

Congenital *Plasmodium vivax* Malaria in a Non-Endemic Country; A Unique Case in the Netherlands

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Abstract

Congenital malaria is a rare complication of *Plasmodium* infection during pregnancy. We present a case of a neonate with a mother who migrated from an endemic area. The mother developed fever during delivery due to *Plasmodium vivax* infection. Despite postnatal negative screening for malaria, the neonate developed fever on day 20 and was diagnosed with *Plasmodium vivax* malaria. The neonate was successfully treated with chloroquine. Follow-up including repeated malaria screening might have spared the neonate a period of illness with consecutive chances of complications.

and rare parasitic infections should be considered when evaluating febrile neonates, too. It is of utmost importance to obtain, geographical and other demographic information. The incidence of malaria in the Netherlands is 150-300 cases annually. The Netherlands is considered a non-endemic country for malaria, thus these cases are travel-related. Driessen et al. [2] reported a total incidence of paediatric malaria in the Netherlands of 32 patients in 20 months. The most predominant parasite was *Plasmodium falciparum* (81%), and infections were mainly acquired in sub-Saharan Africa. Congenital malaria, defined as mother-to-child transmission of *Plasmodium* parasites, is a rare complication of malaria infection during pregnancy in endemic areas. An estimation of the prevalence of congenital malaria is complicated; in endemic areas it is difficult to differentiate between neonatal and congenital malaria [3]. Prevalence is region dependent; differing from 0.03% to 46.7% [3]. A literature search revealed 8 documented cases of congenital malaria in European countries [4-10], as summarized in Table 1. Congenital malaria has never been documented in the Netherlands previously.

Introduction

A common clinical problem encountered in emergency departments is an infant with fever. Neonates with temperature above 38.0 °C require comprehensive diagnostic evaluations including blood, urine, and cerebrospinal fluid cultures [1]. Viral

Table 1: Summary of documented congenital malaria cases in Europe, * interval since last stay in endemic area and pregnancy; ** Urinary Tract Infection

| Authors | Endemic area + interval* | Symptoms in mother | Age of diagnosis/sex | Parasite | Treatment | Outcome | Prophylaxis |
|-------------------|-----------------------------------|---|----------------------|--|---|-------------------|-------------|
| de Pontual et al. | Congo, 2 years | None | 6 weeks/ female | <i>P. malariae</i> | Oral chloroquine Bloodtransfusion | Complete recovery | None |
| Zenz et al. | Ghana, 1.5 years | None | 8 weeks/ male | <i>P. falciparum</i> <i>P. malariae</i> | Oral quinine hydrochloride | Complete recovery | None |
| Prior et al. | India 5-7 months | Fever during pregnancy no treatment | 26 days/ female | <i>P. vivax</i> | Intravenous quinine Bloodtransfusion | Complete recovery | None |
| Del Punta et al. | Pakistan, months before pregnancy | Fever during pregnancy treated as UTI** | 22 days/ female | <i>P. vivax</i> | Oral chloroquine | Complete recovery | None |

| | | | | | | | |
|------------------|-----------------------------------|----------------------------------|-----------------|----------------------|----------------------------|-------------------|------|
| Comellini et al. | Congo | Malaria in week of delivery | 21 days | <i>P. vivax</i> | Oral quinine hydrochloride | Complete recovery | None |
| Vottier et al. | Guyana, 6 months before pregnancy | Malaria during pregnancy treated | 21 days/ female | <i>P. vivax</i> | Oral chloroquine | Complete recovery | None |
| Vottier et al. | Angola, 3 years | None | 19 days/ female | <i>P. ovale</i> | Oral chloroquine | Complete recovery | None |
| Romero et al. | Ecuatorial Guinea, 1 month | None | 3 weeks/female | <i>P. falciparum</i> | Oral mefloquine | Complete recovery | None |

Case Report

Upon presentation at the emergency clinic at the age of 20 days, an irritable febrile male neonate was seen. This child was born at term from a mother who resided in Eritrea. The parents emigrated from Eritrea ten months before birth. During the year prior to pregnancy the mother was treated for malaria (*Plasmodium* species and medication unknown) in a refugee camp in Ethiopia. At our hospital in the Netherlands she gave birth to a healthy boy, with a birth weight above the 50th percentile (gestational age 41 + 3, birth weight 3970 gm). The mother tested previously HIV negative. During labour the mother developed fever; based on *Plasmodium vivax* infection, diagnosed in peripheral blood smear (Figure 1), and real time-PCR confirmed. In our laboratory malaria screening comprises microscopic examination of Giemsa-stained thin and thick blood smears, a Quantitative Buffy Coat Analysis (QBC) and the Binax Now Malaria test. In addition, *Plasmodium* species specific PCR can be performed. The detection limit of the thick blood smear in our laboratory is determined as 5-10 parasites/ μ l blood, for QBC 0.5-1 parasites/ μ l blood. Although the detection limit of the PCR is not yet determined, it can be assumed to be even lower than 0.5-1 parasites/ μ l blood. Due to maternal infection the neonate was tested for malaria on the first day of life; the screening was negative (PCR confirmed). During follow-up one week post-partum no symptoms of malaria were noticed; a malaria screening was not performed. After that, the child was discharged from outpatient monitoring. The mother was successfully treated with chloroquine and primaquine.

