AMERICAN ACADEMY™
OF OPHTHALMOLOGY

Expanded Spectrum of Congenital Ocular Findings in Microcephaly with Presumed Zika Infection

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Purpose: To describe the ocular findings of 3 cases of suspected congenital Zika viral infection with microcephaly and maculopathy.

Design: Retrospective, consecutive case series.

Participants: Three male infants born in northern Brazil whose mothers demonstrated a viral syndrome during the first trimester and who subsequently were born with microcephaly.

Methods: Observational report of macular findings.

Main Outcome Measures: Continued observation.

Results: Three male infants were born with microcephaly to mothers who had a viral syndrome during the first trimester of gestation in an area that subsequently has demonstrated epidemic Zika infection, a flavivirus related to Dengue. Ocular examination was performed. All 6 eyes demonstrated a pigmentary maculopathy ranging from mild to pronounced. In 4 eyes, well-delineated macular chorioretinal atrophy with a hyperpigmented ring developed. Three eyes demonstrated vascular tortuosity and 2 eyes demonstrated a pronounced early termination of the retinal vasculature on photographic evaluation. Two eyes demonstrated a washed out peripheral retina with a hypolucent spot. One eye had scattered subretinal hemorrhages external to the macula. Finally, 1 eye demonstrated peripheral pigmentary changes and clustered atrophic lesions resembling grouped congenital albinotic spots (polar bear tracks).

Conclusions: Zika virus has been linked to microcephaly in children of mothers with a viral syndrome during the first trimester of pregnancy. Ocular findings previously described a pigmentary retinopathy and atrophy that now can be expanded to include torpedo maculopathy, vascular changes, and hemorrhagic retinopathy. Ophthalmologic screening guidelines need to be defined to determine which children would benefit from newborn screening in affected regions. *Ophthalmology 2016;■:1–7 © 2016 by the American Academy of Ophthalmology.*

The southern region of the Americas, Brazil in particular, has experienced an outbreak of Zika viral infection transmitted by the *Aedes* species of mosquito. Originally identified in Uganda in 1947,[1] Zika is a flavivirus related to Dengue and yellow fevers. In the past year, it has been associated with an outbreak of microcephaly and Guillain-Barré syndrome in Brazil. Three cases of maculopathy along with microcephaly were recently reported in children with suspected congenital Zika infection.[2] The authors followed up with a larger case series of 10 patients with microcephaly who were noted to have 17 affected eyes, with findings including focal pigment mottling, chorioretinal atrophy, optic nerve abnormalities, iris coloboma, and lens subluxation.[3] We report herein 3 cases of chorioretinal maculopathy and expanded pigmentary and hemorrhagic retinopathy in children with microcephaly and suspected congenital Zika infection.

Methods

Three consecutive cases of congenital microcephaly with chorioretinal atrophy and pigmentary maculopathy are described in infants of mothers who had viral syndrome findings of fever, rash, and asthenia consistent with Dengue fever in an endemic area during the first trimester of pregnancy. The infants underwent a full ophthalmologic examination with wide-angle fundus photography (RetCam Shuttle; Clarity Medical Systems, Pleasanton, CA) as part of microcephaly evaluation. The institutional review board (Stanford University, Palo Alto, CA) ruled that approval was not needed for this study.

Results

Patient 1

A male infant with microcephaly (head circumference, 28 cm; Fig 1A) was born after 39 weeks of gestation (birth weight, 2750 g) in November 2015. The mother was in Pernambuco (Northeastern Brazil) during pregnancy, where she was diagnosed with Dengue fever, without serologic testing. The antenatal test results were negative for human immunodeficiency virus (HIV) and Venereal Disease Research Laboratory (VDRL) test.

Cranial computed tomography demonstrated lissencephaly, diffuse parenchymal calcifications, and ventriculomegaly. Fundus examination demonstrated focal chorioretinal atrophy in the periphery of both eyes as well as 2 well-delineated chorioretinal atrophic

