Multidrug Resistant Transfusion Vivax Malaria

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ABSTRACT A 17-day-old premature baby girl had received a blood exchange transfusion because of hyperbilirubinemia and got another blood transfusion because of severe anemia on day 45. The diagnosis of transfusion vivax malaria was made when she had severe anemia again on day 78. The most predominant clinical signs were fever, anemia, hepatosplenomegaly, and thrombocytopenia. Treatment with chloroquine 25 mg base/kg BW showed resistance at RIII level on a 7-day follow up. She was retreated with quinine 10 mg salt/age in month divided in 3 doses/day for 7 days. It also showed resistance at late RI level on day 30. Then she was retreated with quinine 10 mg salt/age in month divided in 3 doses/day for 7 days and still showed resistance at late RI level on day 32. Finally she was treated with quinine 10 mg salt/kg BW/dose, tid for 7 days which was effective. During the course of treatment, no adverse reactions were found clinically. This malaria case was transfusion vivax malaria resistant to chloroquine at R III level and to quinine at late RI level. Quinine 10 mg salt/BW/ dose tid for 7 days was effective and safe for infants.[Paediatr Indones 1994; 34:175-178]

Introduction

Indonesia is a tropical country where malaria is still prevalent especially in the eastern part. In Jakarta, many people including the clinicians think that malaria is not more a public health problem.

In Jakarta usually malarial cases are imported by people who have travelled to endemic or malarious areas. In this city where people from every part of Indonesia can be found, the possibility of malaria infection in blood donors must always be considered seriously. 

The extensive use of blood transfusion in medical practice renders transfusion malaria a problem of clinical and public health importance. WHO requires that all blood donors in malaria endemic
areas should be free from malaria for at least 2 consecutive years. However, the Indonesian Red Cross which is the main source of blood for transfusion does not require malaria laboratory examination for screening of blood donors. Exclusion criteria is based on interview.

Very few transfusion malaria cases were reported in Indonesia. This report calls for awareness and attention on induced malaria from the use of unscreened blood for transfusion that may develop into a serious or fatal case.

Case Report

A premature baby girl (weight 1.8 kg) was born in Jakarta on January 17, 1993. Her parents were residents of Jakarta who had never stayed in malaria areas and had no history of malaria. She was hospitalized for intensive neonatal care for 17 days.

On day 7 she received blood exchange transfusion because of hyperbilirubinemia (serum bilirubin concentration=21.0 mg/dl). She was discharged in a good condition with a weight of 2.0 kg. When she was 38 days old, her mother realized that she was pale and had a distended abdomen, her body weight increased to 2.7 kg. She was readmitted for 3 days because of severe anemia (hemoglobin=5.0 g/dl) and received 90 ml blood transfusion to increase her hemoglobin to 16.0 g/dl.

At the age of 78 days, she was again admitted to the hospital because of skin rash, severe anemia (Hb=5.0 g/dl), hepatomegaly (8 cm), splenomegaly (Hackett 4 = H4), slight leukocytosis (11 000/µl), and thrombocytopenia (49 000/µl). Her body weight was 3.5 kg. Vivax malaria was diagnosed from the thin blood smear with a parasite density of 1.3%. Another 80 ml blood transfusion was given to increase her hemoglobin level to 10.2 g/dl, WBC and platelet counts were 9 600/µl and 68 000/µl respectively.

Chloroquine 25 mg base/kg BW was given in 3 doses for 3 days. During the treatment no vomiting was reported but the decrease of parasitemia was less than 75% and the parasite density remained at 0.5% on day 2 after treatment. No parasitemia clearance was observed until day 7 and the parasite density remained at 0.9%. According to the WHO standard of in vivo sensitivity test, this Plasmodium vivax was resistant to chloroquine at R III level.

One month after quinine treatment, she developed fever. The hemoglobin, WBC and platelet were 8.1 g/dl, 10 800 /µl and 124 000/µl respectively. P. vivax was found at 1.6% density in the thin blood smear. It means that P. vivax was resistant to quinine at R I level. Quinine treatment with a higher dose: 15 mg salt /age in month divided in 3 doses/day was given for 7 days. The parasite vanished on day 4 with hemoglobin, WBC and platelets of 6.1 g/dl, 6500/µl, and 123 000/µl respectively. The parasitological follow-up was also done on a weekly basis. Thirty two days after the second quinine treatment, she developed fever again and P. vivax was found at a 0.5% density. It was also resistant at the late R I level. The hemoglobin, leukocyte and platelet values were 9.2 g/dl, 3400/µl and 129 000/µl respectively. Quinine 10 mg salt/kgBW/dose was given three times a day for 7 days and the parasite vanished on day 2. On weekly follow-up for 2 months the blood smear remained negative.

Discussion

Malaria induced by blood transfusion from asymptomatic donors is a problem in Indonesia. Preliminary screening by doing blood smear or serological test or other tests cannot be applied because of lack of trained technicians and funds. For the time being, it is important to pay attention and be aware of induced malaria by blood transfusion. Clinicians should have sufficient knowledge on the principles of malaria diagnosis and its treatment.

