# A RECENT CASE OF CONGENITAL MALARIA IN SINGAPORE

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### ABSTRACT

We report a case of congenital malaria in a 2-month-old baby girl, born in Singapore of a Singaporean mother, who presented with fever for one week, gross hepatosplenomegaly and anaemia (haemoglobin 5.6 g/dL) and thrombocytopenia. Peripheral blood films showed Plasmodium vivax. There was no local transmission at that time, but the mother had spent the first 6 months of her pregnancy in Pakistan, where she had been treated for prolonged fever at 4 months amenorrhoea with ibuprofen alone. The mother and 2 siblings were asymptomatic and repeatedly tested negative on blood films for malaria parasites, but the mother tested positive for antibodies to Plasmodium on the Fluorescent Antibody Test. The child was treated with oral chloroquine and made an uneventful recovery. We postulate that this is believed to be the first recent case of congenital malaria in Singapore since it was declared malaria free in 1982. The diagnosis should be considered in babies of mothers who have travelled to places where malaria is endemic, as maternal infection may be unrecognised, and the child may be asymptomatic at birth.

Keywords: congenital malaria, hepatosplenomegaly, neonatal infection, Singapore

# INTRODUCTION

We often think of malaria in the context of a febrile illness when the patient gives a recent history of travel to a region where malaria is endemic, but we should also consider congenital malaria in the differential diagnosis of a pale febrile infant when the mother has been to an endemic region. We report a case of congenital *Plasmodium vivax* malaria in a 2-month-old baby girl, born in Singapore of a Singaporean mother, who presented with fever, hepatosplenomegaly, anaemia and thrombocytopenia and who had never been out of Singapore. We postulate that this is the first recent case of congenital malaria in Singapore since it was declared malaria-free in 1982.

#### CASE HISTORY

MMK, born in Singapore to a Singaporean mother of Pakistani ethnic origin, presented at 2 months of age to the Department of Paediatrics, Singapore General Hospital with fever for 6 days and cough. She had been born at term by normal vaginal delivery, birth weight 2775g, at the Kandang Kerbau Maternity Hospital. She had been discharged well at Day 3 of life, with a normal glucose-6-phosphate dehydrogenase (G6PD) level, and had been well till her presentation to us. She had never travelled out of Singapore. Physical examination revealed a fever of 39.3°C, pallor, an enlarged liver 6 cm below the costal margin and a spleen of 5 cm. There was a soft systolic murmur but the lungs were clear and there were no other signs suggestive of

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haematological malignancy or intra-uterine infection. Her initial full blood count showed a haemoglobin (Hb) of 7.4 g/dL, haematocrit (Hct) of 21.5%, and mean corpuscular volume 81.4 fL, total white cell count of 11 500 per mm<sup>3</sup>, and a platelet count of 91 000 per mm3. The haemoglobin dropped to 5.3g/dL, the haematocrit to 14.6%, the total white cell count to 6 060 per mm3 and platelet count to 69 000/mm3 over the next few hours. Blood films for malaria parasites (BF for MP) showed Plasmodium vivax with a parasite load of 2+. A bone marrow aspirate was done for gross hepatosplenomegaly and showed a regenerating marrow with cvidence of peripheral platelet destruction. The child responded well to oral chloroquine 50 mg stat followed by 25 mg at 6, 12, 24 and 48 hours and a blood transfusion, but primaquine was omitted in view of the child's age. Chloroquine 25 mg weekly was given for a further 6 weeks on an outpatient basis. She was discharged six days after admission, with a haemoglobin of 8.7 g/dL, a reticulocyte count of 10%, a total white cell count of 14 820 per mm<sup>3</sup>, a platelet count of 239 000 per mm<sup>3</sup>, and blood films negative for malaria parasites for 3 consecutive days. At that time, there were no local cases of malaria reported in Singapore, the only cases having been imported. The child had never been out of the country, but her mother had spent the first 6 months of her pregnancy in Pakistan, where she had been treated for prolonged 'typhoid fever' in her fourth month of pregnancy with ibuprofen alone.

