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Neonatal *Plasmodium vivax* malaria

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Abstract. Congenital malaria is a condition rarely diagnosed, even in endemic countries. This tropical disease is associated with high mortality in the absence of timely recognition and prompt therapy, particularly when is due to *Plasmodium falciparum*, however *Plasmodium vivax* can also lead to relevant morbidity and mortality. We report an unusual case of a 19-day-old male newborn with neonatal vivax malaria, suspected primarily on the basis of positive maternal history, which presented with low birth weight, thrombocytopenia and a significant parasitemia. He responded satisfactorily to chloroquine antimalarial therapy, being successfully discharged 10 days after admission. Blood smears remained negative during the first 2 months of follow up. At 8 weeks of follow-up, she showed remarkable weight gain and was developing normally with age-appropriate anthropometry with no subsequent complications.

INTRODUCTION

Congenital malaria is a condition rarely diagnosed, even in endemic countries (Wiwanitkit, 2006; Thapa *et al.*, 2010). The presentation is usually with non-specific signs and symptoms and most cases are due to *Plasmodium falciparum* (Uneke, 2007; Thapa *et al.*, 2010), which is responsible for most complicated forms of disease during pregnancy and childhood (Rodriguez-Morales *et al.*, 2007). A meticulous past medical history, including that of the maternal gestation is often the initial suspicion-arousing event (Wiwanitkit, 2006; Rodriguez-Morales *et al.*, 2007; Uneke, 2007; Thapa *et al.*, 2010). This tropical disease is associated with high mortality in the absence of timely recognition and prompt therapy, particularly when is due to *P. falciparum* (Rodriguez-Morales *et al.*, 2008). We report an unusual case of a 19-day-old male newborn with neonatal vivax malaria, suspected primarily on the basis of positive maternal history. He responded satisfactorily to chloroquine therapy.

CASE REPORT

A 19-day-old, term, male infant, was initially seen for a three-day history of fever (39ºC), irritability and poor breastfeeding. There was no history of abdominal distension, oliguria, alteration of consciousness, convulsions, or prolonged jaundice in the neonatal period. His mother proceeded from Zaragoza northern Antioquia, Colombia, and was delivered at Medellin, in a primary health institution, by spontaneous vaginal delivery, and there had been without immediate postnatal complications. He received exclusive breastfeeding and all the immunizations according to the national programme (against polio, tuberculosis and hepatitis B). The mother's past medical

history was significant for an episode of fever, chills, vomiting and diaphoresis, at seven months of gestation, which had been not diagnosed and treated. Three days after delivery, she attended the same institution where diagnosis of *Plasmodium vivax* malaria was made. She was apparently treated with chloroquine and primaquine. When she came with her newborn to our institution (General Hospital of Medellin, Antioquia, Colombia), her peripheral blood smears appeared repeatedly negative for malaria. After delivery the mother and the infant remain living in Medellin, a non-endemic zone for malaria.

On examination, the infant appeared hydrated and tachypneic with labored breathing. He weighted 2,440 g at birth which occurred at 38 weeks of gestation. The axillary temperature was 39ºC, and he had a heart rate of 144 per minute, a respiratory rate of 48 per minute, and an oxygen saturation of 94% in room air. The liver was palpable 2 cm below the right costal margin. Examination of the other major systems was non-contributory. A complete hemogram showed the following: hemoglobin 12.8 g/dl, hematocrit 36.1%, total leukocyte count of 8.93 x 10^9/l (neutrophils 36%, lymphocytes 65%), and 70.0 x 10^9/l of platelets. The erythrocyte sedimentation rate was 23 mm (first hour) and C-reactive protein was 5 mg/l (normal reference value <0.3 mg/l). A Giemsa-stained peripheral blood smear showed trophozoites of *P. vivax*, with a parasitemia of 24,480/µl. Diagnosis was confirmed by thin and thick peripheral blood smears at the regional malaria department laboratory, with external quality control. The different *Plasmodium* species are identified morphologically by laboratory experts dedicated to interpret malaria smears at the Malaria Regional Offices in Colombia. In addition, all positive smears and 10% of those considered negative by the regional laboratories were reevaluated by a third national malaria reference microscopists to confirm the diagnosis of malaria. The peripheral blood smear of the mother failed to reveal malarial parasites at presentation. Cultures of the blood and urine were sterile. An abdominal ultrasound had no significant findings.

