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ORIGINAL ARTICLE

Cases of Chikungunya virus infecton by vertical transmission in a university hospital in the first half of 2016

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Abstract

The vertical transmission of the Chikungunya virus has a mechanism that is little known, increasing with each outbreak of arboviruses, being the cause of clinical manifestations in the newborn children of mothers who had Chikungunya in the peripartum. **Objective:** To report five cases of Chikungunya vertical transmission and to describe its clinical manifestations. **Method:** A retrospective descriptive study, based on an analysis of records of infants with manifestations that could be attributed to Chikungunya, whose mothers had suspected the disease in the peripartum. Reverse Transcriptase Reaction was performed, followed by Chain Polymerase Reaction - PCR-RT for Chikungunya research in the blood and CSF of infants. Ten patients were searched and five with PCR-RT positive for Chikungunya were found. **Results:** The period of the manifestation of the maternal disease varied from days before delivery until the day of the babies' birth. Two babies had positive CSF and one of them had encephalitis; three had positive RT-PCR in peripheral blood. Babies were term, male. Two had some joint alteration, such as erythema / edema and subluxation of the hip. Three had a fever. One had cutaneous hyperpigmentation and seizure, two presented irritability. Two had bullous lesions throughout the body. Three infants had thrombocytopenia and two changes in transfontanel ultrasonography. **Conclusion:** There are few cases reports of Chikungunya perinatal in Brazil. It is important that the pediatrician is attentive to maternal history in order to suspect this diagnosis against the nonspecific symptoms.

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INTRODUCTION

The chikungunya virus (CHIKV) is an African alphavirus first described in 1952. A series of outbreaks started in 2005 in islands in the Indian Ocean produced numerous cases of acute fever and severe joint pain, in addition to meningoencephalitis. Cases of chikungunya fever once limited to countries in Africa and Western Asia have been described in the Americas and Europe since 2005. Cases of the disease must be monitored and solutions to combat and treat CHIKV infection found and implemented[1].

The first confirmed cases of CHIKV infection in the Americas date back to late 2013. A year later, the disease had spread to most of the islands of the Caribbean and countries in Central, North, and South America, including Brazil. Since the arrival of the virus in the Americas, the Pan American Health Organization (PAHO) has estimated that 1.3 million individuals have the disease, with nearly 30,000 confirmed cases and 184 deaths from CHIKV infection[1].

Incidence has increased with every outbreak of arboviral disease. In 2015, 38,332 probable cases of CHIKV infection were reported in 696 municipalities in Brazil (18.7 cases/100,000 population), 13,236 of which confirmed. Within the same time period, six individuals died of chikungunya fever. In the first semester of 2016, 83,678 probable cases of CHIKV infection were reported in 1,550 municipalities in Brazil (40.9 cases/100,000 population), 15,053 of which confirmed. Incidence was higher in the Brazilian Northeast, more notably in the States of Rio Grande do Norte (273.4 cases/100,000 population), Bahia (196.4 cases/100,000 population), Pernambuco (186.4 cases/100,000 population), and Sergipe (168.1 cases/100,000 population) [2].

Little is known about the vertical transmission of CHIKV infection and the resulting clinical manifestations that may adversely affect infants in the short and long term. The literature on the matter is scarce and the pathophysiology of the disease is mostly unknown. Additionally, the disease is underdiagnosed and underreported[2].

The first cases of vertical transmission were published in 2006, after an outbreak in Reunion Island in 2005, in which 160 females with CHIKV infection were followed. Three of nine miscarriages were attributed to the virus (< 22 weeks of gestational age)[3]. Of the 151 females suspected of CHIKV infection, 118 tested negative at the time of delivery and none of their infants presented symptoms. Thirty-three tested positive at the time of delivery and 16 (48.5%) infants had neonatal infection by CHIKV[3].

Substantial evidence indicates that the chikungunya virus does not cause fetal malformations[4].

CHIKV infection by vertical transmission must be considered in the differential diagnosis of infants presenting clinical signs suggestive of encephalopathy, bullous skin lesions, and perioral hyperpigmentation, particularly in areas where the disease is endemic[5,7].

The study carried out in Reunion Island described cases of neonatal infection by CHIKV with reports of meningoencephalitis and severe skin disorders. The authors of a study performed in Colombia also reported bullous skin lesions in infants aged three months and younger[6].

This report describes five cases of vertical transmission of CHIKV infection confirmed by RT-PCR along with the clinical manifestations and relevant workup alterations found in the infants presenting the disease.

METHOD

This descriptive retrospective study was based on the charts of infants suspected of vertically transmitted CHIKV infection staying at a neonatal intensive care unit. Infants born to mothers diagnosed with CHIKV infection were tested. Symptoms manifested from two days before delivery to the day of delivery.

Reverse transcription-polymerase chain reaction (RT-PCR) tests were run in serum and CSF samples taken from ten infants for dengue, zika, and chikungunya infection. Five infants tested positive for CHIKV and were included in our study.

