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Congenital Lymphocytic Choriomeningitis Virus Syndrome: A Disease That Mimics Congenital Toxoplasmosis or Cytomegalovirus Infection

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ABSTRACT. *Objective.* To describe the clinical characteristics of intrauterine infection with lymphocytic choriomeningitis (LCM) virus, an uncommonly recognized cause of congenital viral infection.

Patients. Three infants born in the midwestern United States in 1994 and 1995 with clinical features and serologic studies consistent with congenital LCM virus infection and cases of congenital infection identified by review of the medical literature between 1955 and 1996.

Results. Twenty-six infants with serologically confirmed congenital LCM virus infection were identified. Twenty-two infants were products of term gestations, and birth weights ranged from 2384 to 4400 g (median, 3520 g). Ocular abnormalities, macrocephaly, or microcephaly were the most commonly identified neonatal features. Twenty-one infants (88%) had chorioretinopathy, 10 (43%) had macrocephaly (head circumference >90th percentile) at birth, and 3 (13%) were microcephalic (head circumference <10th percentile). Macrocephaly and hydrocephalus developed postnatally in one of the latter infants. Hydrocephalus or intracranial calcifications were documented in five infants by computed tomography or magnetic resonance imaging. Nine infants (35%) died, and 10 (63%) of the 16 reported survivors had severe neurologic sequelae, consisting of spastic quadriplegia, seizures, visual loss, or mental retardation. One-half of the mothers reported illnesses compatible with LCM virus infection, and 25% reported exposures to rodents during their pregnancies.

Conclusions. These cases suggest that congenital LCM virus infection could be an underrecognized cause of congenital infection among infants born in the United States. Because of the clinical similarities of these congenital infections, cases of congenital LCM virus infection can be confused with infections with cytomegalovirus or *Toxoplasma gondii*. *Pediatrics* 1997;100(1). URL: <http://www.pediatrics.org/cgi/content/full/100/1/e9>; congenital infection, arenavirus, lymphocytic choriomeningitis virus, cytomegalovirus, toxoplasmosis.

ABBREVIATIONS. CMV, cytomegalovirus; HSV, herpes simplex virus; CNS, central nervous system; LCM, lymphocytic choriomeningitis virus; CT, computed tomography; WBC, white blood cell; CSF, cerebrospinal fluid.

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Although women encounter many different infectious agents during their pregnancies, relatively few pathogens cross the placenta and damage the developing fetus.¹ Nonetheless, several viruses and protozoa, linked conceptually by the TORCH acronym² (*TOxoplasma gondii*, Rubella virus, Cytomegalovirus, Herpes simplex virus), are capable of infecting pregnant women and inducing birth defects in their offspring. Certain disorders, such as the congenital rubella syndrome, have become infrequent as a direct result of intensive immunization programs,³ whereas others, such as congenital toxoplasmosis, remain a potential threat to the fetuses of nonimmune pregnant women.

Of the viruses associated currently with congenital infections, members of the herpesvirus family are the predominant etiologic agents.⁴⁻⁶ Cytomegalovirus (CMV), the most frequent viral cause of congenital infection, affects several thousand infants annually in the United States.⁴ Congenital infections with varicella zoster virus and herpes simplex virus (HSV) types 1 and 2, although much less frequent, produce similar clinical syndromes in the young infant.^{5,6} The clinical features of these intrauterine herpesvirus infections reflect involvement of the reticuloendothelial system, the retina, the cochlea, and the developing central nervous system (CNS). Infants with congenital CMV, HSV, or varicella zoster virus infections frequently display microcephaly, intracranial calcifications, or other CNS lesions, and have high rates of permanent neurodevelopmental, visual, and auditory sequelae.

Lymphocytic choriomeningitis (LCM) virus, a rodent-borne arenavirus, can infect humans throughout temperate regions of Europe and North America.^{7,8} The virus occasionally causes congenital infections, although the incidence of congenital LCM virus infection among infants born in the United States has not been established. Clinical knowledge regarding congenital LCM virus infection relies largely on the publications of Ackermann et al⁹ and Sheinbergas¹⁰ from Europe and occasional case reports from the United States.^{11,12} Clinicians in the United States generally lack familiarity with this pathogen and its potential association with congenital infection. Moreover, clinicians may confuse congenital LCM virus infections of infancy with other congenital infections, especially CMV or toxoplasmosis, because of their clinical similarities. In this

report we describe three infants with serologically confirmed congenital LCM virus infections and review the literature regarding this potential but often unsuspected infection.