The infant was started on chloroquine (25 mg/kg, 10 mg/kg on days 1 and 2, 5 mg/kg on day 3). He improved satisfactorily with antimalarial therapy. A subsequent peripheral blood smear at 48 hrs post-treatment found trophozoites of *P. vivax*, with a parasitemia of 1600/µl. Four days later, the parasitemia was 160/µl and became negative at 7 days post-treatment. Patient was successfully discharged at 10th day. Blood smears remained negative during the first 2 months of follow up. At 8 weeks of follow-up, he showed remarkable weight gain and was developing normally with age-appropriate anthropometry with no subsequent complications.

DISCUSSION

Malaria is still responsible for a significant burden of disease, estimated to cause more than 300,000 fetal and infant deaths and 2,500 deaths of pregnant women worldwide annually (Menendez *et al.*, 2007; Rodriguez-Morales *et al.*, 2008). Malaria in pregnancy can result in premature labour, intrauterine growth retardation, high perinatal mortality, anemia, miscarriage, low birth weight, and maternal deaths, even in *P. vivax* cases (Rodriguez-Morales *et al.*, 2006, 2007, 2008; Menendez *et al.*, 2007; Thapa *et al.*, 2010). Occasionally, the infection may cause cord parasitemia, early and late neonatal malaria. Placental infection with malarial parasites may result in their transplacental transmission, although the infant born may remain asymptomatic and healthy (Menendez *et al.*, 2007; Thapa *et al.*, 2010).

As has been previously reported, there is lack of consensus on the definition of congenital malaria (Menendez *et al.*, 2007; Thapa *et al.*, 2010). Traditionally, in endemic countries, congenital malaria is diagnosed when the parasite is seen in an infant's peripheral blood smear during the first week of life (Menendez *et al.*, 2007; Thapa *et al.*, 2010). Although we were unable to demonstrate malarial parasites in the

maternal peripheral circulation with routine microscopy at the time of presentation (which was previously diagnosed also with vivax malaria during pregnancy), the diagnosis of congenital malaria in our patient at the age of 19 days was established by the presence of *P. vivax* in the peripheral smear, with a negative history of vector exposure postnatally given the fact that the infant was born and lived in a non-endemic zone.

This case shows that the diagnosis of congenital, neonatal or perinatal malaria should be considered as an important differential diagnosis in infants who are born from mothers coming from malaria endemic countries and areas with or without a history of malarial disease during pregnancy (Rodriguez-Morales *et al.*, 2006; Menendez *et al.*, 2007; Del Punta *et al.*, 2010). The treatment of neonatal vivax malaria requires a blood schizonticide, like chloroquine, whereas primaquine is unnecessary as there is no hepatic stage of the parasite in congenital malaria (Rodriguez-Morales *et al.*, 2006; Menendez *et al.*, 2007; Del Punta *et al.*, 2010). In the treatment, it is also important, as in this case occurred with the mother, likely to be relapse malaria (as suggested by the 3 days postpartum diagnosis), to treat immediately the mother after birth with primaquine, if she is not breastfeeding (as well also chloroquine). Primaquine remains as the drug of choice to treat *P. vivax* relapses, but is contraindicated in pregnancy. This is one of the major limitations in achieving radical cure for *P. vivax* malaria during pregnancy which could minimize the risk of potential neonatal infections with its potential severe complications.

The majority of studies on congenital malaria are in the context of *P. falciparum* infections in Africa. Congenital malaria due to *P. vivax* has been described in few countries (Wiwanitkit, 2006; Menendez *et al.*, 2007; Valecha *et al.*, 2007; Rodriguez-Morales *et al.*, 2008; Del Punta *et al.*, 2010).

Plasmodium vivax malaria may negatively impact maternal and perinatal outcomes as we have shown herein (Wiwanitkit, 2006; Menendez *et al.*, 2007; Valecha *et al.*, 2007; Rodriguez-Morales *et al.*, 2008; Del Punta *et al.*, 2010). Moreover, *P. vivax* is increasingly recognized as a cause of significant morbidity in pregnant women (Rodriguez-Morales *et al.*, 2006; Menendez *et al.*, 2007). There is still little information on the clinical, epidemiological and molecular aspects of this infection during pregnancy and neonatal period, which clearly deserve more studies (Menendez & Mayor, 2007). This is of utmost relevance, particularly in areas, such as Latin America, where *P. vivax* is the predominant *Plasmodium* species, currently associated with a significant burden of morbidity and mortality (Rodriguez-Morales *et al.*, 2008).

Ethical approval

Ethical consent was obtained from the patient for this publication.

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