



# Severe congenital chorioretinitis caused by congenital lymphocytic choriomeningitis virus infection

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## ABSTRACT

**Purpose:** To describe a case of congenital lymphocytic choriomeningitis virus (LCMV), a potentially severe and under-diagnosed etiology of congenital chorioretinitis.

**Observations:** A 5-month old boy presented with esotropia. Examination revealed light perception vision in the right eye and normal fixation and following behavior in the left eye, and a 50PD esotropia with full versions. The external, anterior segment, and pupil exams were normal. Fundus examination demonstrated slightly pale optic nerves, numerous geographic atrophic and hyperpigmented lesions along the vascular arcades in both eyes that extended into the fovea of the right eye. Head computed tomography (CT) imaging demonstrated bilateral cerebral volume loss with consequential ex vacuo dilation of the lateral ventricles and scattered intracranial calcifications. Serum IgG and IgM titers for toxoplasmosis, rubella, cytomegalovirus (CMV), herpes simplex virus (HSV), syphilis, and zika were all negative. Upon communication of negative TORCHS titers, the mother recalled a severe rat infestation of their home during the pregnancy. A LCMV antibody titer was then ordered and which resulted positive for IgG antibodies.

**Conclusions and Importance:** Congenital LCMV infection is an under-recognized cause of congenital chorioretinitis.

## 1. Introduction

Lymphocytic choriomeningitis virus (LCMV), an emerging fetal teratogen and member of the arenavirus family, is an often undiagnosed cause of acquired and congenital infection in humans.<sup>1</sup> Acquired, post-natal humanhuman huinfecion with LCMV usually consists of a brief febrile illness with mild symptoms that tend to fully resolve within 3 weeks often with no long-term sequelae. In contrast, congenital infection with LCMV can cause severe and permanent damage to the fetus, mainly targeting the central nervous system and retina.<sup>2</sup>

### 1.1. Case description

A 5-month-old boy presented with a 2-month history of esotropia of the right eye. On examination, he had light perception vision in the right eye and normal fix and follow vision in the left eye. His pupils were equal and reactive without afferent pupillary defect (APD). The motility exam revealed a 50PD esotropia with full versions. The anterior segment and external exams were normal. Intraocular pressure was normal by palpation. Fundus examination demonstrated smoderately pale optic

nerves with the cup:disc ratio of 0.1 in both eyes, numerous geographic atrophic and hyperpigmented lesions consistent with scarring along the vascular arcades and maculae in both eyes. The pigmentary retinal lesions included the fovea of the right eye but spared the fovea in the left eye (Figs. 1 and 2). The vitreous was clear without active inflammation. The cycloplegic refraction was  $-5.50D$  in the right eye and  $-1.25D$  in the left eye.

Serum IgG and IgM titers for toxoplasmosis, rubella, cytomegalovirus (CMV), herpes simplex virus (HSV), syphilis, and Zika were all negative. A head CT scan without contrast demonstrated broad regions of volume loss within the bilateral posterior cerebral hemispheres at the level of the parietal, occipital, and posterior temporal lobes with anomalous gyration sulcation (Fig. 3a,c). There was also an associated severe volume loss of the posterior supratentorial white matter with ex vacuo dilation of the lateral ventricles (Fig. 3a–b). There was no hydrocephalus. There were also two foci of dystrophic calcification at the lateral margin of the right caudate nucleus and another focus along the ependymal surface of the right lateral ventricle (Fig. 3d).

After communicating the negative TORCHS and Zika titer results to the mother, she mentioned that her home at the time of pregnancy had

