

Vertical transmission of chikungunya virus infection. Case report

Transmisión vertical de la infección por virus chikungunya. Reporte de caso

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Abstract

Chikungunya virus infection is a disease transmitted by vectors, in which vertical transmission was described in years 2005-2006. An infection rate up to 49% in neonates born from mothers with active viremia during labor has been observed. Perinatal infection could result in serious complications and potential cognitive impairment. **Objective:** To describe a newborn with Chikungunya virus infection secondary to vertical transmission. **Clinical case:** A female newborn is analyzed. She presented with fever and exanthema during her first week of life, elevation of transaminases and thrombocytopenia. Her mother had had symptoms compatible with chikungunya virus infection on the day of the delivery. Specific IgM antibodies against chikungunya were documented and the diagnosis was confirmed. **Conclusion:** Given the high perinatal transmissibility rate of chikungunya virus, this diagnosis should be considered in every newborn child of a mother with suggestive symptoms of chikungunya in the days surrounding delivery.

Keywords:

Chikungunya fever, chikungunya virus, infectious disease transmission, Newborn

Introduction

Chikungunya fever is a disease transmitted by vectors that has shown a cyclical presentation. The chikungunya virus is an RNA virus, a disease caused by an Alphavirus of the Togaviridae family. It was first isolated in Africa in the 1950's. In the following decades Chikungunya fever outbreaks occurred in the African continent and parts of Asia^{1,2}.

Since 2004, the virus has expanded its geographical distribution with an outbreak in Kenya, resulting in sustained epidemics in Africa and Asia^{1,2}, which later

spread to Europe and the Americas in recent decades, with several cases reported in almost all the countries of South America^{2,3}.

The transmission of the disease to humans is caused by a bite of an *Aedes* infected mosquito^{1,4}. In the urban cycle, the major vector is *Ae. aegypti* and more recently *Ae. albopictus* adapted to the urban environment, while the jungle cycle involves *Ae. furcifer* and *Ae. africanus*⁴.

During the Chikungunya virus epidemic on the island of "La Reunión", located in the Mascareñas archipelago in the Indian Ocean east of Madagascar on the

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African continent, between the years of 2005-2006 the vertical transmission of the disease was evidenced, with newborns' infection rate up to 49% in mothers with intrapartum viraemia⁵.

In 2013, the first cases of chikungunya virus transmission were confirmed in the Americas and cases of indigenous transmission have been documented in all South American countries with the exception of Chile and Uruguay. In Colombia were 16,629 suspected cases and 118 confirmed cases of chikungunya virus infection, which have been reported up to the epidemiological week number 23 (10 June 2016)⁶.

The objective of this report is to present the case of a newborn with history compatible with vertical transmission of chikungunya virus infection, as well as to review the literature in order to highlight the possible complications of the disease in the neonatal population.

Clinical case

We present the case of a newborn of the first pregnancy, whose mother resides in Segovia (Antioquia, Colombia) with controlled pregnancy. Maternal evaluation

for HIV, hepatitis B and non-treponemal test for syphilis were negative. Spontaneous birth at 39 weeks of gestational age, birth weight 3600 g, height 52 cm. At 5 days of age, the mother consulted for fever, a central localized exanthema and jaundice of 1 day of evolution. The newborn was hospitalized and initially focused on late neonatal sepsis, with tests showing a slightly elevated C-reactive protein of 1.68 mg/dL, an unchanged urine cytochemistry and negative urine culture. The newborn received antibiotic treatment with ampicillin (100 mg/kg every 12 hours) and amikacin (15 mg/kg/day) for 4 days, after which he was discontinued by negative blood cultures. The newborn did not receive antiviral treatment. During the course of the disease, on the sixth day of life, thrombocytopenia was observed with nadir of platelet count at 7 days of life, clotting times within normal limits and increase of oxaloacetic glutamic transaminase. During the time while all studies were carried out, bacterial infection, toxoplasmosis, malaria and infection by other viruses such as dengue, cytomegalovirus, Epstein-Barr and rubella were discarded. On the eighth day of life, she presented supplemental oxygen requirements without evidence of respiratory distress, with normal chest radiographs and no pathological findings to cardiopulmonary auscultation. When the mother was questioned about relevant perinatal events, she reported that at the time of delivery she had fever, malaise, and arthralgia that impeded walking. According to this maternal history and the increasing number of cases in its region of origin, IgM was requested for chikungunya virus, which was positive at 10 days of postnatal life. The patient had a favorable evolution, with improvement of the fever on the fourth day of onset of symptoms and loss of the rash at 13 days of life. Supplemental oxygen was withdrawn and platelet count was increased, with resolution of thrombocytopenia and liver function tests at 14 days of life, without transfusion or other complications. Thus, the newborn was discharged at 8 days of hospitalization. At 6 months of follow-up, the patient was in good health with neurodevelopment according to her chronological age (Table 1).

