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Case Report

Paediatrics Section

Co-infection of *Plasmodium vivax* Malaria and Cytomegalovirus in an Immunocompetent Neonate

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ABSTRACT

Co-infections when occur can pose substantial diagnostic and treatment challenges for clinicians. In this case report we describe a neonate with co infection of *plasmodium vivax* malaria with Cytomegalovirus and discuss whether it can be the result of reactivation of one by the other infection postnatally or if these infections can affect and facilitate the transplacental transmission of each other from the mother.

Keywords: Cytomegalovirus, TORCH, IgM, IgG antibodies, Congenital Infection

CASE REPORT

A 30-days-old male infant (normal term vaginal delivery at hospital, first in birth order, birth weight-2.7 kg) presented to us with high grade fever on and off for last 7 days, lethargy and decreased oral intake for 2 days. There was no history of rash, cough, vomiting, diarrhea, seizures, eye, ear, umbilical discharge or bleeding from any site. On examination he was febrile, pale but not icteric. His temperature was 102°F, heart rate-138/min and respiratory rate-56/min. Abdomen examination revealed splenohepatomegaly (spleen-6cm, liver-4cm BCM). His respiratory, cardiovascular and neurological examinations were unremarkable and anthropometry was within normal limits. A differential diagnosis of TORCH group of infections, neonatal sepsis and hemolytic anemia was considered. Empirical antibiotics were started with ampicillin and gentamicin after drawing the blood samples. His investigations showed severe anemia and thrombocytopenia (hemoglobin-6.8 mg/dl, total leucocyte count-12700/mm^3 and platelets-33000/mm^3). Peripheral smear showed a shift of leucocytes towards left. The reticulocyte count was 5.4% and mean corpuscular volume was 72 fl. Serum bilirubin, Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT), blood urea, Creatinine and serum electrolytes were in normal range. Blood culture was sterile. As the infant continued to be febrile and lethargic after 48 hrs, his investigations were repeated and antibiotics were upgraded to cefotaxime and amikacin. This time the peripheral smear showed trophozoites of *plasmodium vivax* while blood culture was again sterile. Chloroquine was given in a total dose of 25mg/kg over a span of 3 days and the baby became afebrile at 3rd day of antimalarial treatment with improvement in his activity and oral intake. Meanwhile, TORCH serology showed positive result for CMV (IgG and IgM level at 2.22 U/ml and 3.3U/ml respectively) by ECLIA (electro chemiluminescent immunoassay). Urine PCR for CMV was positive but culture could not be performed. The clinical history was reviewed which did not reveal any transfusion of blood products or hospitalization in past 30 days. Mother could not recollect any history of fever or rash during antenatal period. She was sero negative for HIV and her peripheral smear was negative for malarial parasite however she tested positive for anti CMV IgG. The baby was discharged on iron, folic acid and cobalamin after 7days at hemoglobin of 6.8 mg/dl, platelet count of 2.7lac/mm^3 and normal neuroimaging. He was followed up closely every week and hemoglobin increased to 9 mg/dl after one month. His retinal, BERA, and neuroimaging examination was normal at 6 and 12 months of age. Institute ethics approval and parental informed consent was obtained.

DISCUSSION

Malaria and CMV infection are both a disease of overcrowding, still posing a major health challenge for developing countries. Both can cause similar clinical presentation (fever, hepatosplenomegaly, thrombocytopenia) and can be acquired transplacentally. Malaria is a protozoan infection and causes considerable mortality if not treated. On the other hand, CMV is an asymptomatic, self limiting infection in immunocompetent persons but can cause serious illness in immunocompromised subjects and neonates.

The incidence of congenital CMV infection is very low (2.1%) even in populations of high seroprevalence [1]. It is shown to affect 7.8% of asymptomatic pregnant women [2]. Mother can transmit the infection due to primary (acquired during pregnancy) or due to reactivation of latent infection or re-infection of different virus. It is difficult to differentiate between the two and both can cause complications, although it is said that baby is protected by acquisition of transplacental antibodies when it is due to reactivation of the virus. This makes primary infection more dangerous.

Malaria causes reactivation of several viruses but data on its interaction with CMV is negligible. We could find only one study done by Chene A et al., who studied the effect of falciparum malaria on reactivation of all human herpes viruses. They demonstrated that acute malaria was not associated with reactivation of CMV though it caused reactivation of HSV-1 and EBV [3]. This suggests that the chances of acquisition of both infections after birth and then reactivation of one by another are extreme. Thus, the present case seems to acquire both the infections in utero. In support of this assumption we found a single study by Van der Sande et al., who studied the risk factors associated with congenital infection of CMV in Gambia. They found active placental malaria infection to be a significant risk factor (adjusted OR 2.9, 95%CI 1.0-8.4). They hypothesized that one established infection can facilitate the other to be transmitted congenitally. However they did not asses HIV status of mothers or babies which would have been crucial.

They also observed that it was more common in primiparous women similar to the present case. The immune response of them may differ from multiparous women [4]. In the present case the mother did not show raised immunoglobulin M (IgM) antibodies which implicates she must have acquired the infection at least 4-5 months ago.

The possibility of acquisition of both infections after birth cannot still be ruled out. As the mother was not symptomatic during pregnancy nor did she shows malarial parasitemia or IgM antibodies against CMV.

The treatment of congenital CMV in immunocompetent babies is controversial. Many clinicians believe that CMV is self-limiting in immunocompetent patients and the patients should not be exposed to the adverse effects associated with antivirals. The only concern is sensorineural hearing loss in young children even in asymptomatic congenital CMV infection. Intravenous ganciclovir therapy seems to prevent subsequent sensorineural hearing loss [5].

To investigate a neonate (with fever, hepatosplenomegaly, thrombocytopenia) for TORCH. It is unusual to think and look for malaria at this age. As malaria can cause mortality if not treated, it should be suspected even in the absence of a history of immigration to endemic area or malarial symptoms during antenatal period. It is difficult to diagnose malaria on blood smear during low parasitemia and it may go unrecognized. If CMV is diagnosed in such a neonate the clinician stops thinking for other infections.

CONCLUSION

Although our case had asymptomatic infection and did not develop chorioretinitis, cerebral calcifications or hearing loss which may be delayed up to two years of age. His development and anthropometry was appropriate. This case report again emphasizes on the screening for CMV during the antenatal period and warns against the dual pathology especially because these are associated with long term sequelae.

ABBREVIATIONS

Cytomegalovirus (CMV); Toxoplasma, Rubella, Cytomegalovirus, Herpes virus (TORCH); immunoglobulin M (IgM), Epstein Bar Virus (EBV), Electrochemiluminescent immunoassay (ECLIA)

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