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Choriocapillaris Loss in a Pediatric Patient With Congenital Cytomegalovirus Seen on Optical Coherence Tomography Angiography

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Abstract

Purpose: To describe choriocapillaris loss on optical coherence tomography angiography (OCTA) imaging in a pediatric patient with congenital cytomegalovirus (CMV). **Methods:** A case was evaluated. **Results:** A 7-year-old female patient was referred for retinal evaluation of maculopathy in the right eye. She was diagnosed with congenital CMV at 14 months of age, at which time treatment was not deemed necessary. At 7 years of age, the patient was asymptomatic with 20/20 Snellen visual acuity. Funduscopy and colored fundus photographs showed macular scarring. Ancillary testing was performed, with retinal pigment epithelium alterations and disruption of the outer retinal layers seen on OCT and choriocapillaris loss in the area of the macular scar seen on OCTA. **Conclusions:** For patients with congenital CMV, OCTA imaging can show significant changes in choriocapillaris function. These changes do not necessarily correlate with visual function parameters. OCTA may be useful as an additional screening or surveillance modality for patients with congenital CMV or CMV retinitis.

Keywords

congenital cytomegalovirus, optical coherence tomography angiography, optical coherence tomography, macular scar

Introduction

Congenital cytomegalovirus (CMV) is the most common intrauterine viral infection in the United States.[1] Ophthalmologically, congenital CMV most commonly manifests as chorioretinitis, optic atrophy, cortical visual impairment, or strabismus.[2,3] Ocular disease in newborns with congenital CMV has a reported incidence ranging from 5% to 30% and can have devastating visual consequences.[3] The most recent large study of outcomes of patients with congenital CMV found that 7.5% of patients (14/186) with congenital CMV developed visual impairment categorized as severe (visual acuity [VA] worse than 20/200).[2]

CMV has a tropism for neural stem cells, which accounts for its devastating effects on the developing brain and retina.[4,5] Chorioretinal scars in patients with congenital CMV are thought to be evidence of previous CMV chorioretinitis. Chorioretinal scars in these patients are typically considered stable; however, in rare cases patients develop progressive chorioretinitis after birth or late disease reactivation.[6–9]

The pathogenesis of CMV retinitis is thought to be mediated through viral spread to the choroid and retinal pigment epithelium (RPE), with resultant disruption of Bruch membrane and spread of infection from the outer to the inner retinal layers.[5,10] Imaging modalities that highlight chorioretinal blood flow, such as optical coherence tomography angiography (OCTA), may therefore help delineate the pathologic changes seen in congenital ocular CMV and CMV retinitis.

The current reported OCTA findings in CMV retinitis are limited to immunocompromised adults with acquired disease, with this population showing decreased retinal vessel density.[11,12] Whether these findings are applicable to pediatric patients with congenitally acquired CMV is not known. To our knowledge, there is no literature describing OCT or OCTA findings in pediatric patients with congenital CMV. In this case report, we present a pediatric patient with congenital CMV with findings of a macular scar and corresponding choriocapillaris loss on OCTA imaging.

Case Report

A 14-month-old female patient was referred for retinal evaluation of maculopathy in the right eye. Her medical history was significant for mild gross motor delay and congenital bilateral sensorineural hearing loss, for which she had bilateral cochlear

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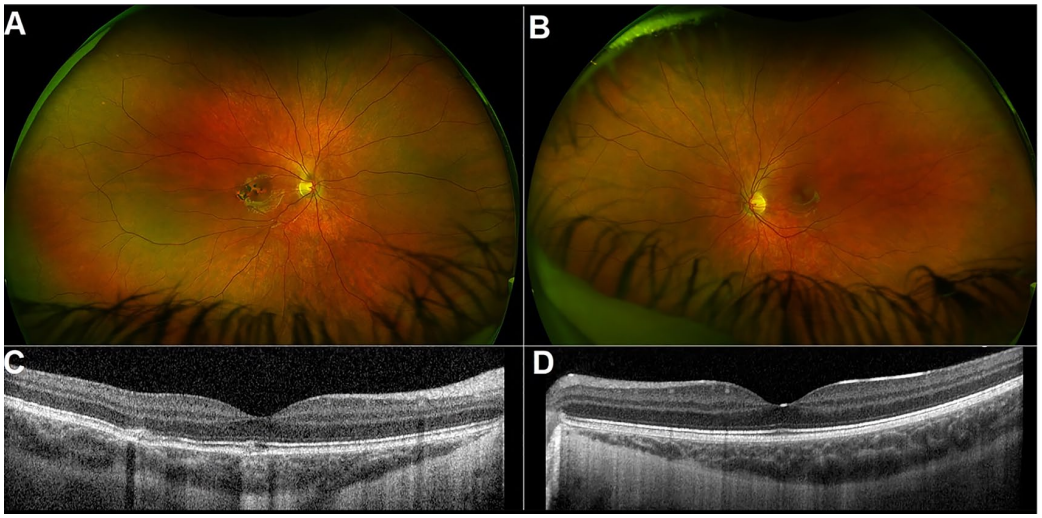