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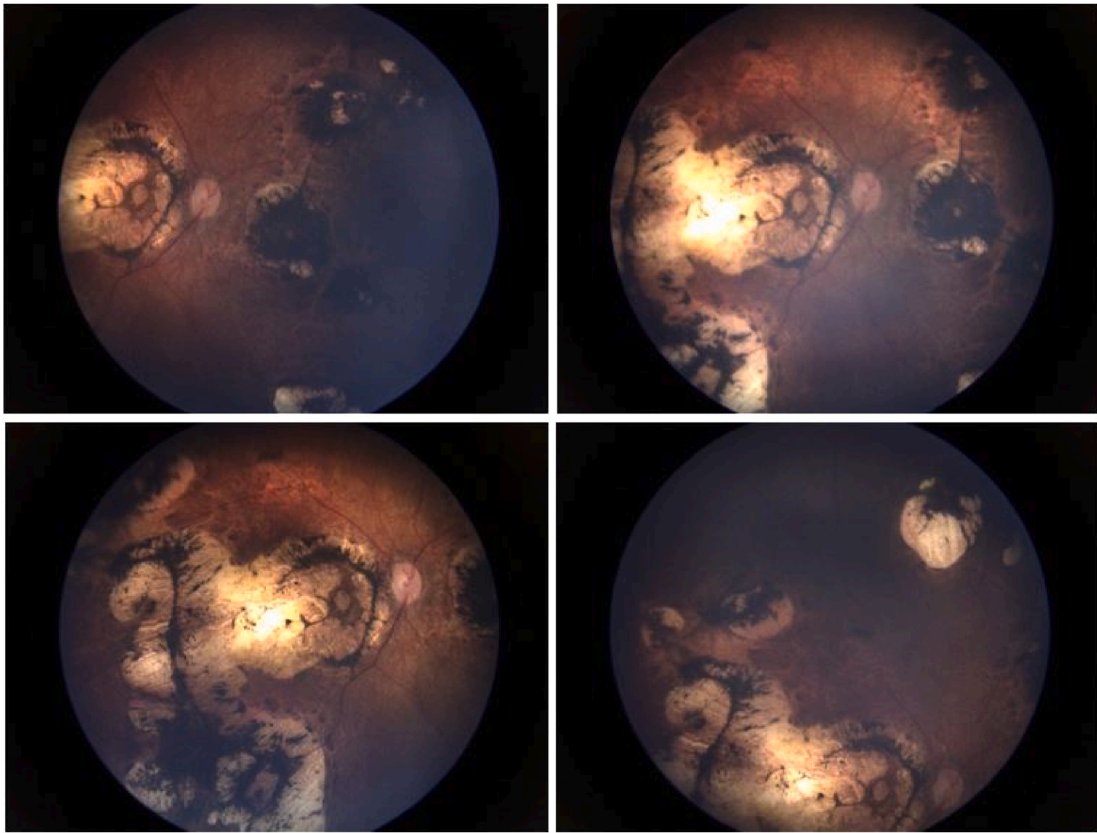


Fig. 1. Diffuse chorioretinal scarring in the macula, including the fovea, and periphery of the right eye (Retcam).