The serum and CSF samples taken from the ten infants for arboviral disease testing were sent for analysis to a laboratory in our institution in which a study on arboviral diseases had been in progress. The mothers of the participating infants consented in written to joining the study. The Research Ethics Committee of our institution approved the study (Ethics Review Certificate - CAAE: 51057015.5.0000.5537).

RESULTS

Clinical manifestations of the disease were observed in the affected mothers from two days before delivery to the day of delivery. All had symptoms consistent with CHIKV infection such as joint pain, fever, maculopapular rash, and two presented bullous skin lesions.

The infants started presenting symptoms after 48 to 96 hours of life, with fever as the most frequent manifestation (60%).

Neurological events such as seizures and severe irritability were seen in 40% of the cases.

Although thrombocytopenia was the most prominent workup alteration affecting 60% of the infants, none had bleeding disorders while they were hospitalized.

Table 1 shows the signs and symptoms presented by the infants, while Table 2 describes their workup and imaging findings.

DISCUSSION

Little is known about the transplacental transmission of CHIKV. Transmission is believed to occur with the disruption of the placental barrier in the peripartum. Significant viremia in this period may contribute to perinatal infection. Although CHIKV infection has not been linked with fetal malformation, infants infected with the virus may develop significant morbidity including blood and joint disorders, seizures, and encephalitis. Neurocognitive development was not addressed in our study.

Table 1. Signs and Symptoms (n = 5).

Signs and symptoms presented by infants diagnosed with CHIKV infection by vertical transmission	
Joint disorders	2/5
Fever	3/5
Hyperpigmentation	1/5
Bullous lesions	2/5
Seizure	1/5
Irritability	2/5
Microcephaly	1/5

Table 2. Tests (n = 5).

Workup and imaging findings of infants diagnosed with CHIKV infection by vertical transmission.	
PCR-RT por sangue	3/5
PCR-RT por líquor	2/5
PCR-RT por líquor e sangue no mesmo paciente	0/5
Trombocitopenia	3/5
Alteração USTF	2/5
Triagem Auditiva (OEA)	1/5

The subset of individuals with neurological involvement studied in our center showed the following alterations: grade I intracranial hemorrhage (ICH), cortical atrophy, and ventricular dilatation. The infant with seizures developed meningoencephalitis and had altered total CSF protein levels. His fontanelle sonography and head computerized tomography scans showed diffuse cortical atrophy with no evidence of calcification. The same infant also had hyperpigmentation, a finding associated with meningoencephalitis in the literature[5].

One of the patients had poor otoacoustic emission test results and was referred for further auditory examination. He also had syndromic facies, microcephaly without evidence of intracranial calcification, congenital heart disease (interventricular communication), and low weight. This patient was referred for further diagnostic examination for a possible genetic condition.

One of the infants with joint disorders had clinical signs of arthritis, enlarged joint volume, redness, and range-of-motion limitations. The other had a hip subluxation, with a type IIa hip in ultrasound examination and signs of instability during dynamic maneuvers. It is not known whether this alteration is associated with CHIKV infection or if it occurred for unrelated reasons as it would in the general population.

The serous fluid harvested from the lesions of the two infants with bullous lesions tested negative for CHIKV infection.

None of the patients had altered serum and CSF RT-PCR tests concurrently. This indicates that viral infection may have occurred at different times in the patients.

CONSIDERAÇÕES FINAIS

The profile of vertically transmitted infections has changed in recent years. Recent outbreaks of severe diseases transmitted from mothers to their offspring have significantly increased the morbidity of children born to infected mothers, in what constitutes a relevant public health issue. Although little is known about the pathophysiology of vertically transmitted CHIKV infection, the disease has been linked to severe cases of neonatal encephalitis and skin and blood disorders. Infants infected with CHIKV must be followed in the long run so that the actual consequences of infection are identified.

Vertical transmission of CHIKV rarely occurs before 22 weeks of gestation, and studies have shown that the virus cannot cross the placental barrier during exposure before delivery. After 22 weeks of gestation, infection is more frequent in mothers with viremia at the time of delivery[3].

Arthropod-borne viruses must be considered in medical history interviews with pregnant women. It is the task of pediatricians to find suspected cases based primarily on the medical history of the mothers and to then order the tests for the virus in mothers and their infants. The discharge of mothers and their infants must be judiciously examined in cases where the mother has not manifested the disease before or soon after delivery. The start of clinical manifestations in the cases reported herein occurred from 48 to 96 hours after delivery, a reminder of the need to rigorously watch for signs and symptoms of perinatal disease.

We still face significant challenges in defining the etiology of the disease on account of the technical limitations inherent to existing testing methods and difficulties having access to tests. Timely access to tests is also required for diagnostic accuracy.

Cases of the disease must be diligently reported so that actions to minimize the occurrence of CHIKV infection and its future complications can be developed and implemented.

Not much is known about the medium and long-term sequelae of the disease. Therefore, children infected with CHIKV should be followed as they grow and develop so that they are offered early adequate care. Preventing the disease is relevant, as is working to rehabilitate affected children.

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