Congenital Cytomegalovirus Infection Initially Managed as Congenital Rubella Syndrome

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ABSTRACT

Congenital cytomegalovirus (CMV) infection (cCMV) is challenging to differentiate from congenital rubella syndrome (CRS) clinically. Virus detection and serological tests are needed. However, they are often not readily available or are expensive.

This is a case of a five-month-old male with bilateral cataracts. He was jaundiced at birth and started having seizure episodes at one month of age. He was also diagnosed with right inguinal hernia and had abnormal bilateral hearing tests. Both eyes were noted to have leukocoria at two months of age. There was dazzle on both eyes and sclerae were anicteric. Examination revealed dense cataracts on both eyes, but their ocular ultrasound results were essentially normal. Due to the bilateral hearing loss and bilateral cataracts, CRS was initially considered despite the absence of heart abnormality since there were reported CRS cases without the complete triad. However, possible co-infection or another disease was considered due to the presence of jaundice, seizures, and hernia, which were never seen in our previous CRS patients nor were reported in the literature. The patient underwent cataract extraction on both eyes without intraocular lens implantation (IOL) as recommended for CRS cataracts to prevent severe inflammation. TORCH (TOxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex) test was negative for rubella but positive for CMV. As such, the patient would have benefitted from early IOL implantation. The patient was then referred to a national medical center for possible treatment. However, since the patient already tested negative for CMV polymerase chain reaction (PCR) there, systemic antiviral therapy was no longer initiated.

This case presented the challenge of clinically differentiating cCMV and CRS.

Key Words: Congenital CMV infection, Congenital Rubella Syndrome, congenital cataract, hearing loss, jaundice

INTRODUCTION

TORCH, which stands for TOxoplasmosis, Rubella, Cytomegalovirus (CMV), and Herpes, refers to a group of infectious agents that, when pregnant women are exposed to, can cause congenital anomalies to the infants.[1] The severity of the anomalies depends on when the exposure happened, with a first-trimester exposure leading to the most severe.[2] Congenital TORCH infections can have similar clinical manifestations such as hearing loss, chorioretinitis, petechiae, and microcephaly. This makes complete laboratory testing such as virus polymerase chain reaction (PCR) and serology tests imperative to differentiate between TORCH agents, including between rubella and CMV. This is significant since the former does not have any treatment while the latter can benefit from systemic antiviral medication.[2-4] Similarly, treatment regimens can differ in some of their manifestations. However, these tests are not readily available or, if available in private facilities, are expensive.

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The number of congenital rubella syndrome (CRS) has been on the rise in our institution in the past year. We diagnose our patients based on the presence of the CRS classical triad of sensorineural hearing loss, congenital heart anomalies, and eye abnormalities, particularly cataract, and their TORCH test results, if available.[5] However, not all CRS patients present with the triad. Some present with just one manifestation, commonly hearing loss.[6] Although there is no known cure for CRS, some of its manifestations are treatable such as cardiac anomalies and cataracts.[7] Ophthalmologists prefer not to implant an intraocular lens (IOL) immediately after cataract extraction since the rubella virus had been isolated from the lens material.[8] The exposure of the virus to the immune-privileged anterior chamber of the eye during the surgery, together with the introduction of an additional foreign body (the IOL), can cause more inflammation and may lead to surgery-requiring complications such as membrane formation, which can cover the visual axis. However, the delay in implanting the IOL, a cheap and optimal option for correction, can negatively affect visual rehabilitation despite using aphakic glasses as an alternative.[9]

Despite being the leading infectious cause of congenital anomalies, only 5-15% of those infected by CMV show clinical manifestations.[10] Congenital CMV (cCMV) also presents with a clinical triad composed of jaundice, petechiae, and hepatosplenomegaly.[11,12] Although symptomatic cCMV patients can get better without treatment, giving 16 milligrams/kilogram body weight of oral ganciclovir twice a day for six months for better neurological and hearing outcomes was recommended.[4,13] Despite presenting with cataracts, there is no recommendation to delay IOL implantation in cCMV after cataract extraction. Implanting an IOL immediately after cataract extraction can result to better visual rehabilitation.

Due to the presence of bilateral cataracts and bilateral hearing loss, we present a patient with clinical congenital CMV infection initially managed as CRS.

CASE

This is a case of a five-month-old male with bilateral cataracts. He was jaundiced at birth but got better with phototherapy. His mother claimed to have no episodes of fever or rashes during pregnancy. At one month of age, he was admitted for seizure episodes and was also managed for anemia with a blood transfusion. At two months of age, he was noted to have leukocoria on both eyes, thus the referral to our institution. He was initially seen for a right inguinal hernia which parents were advised for repair. His hearing test results came back abnormal for both ears. On referral to Ophthalmology, there was positive dazzle on both eyes, no relative afferent pupillary defect, and sclerae were anicteric. Slit beam examination revealed cataract on both eyes. The ocular ultrasound results were essentially normal.