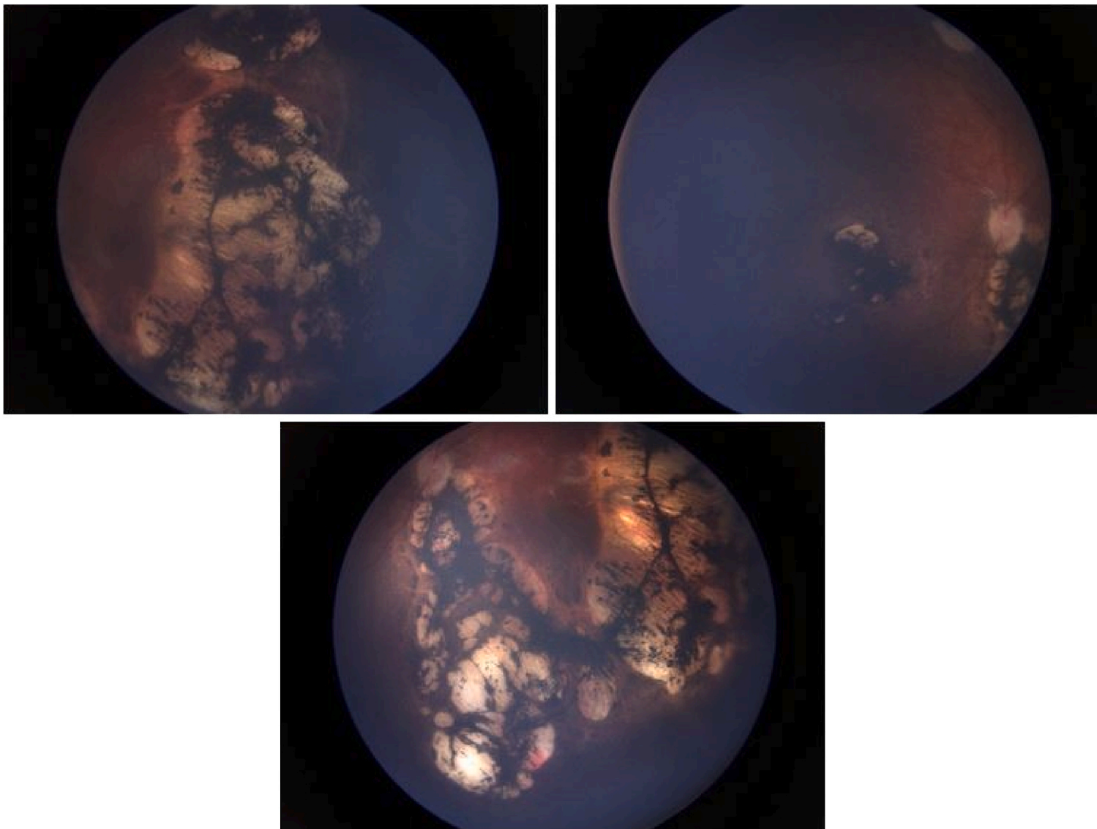
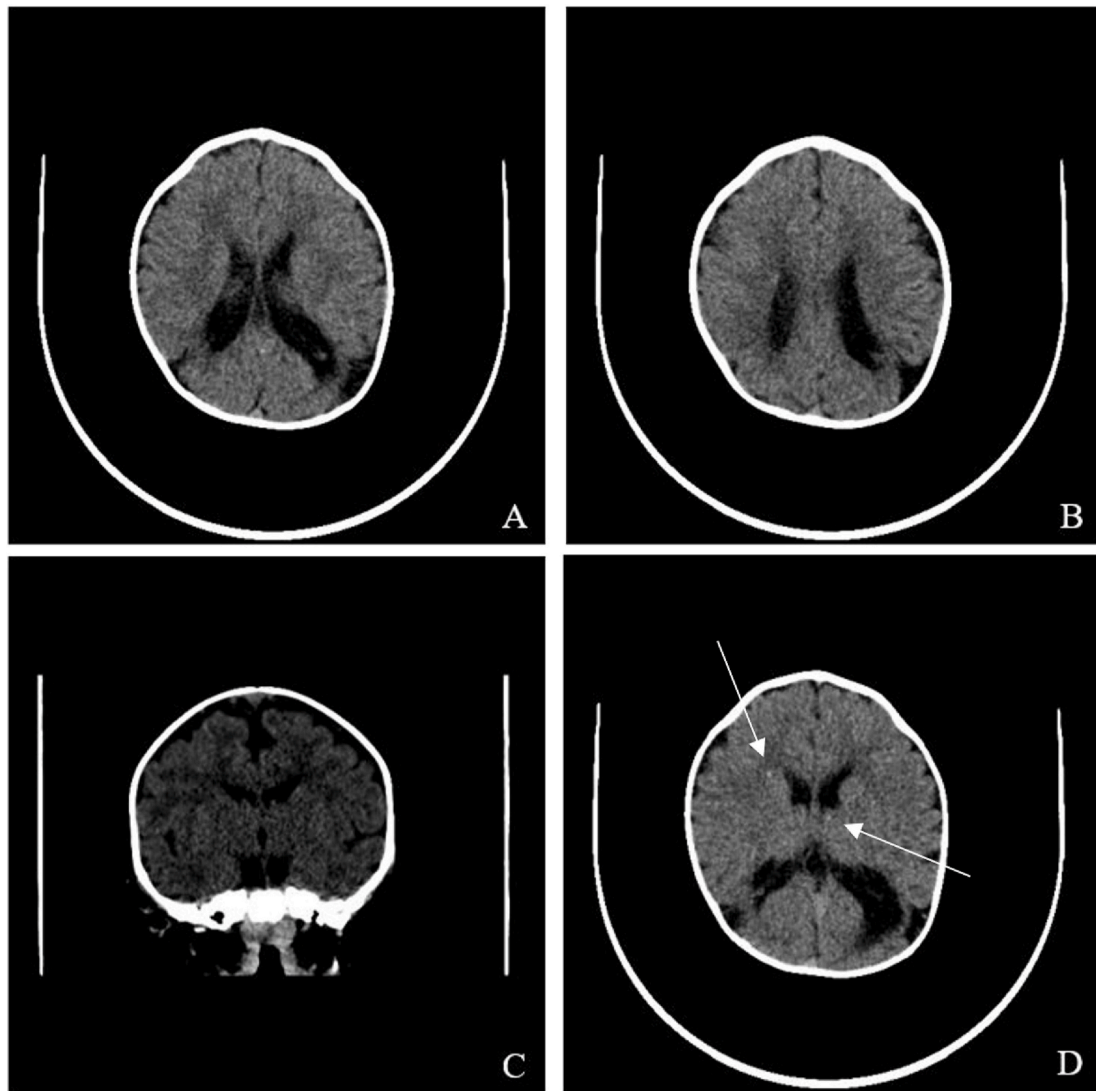


Fig. 2. Diffuse chorioretinal scarring in the macula, excluding the fovea, and periphery of the left eye (Retcam).



