

Case Report

Neonatal *Plasmodium vivax* malaria: an overlooked entity

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Abstract

Although malaria is endemic in India, neonatal disease is considered rare. We report a case of neonatal malaria in a 26-day-old neonate with fever and splenomegaly who was diagnosed after a long and unsuccessful battery of tests for splenomegaly. Routine screening for malaria is essential for all neonates with fever in endemic areas. Early diagnosis and treatment of malaria could effectively prevent infant mortality.

Key words: malaria; neonatal malaria; neonate; splenomegaly

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Introduction

Of all malaria cases reported in 2008, the vast majority (85%) were in Africa, followed by southeast Asia (10%) [1]. India contributes a large number of cases in the south-East Asia region. Although malaria is endemic in India, neonatal disease is considered rare because of the protection provided by the passive acquisition of maternal antibodies and fetal hemoglobin [2]. The nonspecific signs and symptoms of neonatal malaria are often confused with sepsis, which leads to delay in diagnosis and treatment [2-4]. We report a similar incident in which a 26-day-old male neonate was diagnosed as having malaria after a long and unsuccessful battery of tests for splenomegaly.

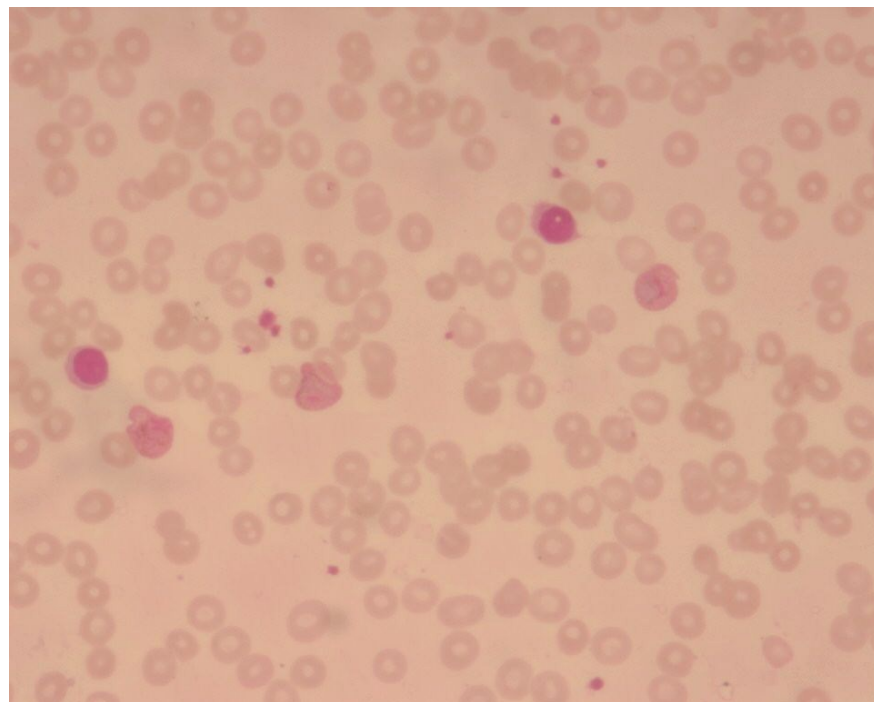
Case report

A 26-day-old male neonate was brought to the paediatrics department of Guru Teg Bahadur Hospital with complaints of intermittent fever, loose stools and abdominal distension for 10 days. There was no history of jaundice or bleeding from any site. He was the first child of a 20-year-old mother, born through normal vaginal delivery. He was febrile (axillary temp of 38⁰C) and his heart rate and respiratory rate were 140/minute and 40/minute respectively. He was pale but non-icteric. The liver and spleen were palpable 3 cm and 6 cm below right and left costal margins respectively. There was no lymphadenopathy. His anthropometric, cardiovascular and nervous system examinations

were unremarkable. There were no signs of vitamin deficiencies and a Bacillus Calmette-Guérin (BCG) vaccine scar was present on his left arm. In order of priority, clinical diagnosis of fever with anemia and splenomegaly secondary to infections (probably viral) / hemolysis / congestion / storage disorders was considered.

A preliminary complete blood count (CBC) and peripheral blood smear revealed normocytic normochromic anemia (hemoglobin (Hb) - 66 g/L, mean corpuscular volume (MCV) - 97.8 fl, mean corpuscular Hb concentration (MCHC) - 32.0 g/L) and mild thrombocytopenia (platelet count – 113 x 10⁹/L). No evidence of red cell fragmentation, nucleated erythroid cells or hemoparasites was seen. The total leukocyte count (15.6 x 10⁹/L) and differential count (Neutrophils – 50%, lymphocytes-47% and monocytes - 03%) were unremarkable. His biochemical tests including liver function tests and arterial blood gas analysis were within normal limits. Chest X-ray was also unremarkable.