Two weeks later the neonate developed fever and was presented at the emergency clinic. The child had a temperature of 38.9 °C with normal heart rate and respiratory frequency. Auscultation of heart and lungs showed no abnormalities. No hepatosplenomegaly was present. A sepsis workup was performed including blood- and urine culture, and a microscopic examination of the urine sediment. Because of maternal malaria infection, malaria screening of the neonate was included. Complete Blood Count revealed a hemoglobin of 13.3 g/dL, leucocytes of 7.3×10^9 g/L, thrombocytopenia 27×10^9 g/L, and an increased C-Reactive Protein of 90 mg/L. Malaria screening revealed trophozoites (Figure 2) and schizonts of *Plasmodium vivax*, with a parasite load of 0.4% (equivalent to approximately 16×10^3 parasites/ μ l blood). Due to proven malaria infection, lumbar puncture was not performed. The patient was admitted to the paediatric department and treated with oral chloroquine for 3 days. Fever and irritability disappeared after initiation of treatment. He was discharged in good clinical condition after 5

days. At outpatient follow up two weeks after discharge, the baby was in good condition; malaria screening was negative.

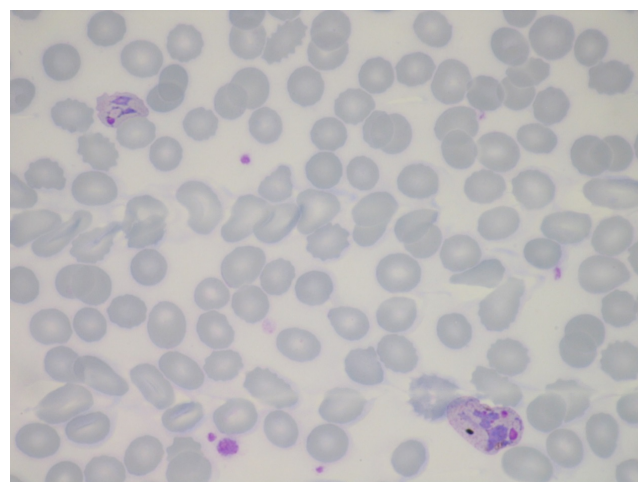


Figure 1: Two enlarged erythrocytes infected with trophozoites which is consistent with *Plasmodium vivax* morphology [Giemsa stained thin blood smear from mother of newborn; blood sample taken during labour (Magnification x 1000)].

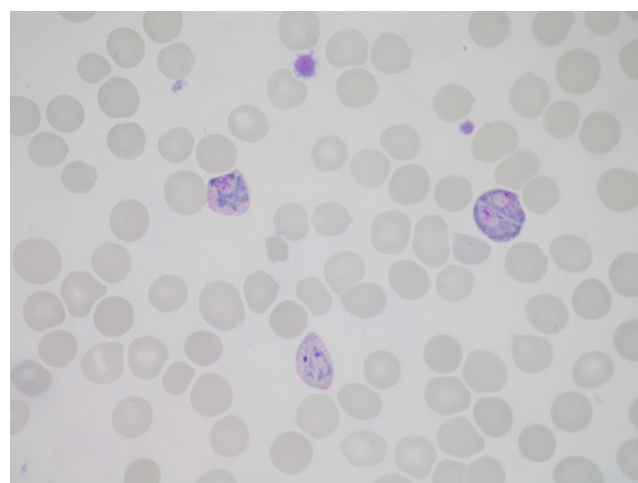


Figure 2: Three enlarged erythrocytes infected with trophozoites which is consistent with *Plasmodium vivax* morphology [Giemsa stained thin blood smear from 20 day old neonate (Magnification x 1000)].

Discussion

The case presented describes a neonate with proven congenital malaria infection with *Plasmodium vivax*, to our knowledge, the first case in the Netherlands. In non-endemic areas diagnosis can only be made if malaria is included in the differential diagnosis of neonatal fever. Although prevalence in literature vary greatly as noted before, pregnant women in high endemic areas have antibodies possibly decreasing transplacental transmission [3]. Migration from high to non-endemic areas, as described in this case, with subsequent loss of immunity due to lack of exposure, could increase the risk of overt malaria in pregnant women and subsequent congenital transmission of parasites. Additionally, pregnancy can provoke activation of the dormant liver stages (hypnozoites), where maternal tertian malaria was not additionally treated with primaquine.

