Evidence of Zika Virus Infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses — Brazil, 2015

Roosecelis Brasil Martins, MD, PhD1; Julu Bhatnagar, PhD1; M. Kelly Keating, DVM1; Lucian Silva-Flannery, PhD1; Atis Muehlenbachs, MD, PhD2; Joy Gary, DVM, PhD1; Cynthia Goldsmith, MS1; Gillian Hale, MD1; Jana Ritter, DVM1; Dominique Rollin, MD1; Wun-Ju Shieh, MD, PhD1; Kleber G. Luz, MD, PhD2; Ana Maria de Oliveira Ramos, MD, PhD3; Helaine Pompeia Freire Davi, MD, PhD4; Wanderson Kleber de Oliveira, MD5; Robert Lanciotti, PhD6; Amy Lambert, PhD6; Sherif Zaki, MD, PhD1

On February 10, 2016, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

Zika virus is a mosquito-borne flavivirus that is related to dengue virus and transmitted primarily by Aedes aegypti mosquitoes, with humans acting as the principal amplifying host during outbreaks. Zika virus was first reported in Brazil in May 2015 (1). By February 9, 2016, local transmission of infection had been reported in 26 countries or territories in the Americas.* Infection is usually asymptomatic, and, when symptoms are present, typically results in mild and self-limited illness with symptoms including fever, rash, arthralgia, and conjunctivitis. However, a surge in the number of children born with microcephaly was noted in regions of Brazil with a high prevalence of suspected Zika virus disease cases. More than 4,700 suspected cases of microcephaly were reported from mid-2015 through January 2016, although additional investigations might eventually result in a revised lower number (2). In response, the Brazil Ministry of Health established a task force to further investigate possible connections between Zika virus infection and microcephaly and fetal demise through detection of viral RNA and antigens in brain tissues from infants with microcephaly and placental tissues from early miscarriages. Histopathologic findings indicate the presence of Zika virus infection in fetal tissues. These findings also suggest brain and early gestational placental tissue might be the preferred tissues for postmortem viral diagnosis. Nonfrozen, formalin-fixed specimens or FFPE blocks are the preferred sample type for histopathologic evaluation and immunohistochemistry, and RT-PCR can be performed on either fresh frozen or formalin-fixed specimens. To better understand the pathogenesis of Zika virus infection and associated congenital anomalies and fetal death, it is necessary to evaluate autopsy and placental tissues from additional cases, and to determine the effect of gestational age during maternal illness on fetal outcomes.

For both newborns, significant histopathologic changes were limited to the brain, and included parenchymal calcification, microglial nodules, gliosis, and cell degeneration and necrosis. Other autopsy tissues and placenta had no significant findings. Tests for toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and HIV were negative in the two mothers who experienced miscarriages. Placental tissue from one miscarriage showed heterogeneous chorionic villi with calcification, fibrosis, perivillous fibrin deposition, and patchy intervillitis and focal villitis, while tissue from the other miscarriage had sparsely sampled normal-appearing chorionic villi.

This report describes evidence of a link between Zika virus infection and microcephaly and fetal demise through detection of viral RNA and antigens in brain tissues from infants with microcephaly and placental tissues from early miscarriages. Histopathologic findings indicate the presence of Zika virus in fetal tissues. These findings also suggest brain and early gestational placental tissue might be the preferred tissues for postmortem viral diagnosis. Nonfrozen, formalin-fixed specimens or FFPE blocks are the preferred sample type for histopathologic evaluation and immunohistochemistry, and RT-PCR can be performed on either fresh frozen or formalin-fixed specimens. To better understand the pathogenesis of Zika virus infection and associated congenital anomalies and fetal death, it is necessary to evaluate autopsy and placental tissues from additional cases, and to determine the effect of gestational age during maternal illness on fetal outcomes.

Updated information about local transmission of Zika virus is available online (http://www.cdc.gov/zika/geo/index.html).