Table 1. Representative results of the patient

<i>Blood results</i>	
Hemoglobin	16.8 g/dL
Hematocrit	47.1%
Leukocytes	8.900 cells/uL
Neutrophils	62% (5.518 cells/uL)
Lymphocytes	26% (2.314 cells/uL)
Monocytes	3% (267 cells/uL)
Platelets	18.000 /uL
<i>Blood chemistry</i>	
Glutamic oxaloacetic transaminase	177 U/l
Glutamic pyruvic transaminase	30 U/l
Conjugated bilirubin	0.78 mg/dl
Total bilirubin	11.16 mg/dl
<i>Infectious disease results</i>	
IgM Cytomegalovirus	Non reactive
IgG Cytomegalovirus	Reactive
IgM Toxoplasma	Non reactive
IgG Toxoplasma	Reactive
IgM Rubella	Non reactive
IgG Rubella	Reactive
IgM EBV	Negative
IgG Varicela Zoster	Positive
IgM Dengue	Negative
NS1 Dengue Antigen	Negative
IgM Chikungunya	Positive
Malaria thick smear	No parasites visualized

Discussion

The epidemic on La Reunión Island revealed the possibility of mother-to-child transmission of the chikungunya virus when they had the infection 4 days before or 2 days postpartum^{3,7}. Chikungunya virus infection can occur in any trimester of pregnancy, but placental histological lesions are uncommon outside the peripartum period, thence fetal involve-

ment with unfavorable outcomes is rare. The reported cases are of newborns that begin with symptoms during the first week of life, which is compatible with the incubation period of the virus. It is believed that vertical transmissions occur due to placental micro-transfusions during labor in mothers with active viremia^{5,8}. The infection is also possible during the passage through the birth canal, but in cesarean delivery patients have not been considered as a protective factor⁷. There is no evidence that the virus is transmitted through breast milk³.

The clinical manifestations of chikungunya virus infection in adults are nonspecific. However, it is more frequently presented with fever, myalgias and arthralgia in about 90% of cases, where the onset of symptoms coincides with viremia². This explains the risk of transmission in symptomatic women at the time of delivery as presented in the previous case, since it corresponds to the period of major viremia and transmissibility.

The hypothesis of neonatal infection acquired after birth by mosquito bite during the first hours of life should be considered, but it is unlikely since the incubation period is between 4 to 7 days and the clinical manifestations are to be observed after the first week of life^{3,5}.

In the present case the patient had fever, rash, thrombocytopenia and elevation of transaminases, which are alterations that have been described in a high proportion in patients with chikungunya infection², the presence of irritability, pain and edema in the limbs has also been frequently described, although not observed in this case⁷.

In about 60% of chikungunya-infected infants clinical and laboratory manifestations are similar to the classic form described in schoolchildren and adolescents, with a febrile illness associated with exanthema with spontaneous resolution of the disease in 1 to 2 weeks⁵. It is important to demarcate it from dengue infection in the clinical presentation, which may also present fever, but the onset of the clinical picture is more torpid, the rash is less frequent and the joint manifestations are absent. Shock and hypotension may occur more frequently and thrombocytopenia is later and marked³. The key point in chikungunya virus infection lies in increased joint involvement, but this may be difficult to determine in the neonatal population.

Up to 40% of infants present complicated or severe forms of chikungunya⁹, which can be manifested as hemorrhagic fever in patients with severe thrombocytopenia, disseminated intravascular coagulation, impaired liver function, myocarditis, respiratory distress or neurological compromise^{5,9}. Regarding the case described above, liver function tests were normalized and thrombocytopenia resolved at 2 weeks of age.

Neurological complications are variable, from compromise of the state of consciousness, meningoencephalitis, seizures or polyneuropathy^{5,9}. Long-term follow-up of these patients with perinatal chikungunya virus infection has been shown to have an increased risk of global neurodevelopmental delay, especially those with encephalopathy in the neonatal period. The predominant alterations are coordination and language¹⁰.

In our patient, due to severe thrombocytopenia, no lumbar puncture was performed in search of central nervous system compromise, there was no clinical evidence of bleeding or cardiovascular dysfunction. The neurological follow-up of the presented case was at 6 months, but it should have been done at 18 and 24 months ideally by performing Bayley Test.

The positive diagnosis from Laboratory for chikungunya virus is based on viral isolation, detection with real-time polymerase chain reaction of the genome in the viraemic stage, specific IgM serology at the acute time or increase in 4-fold titers of specific IgG. The IgM antibodies are identifiable after the fourth day of onset of the disease, which in our patient established the diagnosis. The IgM being pentameric does not cross the placental barrier and is representative of immune response in the newborn, it can persist positive for several months. IgG is elevated after the second week of disease and can persist for several years¹¹.

Currently, there is no specific treatment for chikungunya virus infection or vaccines to prevent it. Anti-inflammatory drugs can be used to control symptoms, especially osteoarticular manifestations.

Treatment for newborns with suspected chikungunya virus infection is based on supportive measures. Although there has been no documented case of in-hospital transmission of chikungunya virus in neonatal units⁷, isolation with bed mosquito net could be considered in institutions where there is evidence of vectors at the intrahospital level. Due to the potentially fatal manifestations of chikungunya congenital infection, we recommend that the offspring of mothers in the period of near-delivery viremia be closely observed during the first days of life. Since there is no evidence of transmission of the virus through breastfeeding we recommend continuing this during the disease.

The potential benefit of polyvalent human immunoglobulin for disease control has been demonstrated in vitro and in animal models with newborn mice where prophylactic immunoglobulin administration from donors in the convalescent phase of the disease had a protective effect of fatal infection¹². A study is currently ongoing in order to determine the potential benefit of human polyvalent immunoglobulin prophylaxis in children of viremic mothers for fatal events (ClinicalTrials.gov NCT02230163).

Conclusion

Vertical transmission infection of chikungunya virus should be considered within the differential diagnosis in the neonates of mothers with suggestive symptoms in the period near delivery, given the high rate of transmissibility. The clinical course of the disease, the potential serious manifestations in this age group, and the virological and serological studies available to achieve a timely diagnosis and adequate management should be known.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Authors state that no economic support has been associated with the present study.

Conflicts of Interest

Authors state that any conflict of interest exists regards the present study.

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