Congenital infection with malaria may occur in all species, but is most commonly associated with *Plasmodium falciparum* and *Plasmodium vivax* [3]. Congenital malaria can present with fever, feeding problems, vomiting, diarrhoea and irritability in neonates. The symptoms typically appear between day 10 and 30 after delivery [3]. Blood investigation may reveal anaemia, thrombocytopenia and hyperbilirubinemia. According to the WHO guideline on the treatment of uncomplicated chloroquine-sensitive *Plasmodium vivax* infections, neonates can be treated with chloroquine. In cases of transplacental infection, additional treatment with primaquine is not mandatory. Prophylaxis for neonates at risk of congenital malaria is not described in literature.

In retrospect, malaria serology performed on the 12th week pregnancy serum of the mother appeared to be positive; antibodies against the pan malaria antigen could be detected. PCR's specific for *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale* and *Plasmodium vivax* performed on the serum did not detect DNA of either of the Plasmodium species. Malaria PCR's in the blood of the neonate at the first day of life were also negative. We hypothesises that in this particular case with a healthy neonate, with a birth weight on the 50th percentile and negative malaria screening, very little *Plasmodium vivax* infected erythrocytes were transferred from mother to child during delivery. Unfortunately umbilical cord blood was not available for PCR testing. After initial negative malaria screening, we assumed mother-to-child transmission of parasites during pregnancy to be excluded.

In retrospect, we recommend repeated malaria screening during weekly outpatient follow-up visits for the first month of life in neonates with symptomatic mothers and in neonates with symptoms. It is hard to identify clear risk factors in neonates.

Many women from endemic countries have parasites in their blood without symptoms of malaria. Repeated malaria screening is recommended because of incubation time and possible false negative results. The final outcome with current policy has had no major consequences for the neonate. In general, *Plasmodium vivax* infection is not severe and mortality is very low. However, complications like severe anaemia and haemorrhage must always be taken into account in younger children. Given the increase of migration from, and tourism to, tropical destinations, malaria is a differential diagnosis in neonates with sepsis or fever of unknown origin in non-endemic areas. In case of initial negative malaria screening, screening should be repeated. Although modern techniques in malaria diagnosis are highly sensitive and specific, a single negative test result still does not exclude malaria infection.

References

1. Haggmann S, Khanna K, Niazi M, Purswani M, Robins EB (2007) Congenital malaria, an important differential diagnosis to consider when evaluating febrile infants of immigrant mothers. *Pediatric Emergency Care* 23: 326-329.
2. Driessen GJ, Pereira RR, Brabin BJ, Hartwig NG (2008) Imported malaria in children: a national surveillance in the Netherlands and a review of European studies. *Eur J Public Health* 18:184-188.
3. Lesko CR, Arguin PM, Newman RD (2007) Congenital malaria in the United States: a review of cases from 1966 to 2005. *Arch Pediatr Adolesc Med* 161:1062-1067.
4. De Pontual L, Poilane I, Ledeur F, Haouchine D, Lachassinne E, et al. Report of a case of congenital malaria *Plasmodium malariae* in France. *J Trop Pediatr* 52: 448-450.
5. Zenz W, Trop M, Kollaritsch H, Reinthaler F (2000) Congenital malaria due to *Plasmodium falciparum* and *Plasmodium malariae*. *Wien Klin Wochenschr* 112: 459-461.
6. Prior AR, Prata F, Mouzinho A, Marques JG (2012) Congenital malaria in a European country. *BMJ Case Rep* 12: 2012
7. Del Punta V, Gulletta M, Matteelli A, Spinoni V, Regazzoli A, et al. (2010) Congenital *Plasmodium vivax* malaria mimicking neonatal sepsis: a case report. *Malar J* Mar 9: 63.
8. Comellini L, Tozzola A, Baldi F, Brusa S, Serra L, et al. (1998) *Plasmodium vivax* congenital malaria in a newborn of a Zairian immigrant. *Ann Trop Paediatr* 18: 41-43.
9. Vottier G, Arsac M, Farnoux C, Mariani-Kurkdjian P, Baud O, et al. (2008) Congenital malaria in neonates: two case reports and review of the literature. *Acta Paediatr* 97: 505-508.
10. Romero Urbano JM, Vázquez López R, Jurado Ortiz A, Martínez Valverde A (2000) A case of neonatal malaria in Spain. *An Esp Pediatr* 52: 377-380.