In Indonesia the most prevalent malarial species are falciparum and vivax malaria. In this case we found vivax malaria after blood exchange transfusion. This could happen because vivax malaria can be successfully transmitted to man with only 10 parasites.

The incubation period of blood induced infection depends on the number of parasites inoculated and susceptibility of the recipient. The period between the transfusion and the appearance of symptoms of this vivax malaria is about one month but other authors reported incubation period of less than one month.

The patient had the common symptoms and signs of malaria, namely fever, anemia, hepatosplenomegaly, slight leukocytosis or sometimes leukaemia and thrombocytopenia.

So far P. vivax resistant to chloroquine has been reported from Nias Islands and Irian Jaya. In Irian Jaya, P. vivax is known as Chesson strain. This case look like Chesson strain. P. vivax infection is resistant to chloroquine at R III level.

The other antimalarial drug available in Indonesia for chloroquine resistant P. vivax is quinine. Quinine is known to be active in asexual erythrocytic stages of all four human malaria parasites but responds less rapidly against P. vivax infections. The commonly recommended quinine dose for infants is 10 mg salt/age in month divided in 3 doses/day for 7 days. To get parasite clearance, we increased the quinine dose according to WHO recommendation and the calculation of dosages of antimalarial drugs for children. This regimen was sensitive and safe for this case.

In P. vivax infection, relapse occurs as result of maturation of hypnozoites in the liver with liberation of merozoites into the blood stream. The merozoites then enter erythrocytes after relatively short or long periods. Theoretically, there is no exoerythrocytic cycle in transfusion malaria and there is no true relapses. The appearance of parasites was due to multidrug resistance.
In summary, the reported malaria case was a transfusion vivax malaria which was resistant to chloroquine at R III level and to quinine at late R I. The patient was cured effectively with quinine 10 mg sali/kgBW/dose three times a day for 7 days with no side effects.

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References

Idiopathic long QT syndrome: Asking the right question
Infants and young children cannot describe symptoms of cardiac syconpse accurately. If the attention in such cases is focused on the seizure activity that may follow, the patient will be treated inappropriately with anticonvulsants. We report such a presentation in four infants and young children (6 to 48 months) with idiopathic long QT syndrome. All patients presented with recurrent seizures. All patients had a corrected QT interval (QTc) > 0.44 s and none had deafness. Diagnosis was suspected by careful history-taking which revealed episodes of loss of consciousness prior to convulsions in all patients. All patients were treated successfully with propranolol and free of symptoms during the follow-up period of 1-2 years. Screening family members showed a prolonged QTc in 9 out of 16, and history of sudden and unexplained deaths in 2 families.

Vivax malaria resistant to treatment and prophylaxis with chloroquine
GS Murphy, HS Basri, Purnomo, et al. [Lancet 1993;341:96-100]
Chloroquine has been the treatment of choice for vivax malaria for more than 40 years. Lately, several case-reports have suggested the emergence of resistance to chloroquine in Plasmodium vivax in Papua New Guinea and Indonesia. We undertook prospective treatment and prophylaxis trials of chloroquine in children and adults with vivax malaria living in Irian Jaya (Indonesian New Guinea). 46 villagers with P. vivax parasitemia were treated with oral chloroquine (25 mg base/kg body weight divided over 3 days) and followed for 14 days. Parasitemia cleared initially but did recur within 14 days in 10 (22%) subjects. All recurrences were in children younger than 11 years, 7 of whom were younger than 4 years; the failure rate among children under 4 was 70%. Seven of the patients with recurrences were given a second course of chloroquine. In all, the infections initially cleared but recurrent parasitemia developed in 5 (71%) within 14 days. Whole-blood chloroquine concentrations were consistently above those previously shown to cure P. vivax blood infections (90 mcg/L). Those whose initial infections cleared and who had no parasitemia on day 14 received weekly prophylaxis with chloroquine. Despite the presence of expected blood chloroquine concentrations, P. vivax parasitemia developed in 9 out of 17 subjects receiving prophylaxis during 8 weeks of follow-up (median time to parasitemia 5.3 weeks). Chloroquine cannot be relied on for effective treatment or chemoprophylaxis of P. vivax blood infections acquired in this region.

Vaccination with SP66, a chemically synthesised vaccine, against Plasmodium falciparum malaria in Colombia
MV Valero, LR Amador, C Galindo, et al. [Lancet 1993;341:705-10]
Preclinical and clinical studies have established safety and immunogenicity of chemically synthesised SP66 malaria vaccine. This study was a phase III randomised, double-blind, efficacy trial completed in La Tola, Colombia. We gave to 1548 volunteers over one year of age three doses of either the vaccine (n=738) or placebo (n=810). Active and passive case detection methods were used in documenting clinical episodes of malaria among the study subjects. The follow-up period began one month after the third dose and lasted for one year. There were 168 and 297 episodes of Plasmodium falciparum malaria documented in the SP66 group and placebo group, respectively; this correspond to a crude protective efficacy of 38.8%. Incidence rates for first or only P. falciparum malaria episodes were