Figure 1. Color fundus photographs of a 7-year-old girl with congenital cytomegalovirus show (A) a stellate-pattern macular scar with well-pigmented margins in the right eye and (B) a normal left eye. Optical coherence tomography shows (C) multiple areas of retinal pigment epithelium and outer retinal disruption with hypertransmission corresponding to atrophy in the right eye and (D) a normal left eye.

implantation. Her additional birth history was unremarkable aside from a maternal history of gastroenteritis at 8 weeks of gestation and a positive group B *Streptococcus* status during delivery. A neurologic evaluation with brain magnetic resonance imaging showed bilateral symmetric white-matter abnormalities affecting the subcortical and deep white-matter structures, predominantly in the temporal lobes. Subsequently, leukoencephalopathy and congenital infection with toxoplasmosis, rubella, CMV, herpes simplex, or other agents were considered in the differential diagnosis.

A baseline ophthalmic examination showed a Snellen VA of 20/89 OD and 20/94 OS. Funduscopy of the right eye showed a stellate-pattern macular scar with well-pigmented margins. The left fundus was unremarkable. Further evaluation with electroretinography (ERG) showed mild but significant deficits in scotopic and photopic responses. Given the examination findings and the patient's history of congenital bilateral sensorineural hearing loss, a serum CMV immunoglobulin G level was obtained and was elevated at 7.50. Subsequently, a polymerase chain reaction from the newborn dried blood spots confirmed a diagnosis of congenital CMV infection. At this stage, no CMV-specific treatment was deemed necessary by the infectious disease consultants. Nine months later, a neurologic follow-up evaluation was performed, showing resolution of the patient's gross motor delays and a significant improvement in her speech skills after implantation of the cochlear devices.

When evaluated at 7 years of age, the patient's Snellen VA was 20/20 bilaterally. A dilated fundus examination showed an unchanged macular scar in the right eye (Figure 1A) and a normal left fundus (Figure 1B). OCT showed multiple areas of RPE and outer retinal disruption with hypertransmission corresponding to atrophy in the right eye (Figure 1C). OCT was normal in the left eye (Figure 1D). Moreover, loss of choriocapillaris and choroidal vessels corresponding to the macular scar in the right eye were seen on OCTA (Figure 2, A and B).

Conclusions

Retinal pathologies are one of the most common ocular manifestations of congenital CMV. A recent meta-analysis of children with ocular manifestations of CMV found chorioretinitis, macular scars, or peripheral retinal scars in 29% of children (75/259) with symptomatic congenital CMV (defined as any systemic manifestation of CMV) and in 23.4% of children (11/47) with asymptomatic congenital CMV.[13] The percentage of macular scars in the 2 groups was 2.3% (6/259) and 12.8% (6/47), respectively. Although a dilated fundus examination remains the gold standard for evaluation of retinal pathology secondary to congenital CMV, new imaging modalities can deepen the understanding of the implications of congenital CMV on the developing retina and also detect subtle, previously undetected signs of retinal pathology.

Our pediatric patient had RPE changes and outer retinal disruption on OCT and corresponding choriocapillaris loss on OCTA observed several years after confirmation of the congenital CMV diagnosis, with long-term retinal changes likely caused by previous chorioretinitis. Mild ERG deficits were seen. Fortunately, however, our patient's VA was unaffected.

Although no published cases of macular scars secondary to congenital CMV have previously been analyzed via OCT and OCTA, we can integrate our findings within the broader realm of acquired CMV retinitis. In patients with resolving CMV retinitis, a study using serial spectral-domain OCT images of eyes with full-thickness retinitis showed that these eyes ultimately developed choriocapillaris atrophy, choroidal thinning, and retinal scars in the area of the previously active lesions.[14]