http://dx.doi.org/10.1016/j.ophtha.2016.05.001
ISSN 0161-6420/16

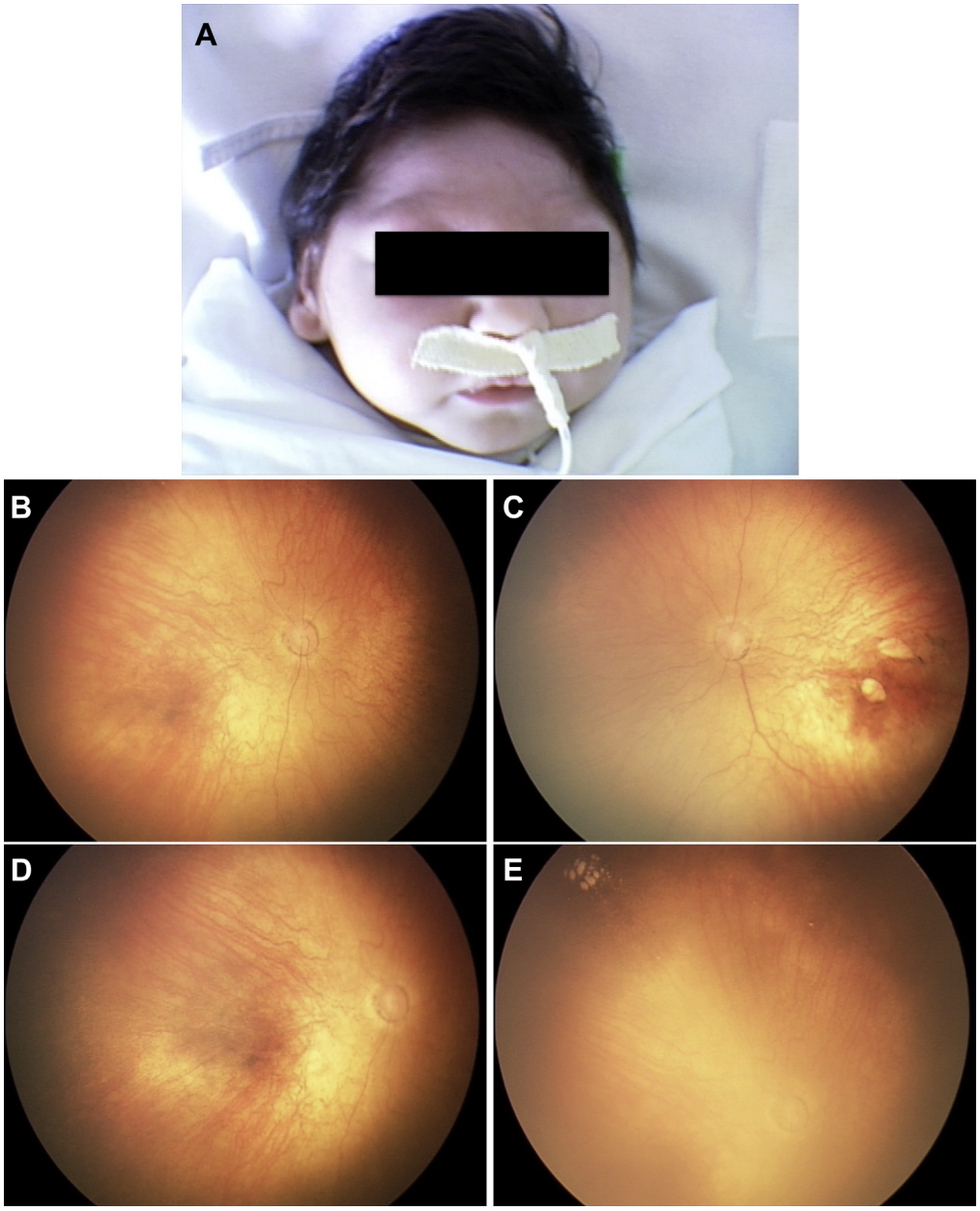

Figure 1. **A**, Characteristic features of microcephaly. **B**, **C**, Fundus photographs showing bilateral mild pigmentary retinopathy affecting the macula of each eye: (**B**) vascular tortuosity in the right fundus and (**C**) 2 well-delineated ovoid lesions with temporal pointed tails in the fovea and just superior in the left eye. **D**, Fundus photograph of the right eye demonstrating early termination of the retinal vessels. **E**, Fundus photograph of the left eye demonstrating polar bear tracks in the superonasal area. **F**, Fundus photograph showing vaso-obliteration of the retinal vasculature temporally in the right eye (left of the dotted line) with the underlying choroid clearly visible. **F**, **G**, **H**, **I**, Fundus photographs of both the right and left eyes showing a washed-out or mottled retina with faint hypolucent spots that resemble peau d'orange in the peripheral retina (arrows).

lesions with temporal pointed tails, 1 ovoid lesion in the fovea, and a more torpedo-shaped lesion just in the superotemporal region in the left eye. Both eyes had mild spicular hyperpigmentation scattered throughout the macula (Fig 1B, C). The temporal retinal vasculature appeared to be absent, with extensive vascular tortuosity in the right eye (Fig 1B [left of the dotted line], D, F). There were grouped congenital albinotic spots in the superonasal region of the left eye (Fig 1E), as well as vascular tortuosity (Fig 1C, E). There was a washed-out appearance of the peripheral retina in the inferior and nasal regions in the right eye and in the temporal region in the left eye, with faint hypolucent spots (Fig 1F–I, arrows).

Patient 2

A male infant with microcephaly (head circumference, 26 cm; Fig 2A) was born prematurely after 34 weeks of gestation (birth weight, 1495 g) in November 2015. The mother was in Pernambuco during the 13th week of pregnancy, where she had a viral illness with fever, rash, and asthenia, requiring hospitalization for 4 days. The antenatal test results were negative for VDRL, HIV, toxoplasmosis, and cytomegalovirus immunoglobulin M antibody. The cytomegalovirus immunoglobulin G antibody concentration was 204.8 IU/ml.