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Development of Secondary Microcephaly After Delivery: Possible Consequence of Mother-Baby Transmission of Zika Virus in Breast Milk

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Statistical Analysis C
Data Interpretation D
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Patient: —
Final Diagnosis: Diagnosis of secondary microcephaly
Symptoms: 23 days after birth revealed that the baby's head circumference remained at 33 cm (z score=–2.330)
Medication: —
Clinical Procedure: Analysis of samples by reverse transcriptase – polymerase chain reaction (RT-PCR) revealed the presence of ZIKV only in breast milk
Specialty: Pediatrics and Neonatology

Objective: Unusual clinical course
Background: The Zika virus is an arbovirus that has as main source of transmission the bite of infected insects of the genus Aedes and has been associated with cases of congenital malformation and microcephaly in neonates. However, other sources of transmission have been identified since the emergence of this virus in the world population, such as vertical transmission by semen and possibly other body fluids such as vaginal secretion and breast milk.
Case Report: An infant, born to a mother whose previous delivery was a baby with severe microcephaly, was normal and was negative for Zika virus at birth but developed secondary microcephaly 1 month later, that persisted. The baby was exclusively breast-fed and Zika virus was present in the mother's milk.
Conclusions: We report the detection of Zika virus exclusively in the breast milk of a woman after her second delivery of an infant, who later developed microcephaly. This case is consistent with possible vertical transmission.

MeSH Keywords: Arbovirus Infections • Infectious Disease Transmission, Vertical • Milk, Human

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Background

Zika virus, an arbovirus belonging to the *Flaviviridae* family was first described in 1952 in the Zika Forest of Uganda [1]. Infection with Zika virus is responsible for a mild exanthematic disease and most of the cases (about 80%) are asymptomatic. In 2007, a Zika virus outbreak in French Polynesia was associated with neurologic complications, especially Guillain-Barré syndrome [2]. In 2015, the first cases of Zika virus were reported in Brazil. An unexpected rise in congenital microcephaly was noticed, and a link between these 2 occurrences was proposed [3,4]. This association was subsequently confirmed, and the congenital Zika syndrome was described [5]. Viral transmission occurred primarily through mosquito bites, although sexual passage through semen where the virus can persist for up to six months, vertical transmission through the placenta, and by transfusion of blood components was also confirmed [6–8]. Zika virus was also been reported in breast milk, although this mode of transmission to the newborn is still controversial [9,10].

We now report a case of secondary microcephaly in a baby whose mother was positive for Zika virus only in her breast milk and who delivered a prior baby with severe microcephaly.

Case Report

A 30-year-old female became pregnant again 19 months after delivery of a baby with severe microcephaly. The first baby, a girl, was positive for IgG antibody to Zika virus and to chikungunya virus although the mother was antibody-negative to both. The second pregnancy was uncomplicated with 5 normal gestational ultrasounds. A female baby was delivered by cesarean section at a gestational age by ultrasound of 39 weeks and by last menstrual period of 39 weeks and 6 days. Birth weight was 2650 g (z score=–1288); length 47 cm (z score=–1.2831) and head circumference 33 cm (z score=–0.379). All these parameters were considered normal by INTERGROWTH-21st standards. Both mother and baby were negative by STORCH (acronym for disease group comprising syphilis, toxoplasmosis, other infections, rubella, cytomegalovirus infection, and herpes simplex). Blood, saliva, urine, and colostrum were collected for laboratory examinations. Analysis of samples by reverse transcriptase –polymerase chain reaction (RT-PCR) revealed the presence of Zika virus only in breast milk. Both mother and baby were Zika virus-negative by serology and RT-PCR.

The infant was exclusively breastfed since delivery. A re-evaluation at 23 days after birth revealed that the baby's head circumference remained at 33 cm (z score=–2.330). This lack of head growth was consistent with a diagnosis of secondary microcephaly [11] as defined by the World Health Organization. Other possible causes of microcephaly such as abnormal ventricles, craniosynostosis, congenital hypothyroidism, were excluded.

A final evaluation, at 7 months 29 days showed a weight of 8.1 kg; length 68.5 cm and head circumference 40.5 cm, with z scores of 0.20; –0.02; –2.10, respectively. This continued reduced head growth confirmed the diagnosis of secondary microcephaly. Additional neurological examinations were all normal.

Discussion

After the 2015 Zika virus outbreak in Brazil, many cases associating microcephaly with Zika virus infection were reported. Subsequent studies were conducted to define the mechanism(s) of mother-fetal transmission and identify additional neurological consequences for the fetus. Considering that Zika virus can be transmitted vertically or intrapartum/perinatally, it is difficult to define when transmission occurs.