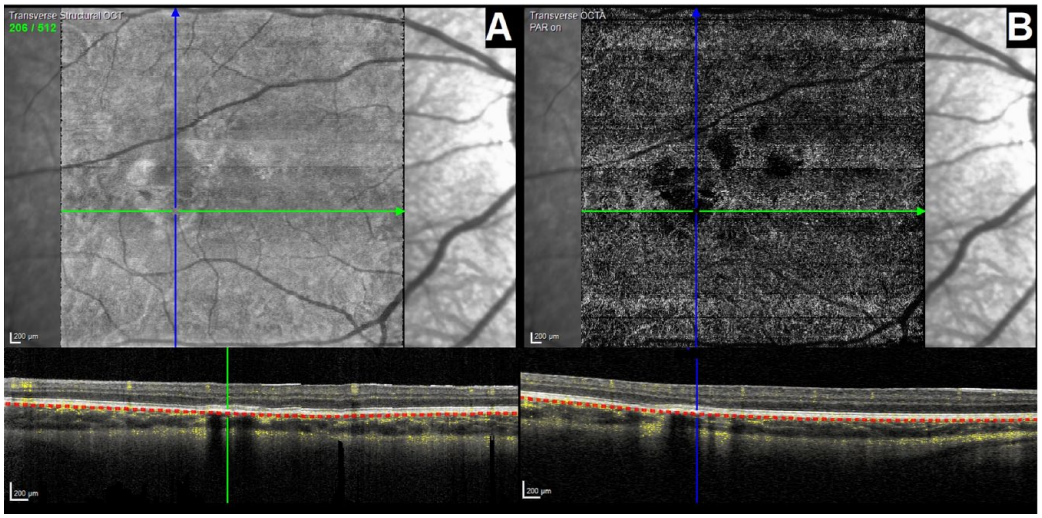

Figure 2. Optical coherence tomography angiography (OCTA) shows choriocapillaris flow deficits in the area of the macular scar in the right eye. (A) Structural en face swept-source OCT (SS-OCT) shows hyperreflective areas corresponding to areas of outer retinal disruption. En face SS-OCTA at the level of the choriocapillaris shows several areas of hypointense flow deficits corresponding to the atrophic macular scar.

Chorioretinal vasculature has been previously analyzed in patients with active and inactive CMV retinitis using fluorescein angiography (FA) and indocyanine green angiography (ICGA). Ueda et al[15] assessed both imaging modalities in an adult patient with active CMV retinitis as well as atrophic lesions. The active lesions showed hypofluorescence in the early and late phases on both FA and ICGA, consistent with chorioretinal inflammation, while atrophic lesions showed staining on FA and ICGA consistent with RPE injury and choroidal damage. Tagami et al[16] described FA changes in a patient with symptomatic congenital CMV who did not have chorioretinitis but who showed major retinal vascular occlusions and arteriovenous anastomoses on FA that regressed after treatment with systemic ganciclovir.

OCTA is a relatively new, noninvasive imaging technique that can provide detailed 3-dimensional visualization of chorioretinal blood flow vs the 2-dimensional visualization provided by FA and ICGA. With OCTA, a dye injection is not required, which is especially relevant in a pediatric population. Two studies have described OCTA findings in acquired CMV retinitis in immunocompromised individuals. Both showed decreased retinal vessel density in the superficial and deep capillary plexuses of the macula, even in eyes without macular involvement.[11,12] This suggests that subtle vascular changes may be present in patients with ocular manifestations of congenital CMV, even if a macular scar is not present. Du et al[11] also investigated vascular changes in the choroid in both active and inactive CMV retinitis and found a decrease in the foveal choroidal vascular index, which is also used to quantify changes in the vascular status of the choroid in patients without macular involvement. In our case, the choriocapillaris dropout could be related to the macular scar. Previous studies of macular scarring related to other infectious etiologies such as toxoplasmosis and *Candida*[17–20] or noninfectious etiologies such as age-related macular degeneration[21] reported a decrease in perfusion of choriocapillaris that coexisted with scarring of the macula.

The choriocapillaris loss exhibited on OCTA in our case thus aligns with what was observed in these studies of adult populations, indicating permanent anatomic changes in chorioretinal vasculature secondary to CMV. Additional studies consisting of a larger sample with congenital CMV are warranted to further describe findings in pediatric populations, including in those with or without macular scars.

Given the findings of subtle vascular changes in the macula in adult patients with CMV retinitis, even without macular involvement, evaluating pediatric patients with chorioretinitis related to congenital CMV would elucidate whether similar or more pronounced findings are present when the virus is acquired earlier during retinal development. Because of enhanced awareness, expanded maternal and newborn screenings, and improved availability of viral genome tests, we are able to identify more congenital CMV cases than ever. The use of new imaging modalities such as OCTA may help clinicians better evaluate these patients and determine which require close ophthalmologic follow-up, especially given the high correlation between ophthalmologic abnormalities and other central nervous system involvement.[22]

In conclusion, this pediatric patient with congenital CMV and a resulting macular scar showed RPE alterations and disruption of the outer retinal layers detected via OCT, accompanied by concomitant choriocapillaris atrophy evident on OCTA. These changes were observed several years after the initially confirmed diagnosis of congenital CMV, suggesting that retinal modifications endure even when excellent VA is preserved.

Authors' Note

Drs. Kozek and Morcos contributed equally to this work.

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health information were performed in a US Health Insurance Portability and Accountability Act–compliant manner. The requirement for approval from the Massachusetts General Brigham Institutional Review Board was waived given the retrospective nature of the study.

Statement of Informed Consent

The patient's guardian provided verbal informed consent before the publication of the case report.

Declaration of Conflicting Interests

Dr. Patel is a consultant to Regeneron, Dutch Ophthalmic, Genentech, EyePoint Pharmaceuticals, and Alcon Vision. None of the other authors declared relevant financial disclosures.

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