**Fig. 3.** Computed tomography (CT) imaging of the brain without contrast demonstrates (a,b) bilateral cerebral volume loss and ex vacuo dilation of lateral ventricle, (c) regional gyration sulcation, and (d) foci of periventricular dystrophic calcification.

been infested by rats. Because of this new information, blood LCMV titers were ordered which came back with a negative IgM titer and a positive IgG titer of 1:320 consistent with a remote LCMV infection. The patient was not placed on any antiviral treatment since there was no active chorioretinitis. Safety glasses were prescribed and occlusion therapy of the fellow left eye was attempted to improve any reversible component of amblyopia. The infant always fell asleep with the patch or cried inconsolably. Patching was then discontinued. The child is now followed every 6 months and will eventually have strabismus surgery before starting school.

## 2. Discussion

There are few reported cases of congenital LCMV in the world literature.<sup>3,4</sup> The primary reservoir for LCMV is infected rodents, and transmission to humans is thought to occur via inhalation of the aerosolized virus or direct contact with contaminated fomites.<sup>1,5</sup> The current incidence of clinically significant human LCMV infection is unknown. Reported serologic positivity rates have ranged between 1.2% in southern Germany and 37.5% in Slovakia, depending on the proximity of human and rodent habitation.<sup>6-8</sup> If acquired during pregnancy, transplacental passage to the fetus leads to a congenital infection for

which the complications and severity seem to depend on the gestational timing of the infection.<sup>9</sup>

In a previous study, Barton et al.<sup>1</sup> analyzed 45 cases of congenital LCMV and found that 42 of them involved chorioretinitis, where the most common abnormality was peripheral chorioretinal scarring. This finding is consistent with our patient who had extensive hyperpigmented scarring in the peripheral retina that extended into the macula bilaterally and included the fovea in the right eye (Fig. 1).

In a separate study, Bonthuis et al.<sup>2</sup> reported that in 20 children who were serologically positive for congenital LCMV infection, the most common neuroimaging abnormality was a combination of microcephaly and periventricular calcifications.<sup>2</sup> Though our patient was not microcephalic, he did have significant volume loss of the bilateral posterior hemispheres and the posterior supratentorial white matter and periventricular calcifications.

Congenital LCMV often goes undiagnosed, likely due its similarities in clinical presentation to more common TORCHS infections. Chorioretinitis, periventricular calcifications, or other CNS lesions typical of LCMV are also found in various other congenital infections including toxoplasma gondii, cytomegalovirus, herpes simplex virus, and varicella zoster.<sup>10</sup> Despite the similarities, there still remain some differences in presentation that could help differentiate between these infections. For

example, congenital toxoplasmosis is often active at the time of delivery, whereas LCMV is cleared in most cases by the time of birth.<sup>2</sup> The negative IgM titer, and positive IgG titer seen in our patient are all consistent with this finding. Additionally, a history of exposure to rodents during pregnancy lends support to a congenital LCMV infection. Among the 20 women who gave birth to children with congenital LCMV in the study done by Bonthius et al.,<sup>2</sup> approximately half of the women reported known exposure to wild mice during the pregnancy.

Although there is currently no cure for congenital LCMV, treatments may be developed in the future. Ribavirin could possibly be effective due to its activity against LCMV in vitro.<sup>11</sup> Based on the findings in this case as well as previous reported cases, awareness of LCMV as a potential cause of severe blinding congenital chorioretinitis is imperative. LCMV infection should be added to the growing list of congenital infections that cause chorioretinitis or chorioretinal scarring, fetal or newborn hydrocephalus, and intracranial calcifications.<sup>1,12</sup>

#### Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

#### Authorship

All authors attest that they meet the ICMJE criteria for authorship.

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#### Financial conflicts of interest

NA, GM, EP: the authors have no conflicts of interests to declare.

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