The blood, urine and cerebrospinal fluid cultures failed to grow pathogenic organisms. None of the various serological tests to exclude infectious etiology such as cytomegalovirus, syphilis, human immunodeficiency virus, or hepatitis B virus showed a positive result. The rapid card tests for detection of plasmodium lactate dehydrogenase (pLDH2) for *Plasmodium vivax* and histidine rich protein 2 (HRP-2) for *Plasmodium falciparum* in blood could not be performed for this neonate born to poor parents. The

Figure 1. Infected erythrocytes showing amoeboid trophozoites of *Plasmodium vivax*

screening hemoglobin electrophoresis (starch agarose gel, pH 8.6 - Hb adult - 92.2%, Hb fetal - 5.0% and Hb A2 - 2.8%) and methemoglobin reduction test to exclude hemolytic anemia were also within normal limits. There was no ABO-Rh incompatibility between the mother and infant. Ultrasonography revealed organomegaly; liver and spleen measured 8 cm and 9.6 cm respectively. There was no evidence of abnormal portal venous blood flow or congestion on Doppler examination.

Eight days hence repeat CBC, peripheral smear, and bone marrow aspiration tests were performed. The peripheral smear showed malarial parasitemia: a few trophozoites of *Plasmodium vivax* (both early and late) with amoeboid cytoplasm, large chromatin dots and fine, yellowish-brown pigment were seen (Figure 1). The bone marrow aspirate was essentially unremarkable. A history of fever with chills in her eighth month of pregnancy could be elicited from the mother; however, presently she did not have fever or parasitemia and her immunochromatographic rapid test for qualitative detection of malaria antigen antigen (pLDH for *P. vivax* and HRP-2 for *P. falciparum*) was negative. The child was treated with chloroquine (base) at a dose of 10 mg/kg followed by 5 mg/kg at 6, 24 and 48 hours. There was prompt relief from fever and gradual regression of spleen size in a week.

Discussion

Most literature on paediatric malaria originates from Africa, a hyper endemic region where it is the single largest killer of children between 28 days to 4 years of age [5]. Although India is the largest contributor to the disease in the southeast Asia region, it a low risk nation for malaria [1]. Being a low endemic region, the median age of presentation tends to be later (8 years) in contrast to the mean age of 26 months reported from Africa [6].

Neonatal malaria is described as disease presenting within the first twenty-eight days of life [4]. Cases presenting later may also be included if the possibilities of postpartum infection by either mosquito bite or blood transfusion have been confidently ruled out [7], which is particularly difficult in endemic regions, including India. Congenital malaria is defined as presence of asexual stages of the parasite in cord blood at the time of delivery or in the peripheral smear of the infant in the first seven days of life [3]. While *falciparum* malaria has been implicated in most studies from Africa [2-4], *Plasmodium vivax* associated disease has been described from non African areas including southeast Asia [8-11]. With the current trend of international travel and immigration, neonatal malaria is likely to be encountered in non endemic regions also [8].

Neonatal malaria is rare; it occurs in 0.1% of immune and 10% of non-immune mothers in endemic areas. However, placental infection occurs in as many as one-third of women who acquire infection during pregnancy [7]. The spontaneous clearance of infection in neonates in endemic areas may be as high as 93% [2]. This has been attributed to the protective effect of maternal antibodies that are passed to the newborn and to the protective role of fetal hemoglobin in slowing the rate of parasite development. Since malaria is thought to be rare in neonates in malaria endemic regions, blood film examination for the parasites is not routinely performed [2]. However, recent reports from Africa suggest that the incidence of congenital / neonatal malaria is rising, possibly due to the increased resistance and virulence of the parasite resulting from altered antigenic determinants as well as increased reporting [2,3].

The clinical features of malaria in newborns are non-specific and overlap with those of sepsis. The typical malaria paroxysm is absent, with the infant instead having fever, refusal to suck, excessive crying and irritability, and anemia [3,4]. Even in endemic regions such as India, newborn babies with fever are invariably considered to have an infection and often receive antibiotics but not anti-malarial drugs. A history of maternal fever is a helpful clue to neonatal malaria [2,8]. Even though demonstration of the malarial parasite remains the gold standard for diagnosis, it is prone to inter-observer variation, especially in low parasitemia. Antigen capture dipstick assays have the advantage of being useful in field settings, but their cost is a prohibitory factor. Assay detecting histidine rich protein 2 (HRP-2) is specific for *Plasmodium falciparum*, whereas the parasite lactate dehydrogenase (LDH) assay can identify both *P. falciparum* and *P. vivax*. The sensitivity of rapid diagnostic tests has been noted to be in the range of 78.5-89.6% [12,13].

Anemia is an under-recognized laboratory finding in neonatal and congenital malaria; up to 42.3% of parasitized neonates may have hemoglobin values less than 120g/L [3]. This condition can be caused by a combination of factors, such as hemolysis of parasitized erythrocytes, bone marrow depression, or pre/co-existing nutritional deficiency. Massive splenomegaly in malaria though described in adults is an uncommon presentation in a neonate. Other consequences include symmetric foetal growth retardation and low birth weight [14].

The therapy for the infecting plasmodium species is curative. As the infection is produced by the transmission of the infected erythrocytes rather than forms that invade the liver, the infant does not require treatment for the exo-erythrocytic stages of the parasite, although the mother does.

To conclude, neonatal malaria is not as rare as it was earlier thought to be. In endemic regions and in infants of immigrant mothers in developed countries, malaria should be suspected in any neonate with fever and anemia with splenomegaly. Early diagnosis and treatment could effectively prevent infant mortality.

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