Due to the bilateral hearing loss and bilateral cataracts, he was initially diagnosed with CRS. Although the patient did not have congenital heart abnormality, CRS was still considered since there were reported cases where the clinical triad was not present and due to the recent increase in cases in the institution.[6] However, possible co-infection or another disease was also considered while waiting for the TORCH result due to the presence of jaundice, seizure episodes and hernia, which were never seen in our previous CRS patients, nor were reported in literature despite some CRS patients being reported to have developmental delay.[14]

On admission for the cataract surgery, the Pediatric service assessed him as stunted and wasted. His thyroid-stimulating hormone and free T3 were elevated at 9.8 micro International Unit per milliliter (μIU/mL) and 9.8 μIU/mL, respectively. On the second day of admission, he had an episode of seizure described as upward rolling of eyes, stiffening of extremities, and loss of consciousness for a minute.

Intraoperatively, both corneas were normal-sized corneas at 11 x 10 millimeters (mm) and both globes had within normal limits axial lengths at 17 mm. He underwent cataract extraction and posterior capsulotomy for both eyes without intraocular lens (IOL) implantation. On indirect ophthalmoscopy, both posterior poles did not have the characteristic salt and pepper retinopathy of CRS. The patient was given aphakic glasses for optical correction. The clinical features of the patient were summarized in Table 1.

Table 1. Summary of the clinical features of the patient

	Case
Eyes	Bilateral cataract
Ears	Bilateral sensorineural hearing loss
Neurological	Seizure
Hematological	Jaundice, anemia
Abdominal	Poor feeding results in stunting and wasting
Endocrinological	Elevated thyroid hormones
Others	Inguinal hernia

The TORCH result came back positive only for CMV IgG and IgM antibodies. As such, the diagnosis was then changed to cCMV. He was then referred by Pediatric service to a national medical center for CMV treatment. However, antiviral therapy was not started since CMV was no longer detected with PCR. At two years old, the patient is currently being rehabilitated for global developmental delay and maintained on Oxcarbazepine 1.6 mg twice a day for focal structural epilepsy. His latest ophthalmological examination revealed an atrophic optic nerve in the right eye. He still uses aphakic glasses.

DISCUSSION

Our patient was a diagnosed case of cCMV initially managed as CRS. The positive IgM and IgG for CMV and his clinical presentations of hearing loss, cataract, optic

nerve atrophy, seizure, hernia, and elevated thyroid hormones were used as the basis for the final diagnosis.

The presence of cataract and its bilaterality made us initially consider CRS since, despite cataract being associated with cCMV, only 5-15% of those infected with CMV become symptomatic. Among the six articles on cCMV reviewed for this paper, only one included cataract as its manifestation and was characterized as the anterior polar type.[10] All three articles on CRS reviewed for this paper cited cataract as clinical manifestation, with one even specifying bilateral involvement.[7-9] Although Lu and Yang detected only CMV IgM and IgG in 10-11 patients of their 37 with bilateral cataract with no rubella antibodies, their positivity rates for CMV IgM and IgG in the control group were relatively close to the study group (IgM: 11.8% vs. 15.5%; IgG: 17% vs. 23.3%).[15] A case report of supposed cCMV documented bilateral cataracts as manifestation. However, the diagnosis was based only on the detection of CMV IgM and IgG, the cataracts and a "new" finding of cholelithiasis.[16] There were no other reported cCMV manifestations seen in the reported case.

Our patient presented with jaundice at birth which resolved with phototherapy, giving the impression that it was physiological. There were no data if the bilirubin levels at birth were elevated and on the type of bilirubinemia, if present. Although the patient received a blood transfusion for anemia, there was also no data on its type. There was note of cortical atrophy on CT, but no calcifications were seen. Although there was no "salt and pepper retinopathy" characteristic of CRS appreciated after cataract extraction, there was also no "pizza pie retinopathy" characteristic of CMV retinitis seen. Our case report shows that cCMV can present with bilateral cataracts. Our diagnosis of cCMV was based not only on the CMV IgM and IgG and the cataracts but also on the presence of the other reported clinical manifestations of cCMV. This case report highlights that ophthalmologists and pediatricians shall maintain a high index of suspicion for the other TORCH agents in the setting of limited testing capability since it can significantly change the management.

Intraocular lens implantation, which offers a better optical correction than aphakic glasses, could have been done to the patient since it turned out that he has a cCMV infection instead. Similarly, although systemic antiviral treatment was no longer started in our patient, the patient can have neurologically and audiologically benefitted from the therapy if caught earlier.[4,10]

CONCLUSION

This case presented the challenge of clinically differentiating between cCMV and CRS. Although TORCH testing is vital in differentiating between the two, a high index of suspicion shall be maintained in the setting of unavailability or inaccessibility due to cost of TORCH tests.

Statement of Authorship

The author contributed in the conceptualization of work; acquisition and analysis of data; drafting and revising; and final approval of the version to be published.

Author Disclosure

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