Colt et al. reported the presence of Zika virus RNA in breast milk from 3 infected mothers. Two of the babies had evidence of Zika virus exposure by serology and/or by its transient detection in urine. All 3 babies remained healthy and asymptomatic [12]. In the present case, while there was no molecular or immunological evidence of Zika virus in the newborn. Her development of secondary microcephaly only after delivery, the exclusion of other apparent causes, and the development of Zika virus-related severe microcephaly in a previous baby from the same mother strongly suggests that the baby became infected with Zika virus that affected brain development after ingestion of breast milk. Reasons for the mother's failure to respond immunologically to Zika virus are unknown. She was not immunosuppressed and had normal levels of antibodies to other infectious agents. The mother's possible exposure to other flaviviruses might have masked or diminished her immune response to Zika virus reinfection prior to her second pregnancy and a possible mechanism for intra-familial transmission of Zika virus might have been Zika virus persistent infection in her partner's semen. It remains to be determined if Zika virus was present in her milk as a free virus or was associated with macrophages, lymphocytes, or other cells. Unfortunately, in the present case we were unable to evaluate these possibilities.

Differences in the severity of microcephaly in the 2 babies might have been due to the simultaneous present of a second flavivirus, chikungunya virus, in the first but not the second neonate. Concurrent infection by more than one flavivirus has been shown to alter immune responses [13].

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Conclusions

Detection of Zika virus exclusively in breast milk after a second delivery, coupled with the child being born healthy but developing microencephaly only 1 month after delivery which persisted to date, was consistent with the possible transmission of Zika virus to the baby in breast milk and the initiation of neurological damage only after birth. The World Health Organization continues to support breastfeeding, considering the benefits of this practice, even for those mothers with suspected or confirmed Zika virus infection [14]. Further studies are needed to better define the dynamics of Zika virus transmission via breast milk and its potential harm to newborns.

Ethical approval

Our data were obtained under the Cohort Zika Jundiaí Consortium, already approved on ethical committee (CAAE 53248616200005412); Research Ethics Review Committee (WHO ERC), World Health Organization (ZIKV100/2018).

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Conflict of interest

The authors declare no conflict of interest.

References:

1. Dick GW, Kitchen S, Haddow A: Zika virus (I). Isolations and serological specificity. Trans R Soc Trop Med Hyg, 1952; 46(5): 509–20
2. Oehler E, Watrin L, Larre P et al: Zika virus infection complicated by Guillain-Barré Syndrome – case report, French Polynesia, Dec 2013. Euro Surveill, 20146; 19: 9
3. Zanluca C, Melo VC, Mosimann Al et al: First report of autochtonous transmission of Zika virus in Brazil. Mem Inst Oswaldo Cruz, 2015; 110: 569–72
4. European Centre for Disease Prevention and Control. Microcephaly in Brazil potentially linked to the Zika virus epidemic [Internet]. Stockholm: ECDC; 2015 [cited 2018 Oct 9]. Available from: *https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/zika-microcephaly-Brazil-rapid-risk-assessment-Nov-2015.pdf*
5. Moore CA, Staples JE, Dobyns WB et al: Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. JAMA Pediatr, 2017; 171(3): 288–95
6. Atkinson B, Thornburn F, Petridou C et al: Presence and persistence of Zika virus RNA in semen, United Kingdom, 2016. Emerg Infect Dis, 2017; 23(4): 611–15
7. Motta IJF, Spencer BR, Silva SGC et al: Evidence for transmission of Zika virus by platelet transfusion. N Engl J Med, 2016; 375(11): 1101–3
8. Bouef P, Drummer HE, Richards JS et al: The global threat of Zika virus to pregnancy: Epidemiology, clinical perspectives, mechanisms, and impact. BMC Med, 2016; 14(1): 112–20
9. Mann TZ, Haddad LB, Williams TR et al: Breast milk transmission of Flaviviruses in the context of Zika Virus: A systematic review. Paediatr Perinat Epidemiol, 2018; 32(4): 358–68
10. Giovanetti JX, Goes de Jeses J, Lima de Maia M et al: Genetic evidence of Zika vírus in mother's breast milk and body fluids of a newborn with severe congenital defects. Clin Microbiol Infect, 2018; 24(11): 1111–12
11. von der Hagen M, Pivarcsi M, Liebe J et al: Diagnostic approach to microcephaly in childhood: a two-center study and review of the literature. Dev Med Child Neurol, 2014; 56: 732–41
12. Colt S, Garcia-Casal MN, Peña-Rosas JP et al: Transmission of Zika virus through breast milk and other breastfeeding-related bodily fluids: A systematic review. PLoS Negl Trop Dis, 2017; 11(4): e0005528
13. Badolato-Correa I, Sanchez-Arcila IC, Alves de Souza TM et al: Human T cell responses to Dengue and Zika virus infection compared to Denhue/Zika coinfection. Immun Inflamm Dis, 2018; 6: 194–206
14. World Health Organization: Guideline: Infant feeding in areas of Zika virus transmission. Geneva, 2016

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