years after infection. PCR and antigen detection tests have limited availability. Hence, most of the donated blood across the country is not screened for malaria and experts recommend malaria immunoprophylaxis to all blood recipients which is not feasible practically. This practice may also pose significant problem in immunosuppressed patients, neonates and children. Reports on transfusion transmitted malaria from India are not available as in the absence of awareness; the cases may be attributed to the mosquito-acquired malaria. High prevalence of malaria in multitransfused thalassemia patients, points towards transfusion as a risk factor. There is a need for definite guidelines on blood screening to prevent transfusion - transmitted malaria.

The present study clearly indicates that Thalassaemic patients are more prone to transfusion transmitted malaria, since they require regular transfusions as well as due to the use of fresh blood for them. Transfusion transmitted malaria differs from mosquito transmitted malaria in the way that the incubation period is shorter, relapses do not occur and therefore treatment with Primaquine is not indicated.

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