The mother also gave a history of having had 3-4 episodes of what was thought to be 'typhoid fever' between 1985- 1989, and recalled having had jaundice in 1987 in Pakistan. None of these illnesses was identified or treated as malaria. The mother and the patient's two brothers were asymptomatic and repeatedly tested negative for malaria parasites on peripheral blood films, but were subsequently found to have antibodies to Plasmodium by Indirect Fluorescent Antibody (IFA) testing(1) done at the Parasitology Laboratory of the NUS Department of Microbiology. The mother's IFA titre was positive at 1:16. The mother and siblings were treated with chloroquine and primaquine. The child's hepatosplenomegaly regressed completely by 1 year of age and her haemoglobin level rose to 11.0 g/dL and her mean corpuscular volume to 77.3 fL (normal range 76-96 fL) 10 months later. She has continued to thrive, with a weight maintained at the 25-50th centile and height at about the 50-75th centile. There has been no recrudescence of malaria over 2 years and 6 months of follow-up.

## DISCUSSION

Congenital malaria is not uncommon in many parts of the world but is rare in areas of high endemicity<sup>(1)</sup>. Menon, in Kuala Trengganu, reported 2 cases of congenital malaria out of 37 cases of malaria in pregnancy over 3 years from 1969-71<sup>(2)</sup>. More recently, Sidhu and Ng in Kuala Lumpur did not find a single case of congenital malaria out of 64 cases of malaria between 1984-88<sup>(3)</sup>. It has not been reported in the Singapore literature in the last 10 years. We report a case of a 2-month-old child who was found to have *Plasmodium vivax* infection, born to an asymptomatic mother who had lived in an endemic area before and during her pregnancy.

Congenital malaria occurs in the offspring of up to 0.3% of immune mothers and up to 7.4% of non-immune mothers with malarial infections<sup>(4)</sup>. In areas of high endemicity, it is common for pregnant women to be parasitemic, and the rates of placental infection range from  $16\% - 34\%^{(5)}$ . Parasites may also appear in the cord blood at delivery, but it is very unusual for neonates to sustain parasitemia or suffer disease<sup>(6)</sup>. Babies born to non-immune mothers are more likely to suffer disease<sup>(7)</sup>. Passively transferred IgG has been postulated to be protective *in utero* and in the first few months of life; the onset of symptoms in congenital malaria is typically at 4-6 weeks of life, which is the estimated half life of maternal IgG in the infant. Absence of antibody would also explain the higher incidence of congenital malaria in non-immune mothers<sup>(8)</sup>.

The disease most commonly presents in the first 8 weeks of life with fever, vomiting, anaemia, hepatosplenomegaly and jaundice and mild diarrhoea<sup>(7,9)</sup>. The examination of a single peripheral blood smear may not yield the diagnosis, even when a suspicious history has been obtained; hence this diagnosis should be sought early and aggressively in the appropriate clinical setting<sup>(9)</sup>.

The mother may have come from a malarious area but may have a normal physical examination and negative blood film for malaria parasites. Congenital malaria can occur despite the absence of any evidence of active malarial infection in the mother in pregnancyt<sup>(1,8-10)</sup>. Gestation and delivery may have been uneventful except for a febrile illness<sup>(8)</sup>. In a review of 50 reported cases of congenital malaria in the United States from 1950-1991, Hulbert found that of 35 mothers who had recently immigrated into the United States, the period that they had been in the country before delivery, varied from <10 months (61%) to <18 months (91%) and even up to 84 months, indicating that even a remote history of foreign travel to a malaria endemic zone may be of importance<sup>(9)</sup>. Maternal blood films were negative for malaria parasites in 38% of the cases of congenital malaria in Hulbert's series<sup>(9)</sup>.

Singapore has been declared malaria-free by the WHO from November 1982<sup>(12)</sup>. There was a large localised outbreak in 1993, when 40 cases of Plasmodium vivax malaria were reported in the Tanjong Rhu/East Coast Park region. There has also been a rise in the incidence of imported malaria among foreign workers. increasing from 25 cases in 1989 to 116 cases in 1993. The potential for local transmission is still present in certain malariareceptive areas, especially where construction work is being carried out on reclaimed land(13). The ASEAN region is by no means free from malaria, and the clinician should ask a thorough history of recent travel or past residence in endemic regions. Pakistan, India, Bangladesh, Thailand, Vietnam, Cambodia, Myanmar, the Philippines, Indonesia and Malaysia are considered endemic for malaria, although in Peninsula Malaysia about 90% of the population live in areas considered free from malaria and the disease is only endemic in the hilly and less developed areas of the centre, the north and the north-eastern part of the Peninsula(14).

