Case Report

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Multiple Mechanisms Of Visual Impairment In Congenital Zika Syndrome.

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Running Title:
Visual impairment in Congenital Zika Syndrome

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ABSTRACT

Purpose: To describe and analyze the involved mechanisms of visual impairment in a patient with microcephaly and presumed Congenital Zika Syndrome.
Settings and study design: This is a clinical case presentation and was carried out at CAVIVER, a non-governmental organization clinic for children with visual impairment in the city of Fortaleza CE, located in the Northeast region of Brazil. The ophthalmological evaluation included retinoscopy, slit-lamp examination, binocular indirect ophthalmoscopy, eye fundus digital imaging, visual acuity testing with Teller acuity cards and strabismus assessment.
Casereport: A 13 months-old girl was referred to the ophthalmological clinic presenting microcephaly. Head circumference at birth was 26cm. Ophthalmologic abnormalities included: macular circumscribed chorioretinal atrophy, focal mottled retinal pigment epithelium, optic nerve hypoplasia with double ring sign, early onset strabismus (exotropia), nystagmus and low visual acuity. Macular atrophic scar and optic nerve hypoplasia with a double ring sign were present in both eyes. Refractive error of -14.00 sph -2.50 cyl (180º) in both eyes was detected. Vision function and visual developmental milestones analysis were abnormal.
Conclusion: Multiple mechanisms as anatomical, neurological, optical and functional abnormalities lead to severe visual impairment in this patient with microcephaly due to presumed Congenital Zika Syndrome.

Keywords : Microcephaly, Congenital Zika Syndrome, low vision, visual impairment, macular atrophy.

INTRODUCTION

A large number of newborns were affected during the Zika virus outbreak occurred in some Northeast regions of Brazil during the years 2015 and 2016 (1).
The characterization of Congenital Zika Syndrome (CZS) and recognition of this phenotype is necessary in order to allow the clinical diagnosis of this entity. The main features, as major signs, that differentiate CZS from other congenital infections are: 1. microcephaly with craniofacial disproportion, narrow and laterally depressed frontal bone and occipital prominence with abnormal skull morphology; 2. central nervous system malformation, thin cerebral cortex with subcortical calcifications; 3. macular scarring; 4. congenital contractures or arthrogryposis; and 5. early hypertonia and extrapyramidal involvement (2).
The most frequent ocular anomalies found in this group of affected patients are macular scarring with chorioretinal areas of atrophy, mottled retinal pigment epithelium changes, optic nerve hypoplasia, strabismus, nystagmus, and low vision (3-5).
This case report aims to describe the ophthalmological features and to analyze the associated mechanisms causing visual impairment in a patient with microcephaly by presumed CZS.

CASE REPORT

A 13 months-old girl presenting microcephaly was referred to the CAVIVER Eye Clinic, a non-governmental organization

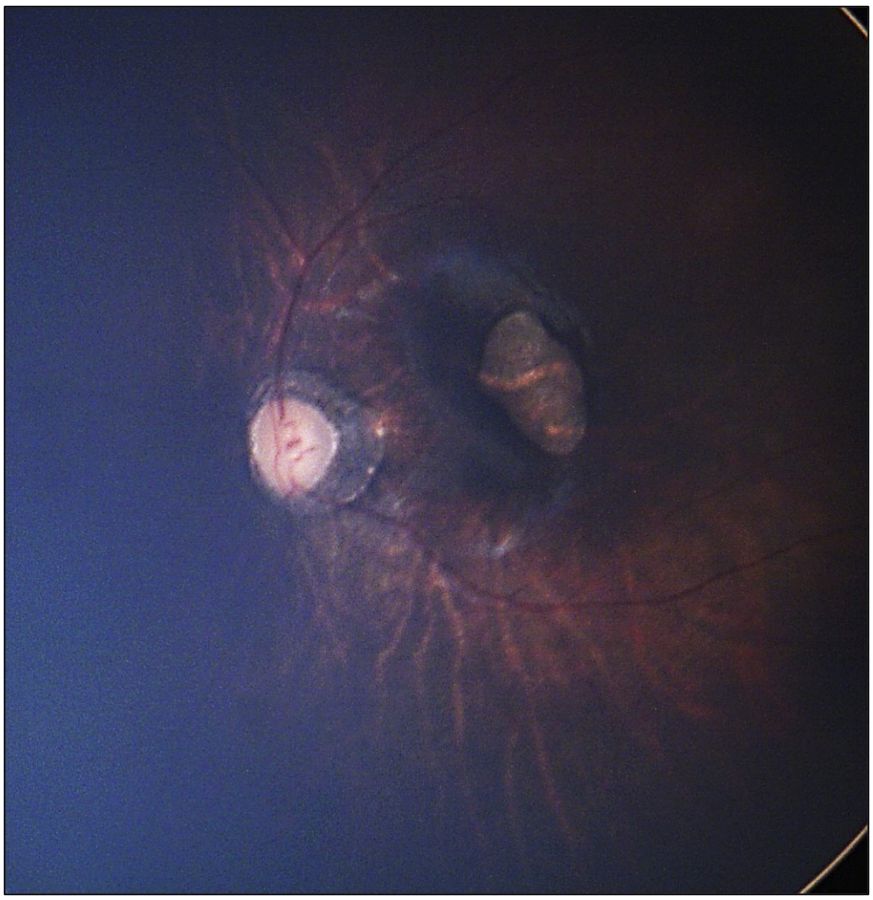
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institute for children with visual impairment in the city of Fortaleza CE, located in the Northeast region of Brazil. Her head circumference at birth was 26 cm. Genetic and infectious diseases were analyzed and tested as causes of microcephaly and were ruled out.