Our patient did not receive any primaquine, though we gave primaquine to the patient's mother and two brothers. There is no exo-erythrocytic phase in the course of congenital or transfusionacquired malaria, so only the erythrocytic phase requires treatment. This circumvents the concern of adverse reactions, most notably intravascular haemolysis, that is sometimes seen in patients who are given primaquine<sup>(6)</sup>.

It is also useful to note that the diagnosis of transfusionacquired malaria should be considered in the appropriate setting<sup>(15,16)</sup>. Symptoms of this disease generally occur sooner than those of congenital malaria<sup>(15)</sup> and include fever, anaemia and hepatosplenomegaly, but intervals of 7-10 weeks between transfusion and onset of symptoms have been reported<sup>(17)</sup>. The use of stored blood does not prevent the transmission of transfusion-acquired malaria, as plasmodia have been shown to survive in stored blood for up to 2 weeks<sup>(18)</sup>.

## CONCLUSION

This case illustrates the need to keep an open mind for the causes of hepatosplenomegaly and pallor in an infant, if treatment for malaria is not to be delayed. Our working diagnosis was that of a haematological malignancy or intra-uterine infection and the blood film for malaria parasites was done because of the mother's travel history<sup>(12)</sup>.

The following points may be reiterated:

- Congenital malaria can occur in babies of asymptomatic mothers, who have had no evidence of malaria in pregnancy<sup>(1,8-10)</sup>.
- The history of mother's foreign travel or residence in an endemic region may be remote in time, but cannot be ignored in a febrile mother or child<sup>(9)</sup>.
- 3. The diagnosis is not difficult once the possibility is considered.

#### References

- 1. Covell G. Congenital malaria. Trop Dis Bull 1950: 47: 1147-67.
- 2. Menon R. Pregnancy and malaria. Med J Malaysia 1972: 27: 115-9.
- Sidhu PS, Ng SC. A retrospective study on malaria cases admitted to the University Hospital, Kuala Lumpur, 1984-1988. Med J Malaysia 1991; 46: 177-82.
- MacGregor IA. Epidemiology, malaria and pregnancy. Am J Trop Med Hyg 1984; 33: 517-25.
- Jeliffe EFP. Low birth weight and infection of the placenta. Bull World Health Organ 1968; 38: 69-78.
- Strickland GT. Ed. Hunter's tropical medicine. 7th ed. Philadelphia: WB Saunders, 1991: 586-615.
- Molyneux ME. Malaria clinical features in children. J R Soc Med 1989; 82 Supplement 17: 35.
- Quinn TC, Jacobs RF, Mertz GJ, Hook EH 3rd, Locksley RM. Congenital malaria: A report of 4 cases and a review. J Paed 1982; 8: 229-32.
- Hulbert TV. Congenital malaria in the United States, report of a case and review. Clin Infect Dis 1992; 14: 922-6.
- Davies HD, Keystone J, Lester ML. Gold R. Congenital inalaria in infants of asymptomatic women. Can Med Assoc J 1992; 146 (10): 1755-76.
- Harvey B, Remington JS, Sulzer AJ. IgM antibodies in a case of congenital malaria in the United States. Lancet 1969; 1: 333-5.
- Ministry of the Environment. Singapore declared malaria free by WHO. Epidemiological News Bulletin, Singapore 1983; 9(2): 6-9.
- Ministry of the Environment. Malaria outbreaks at Tanjong Rhu/ East Coast Park, 1993. Epidemiological News Bulletin, Singapore 1994; 20(3): 13-5.

- World Health Organisation. Malaria: Epidemiological data 1989-91. WHO Weekly Epidemiological Record, No 35, 27 August 1993.
- Arvin AM, Ruskin J, Yeager AS. Protozoan and helminth infections (including *Pneumocystis carinii*) In: Remington JS, Klein JO, eds. Infectious diseases of the fetus and newborn infant. 3rd ed. Philadelphia: WB Saunders, 1990: 535-8.

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- Shulman IA, Saxena S, Nelson JM, Furmanski M. Neonatal exchange transfusion complicated by transfusion-induced malaria. Paediatrics 1984; 73: 330-2.
- Piccoli DA, Perlman S, Ephros M. Transfusion acquired *Plasmodium* malariae infection in two premature infants. Paediatrics 1983; 72: 560-2.
- Bruce-Chwatt L. Blood transfusion and tropical disease. Trop Dis Bull 1972; 69: 825-62.

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