A comprehensive ophthalmologic evaluation was performed including retinoscopy, ocular motility, slit-lamp examination, indirect binocular ophthalmoscopy, and wide-angle digital fundus imaging with the RetCam (RetCam® Shuttle; Clarity Medical Systems). Visual acuity (VA) was evaluated with the Teller Acuity Cards Test (Teller Acuity Cards™ II) performed at 38 cm and paired according to the matched age reference table. Functional vision was analyzed and strabismus assessment was performed.

Anterior segment analysis was normal without corneal, iris or lens abnormalities. Circumscribed macular atrophic scar and optic nerve hypoplasia with a double ring sign were present in both eyes. Myopic changes and mottled pigment dispersion of posterior pole were observed. Fundus digital images were obtained (**Figure 1**). Large angle exotropia and nystagmus were detected.

Figure 1. Fundus digital image of the related 13 months-old girl showing macular circumscribed chorioretinal atrophy.



The refractive status was -14.00 sph -2.50 cyl (180º) in both eyes. Lack of accommodation was detected by dynamic retinoscopy evaluation. Visual acuity was 20/360 (bellow normative tolerance limit for age matched) in both eyes. Functional vision was below normal developmental milestones for the patient age matched.

Neuroimaging study by brain computerized tomography (CT scan) confirmed microcephaly, brain abnormalities and subcortical areas of calcification. The patient also presented arthrogryposis and motor disabilities with some degree of hypertonia.

DISCUSSION

This report discusses a case involving a child CZS who presented multiple associated mechanisms contributing to severe visual impairment. While retinal and optic nerve abnormalities are common causes of vision loss, previous studies suggest that children with CZS may experience visual impairment even in the absence of such abnormalities (6). The child in this case exhibited associated clinical conditions, including neurological, anatomical, and functional alterations in both eyes and in the central nervous system. Additionally, global neurological and cognitive developmental delays, along with motor disabilities, were

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evident. These findings indicate that central or cerebral visual impairment (CVI) could be a significant factor contributing to visual impairment in children with presumed CZS.

The patient presented with microcephaly and severe brain malformation associated with significant ocular anatomical alterations, including high myopia, bilateral macular scarring, and optic nerve hypoplasia. These conditions contribute to major visual dysfunctions, such as nystagmus, a large-angle exotropia, lack of accommodation, absence of stereopsis, and low vision. These characteristics directly impact visual functionality significantly limiting visual integration.

Vision function and functional visual developmental milestones tests results below age range matched scores. Surprisingly the child presented visual responses and social smile to parents and siblings. The patient was referred to a specific early vision intervention program, with a multidisciplinary team specialized and trained in the care of children with CZS.

Global and motor delay may limit the child's response to vision testing. Fatigue, irritability, seizures and use of anti-convulsant medication may interfere with vision function and test results (7-9).

While it is expected that these children will have normal lifespans, they are likely to be severely limited in their functional skills and require constant care. However, almost nothing is known regarding capacities attainment in children with CZS, or the factors that contribute to variability in outcomes. In a previous related assessment in children with CZS, none of the infants were able to demonstrate any age-appropriate visual development milestones (3,4). These findings highlight the importance of interventions aimed at promoting verbal exchanges between caregivers and infants and exploring methods for children to effectively communicate and express their desires and needs. Research on early brain development indicates that visual and hearing pathways develop first, serving as a foundation for communication and cognitive functions. Another Brazilian study conducted in children with presumed CZS born with microcephaly revealed significant neurodevelopmental delays, impacting language acquisition, gross and fine motor skills, and social and personal development (10).

The long-term developmental outcomes for infants with CZS remain uncertain but are anticipated to be severe due to documented brain and central nervous system dysfunctions presented in long-term follow-up of prospective cohorts. Nevertheless, these children will continue to grow and develop, making it essential to understand the developmental skills they can acquire to tailor appropriate interventions over time.

These children should undergo annual neurodevelopmental evaluations until school age and regular eye assessments in the first years of life. As CZS is a newly identified condition, close monitoring and comparisons with age-matched uninfected peers living in similar environments are crucial. Additionally, programs targeting daily abilities and activities must be integrated into their care plans (3).

The overlapping mechanisms of visual impairment – spanning structural, neurological and developmental factors – are challenging to disentangle, emphasizing the need for future detailed research and longitudinal studies to better understand how these factors interconnect and impact visual development in affected children.

CONCLUSIONS

Many associated ocular and neurological clinical manifestations contribute to visual impairment in this patient with CZS. Macular circumscribed chorioretinal atrophy, focal mottled retinal pigment epithelium changes, optic nerve hypoplasia, high refractive error, and severe brain malformation were detected. The combination of anatomical, optical, and neurological manifestations leads to visual function abnormalities such as nystagmus, large angle exodeviation, lack of accommodation, and absence of depth perception, that resulted in severe visual impairment in this patient with microcephaly due to CZS.

It is extremely advisable to refer these children with CZS to specialized early global intervention programs.

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