CASE REPORTS

Case 1

This female infant was the 3660-g product of a 41-week gestation in a 17-year-old primagravida single woman of Native American and Hispanic descent. The pregnancy was complicated by vomiting and malaise during the first 2 months of the pregnancy, as well as an illness with vomiting, headache, eye pain, and dizziness during the sixth month. Ultrasonography 2 days before delivery disclosed fetal hydrocephalus.

Moderately heavy meconium was present at delivery, and the infant had Apgar scores of 4 at 1 minute and 8 at 5 minutes. Physical examination revealed a head circumference of 44.5 cm ($>>97$ th percentile), widely separated cranial sutures, and sunsetting eyes. Initial studies, consisting of a complete blood count, electrolytes, serum transaminases, and chest radiograph, were normal. Head computed tomography (CT) without contrast was compatible with aqueductal obstruction (Fig 1A). No intracranial calcifications were identified.

The infant underwent ventriculoperitoneal shunt placement on the first day of life. The ventricular fluid had a protein content of 161 mg/dL, a glucose content of 41 mg/dL, and contained 1 white blood cell (WBC)/ μ L. A hearing screen was normal at 4 days of age. Before discharge, the infant's head circumference was 38.5 cm.

Ophthalmologic examination at 6 weeks of age revealed no fixation or following, pupils that reacted minimally to light, marked limitation of up gaze, and bilateral exotropia and sunsetting signs. Funduscopy disclosed marked scarring bilaterally with chorioretinal atrophy and scalloping resembling the ocular features of Aicardi syndrome.

Examination at 2 months revealed a head circumference of 41 cm, approximately the 50th percentile. She had roving extraocular movements without visual tracking, mild dolichocephaly, and a left cortical thumb. Her liver and spleen were not enlarged, and

she had no skin lesions. She had mild delays in gross motor ability and substantial delays in items requiring vision.

Studies for infectious pathogens obtained during the first month of life included a negative urine culture for CMV and negative serologic studies for rubella, HSV, syphilis, and *Toxoplasma gondii*. By contrast, sera for LCM virus, assayed by the Iowa Hygienic Laboratory using a complement fixation method and by the Centers for Disease Control and Prevention using an enzyme-linked immunosorbent assay method, were consistent with intrauterine infection with LCM virus (Table 1). Evaluation by a pediatric geneticist disclosed no other dysmorphic features, and the patient's family history was negative for birth defects. Subsequent head CT (Fig 1B) revealed diminished ventricular size.

Review of the prenatal history revealed no exposure to cats, but disclosed apparent exposure to mice during the first 2 months of the pregnancy. The child's mother indicated that the apartment below her mother's apartment, where she lived at the time, was infested with mice and that approximately 4 mice were caught weekly in traps set in her mother's apartment.

Case 2

This female infant was the 3210-g product of a 40-week gestation of a 28-year-old gravida 2, para 2, single white woman. The pregnancy was complicated by late prenatal care, and the infant was born vaginally using vacuum assistance. Her Apgar scores were 7 at 1 minute and 9 at 5 minutes. Microcephaly, occipital frontal head circumference of 29.5 cm (<10 th percentile), was noted at birth, and she had blisters on her chest and neck.

At 2 days of age vesiculo-bullous lesions and sloughing of her labial skin developed. Examination revealed an irritable, although alert, infant who had mildly increased tone throughout. Ophthalmologic examination was normal. A head CT without contrast (Fig 2) disclosed periventricular calcifications. Cerebrospinal fluid (CSF) examination revealed a protein content of 134 mg/dL, glucose content of 63 mg/dL, 1 red blood cell/ μ L, and 3 WBC/ μ L (one lymphocyte and two histiocytes).

An extensive microbiologic evaluation included negative results for the following: herpes simplex virus (HSV) direct antigen and culture of skin lesions, cultures of CSF for HSV and enteroviruses, urine culture for CMV, and serologic studies for *Trepo-*

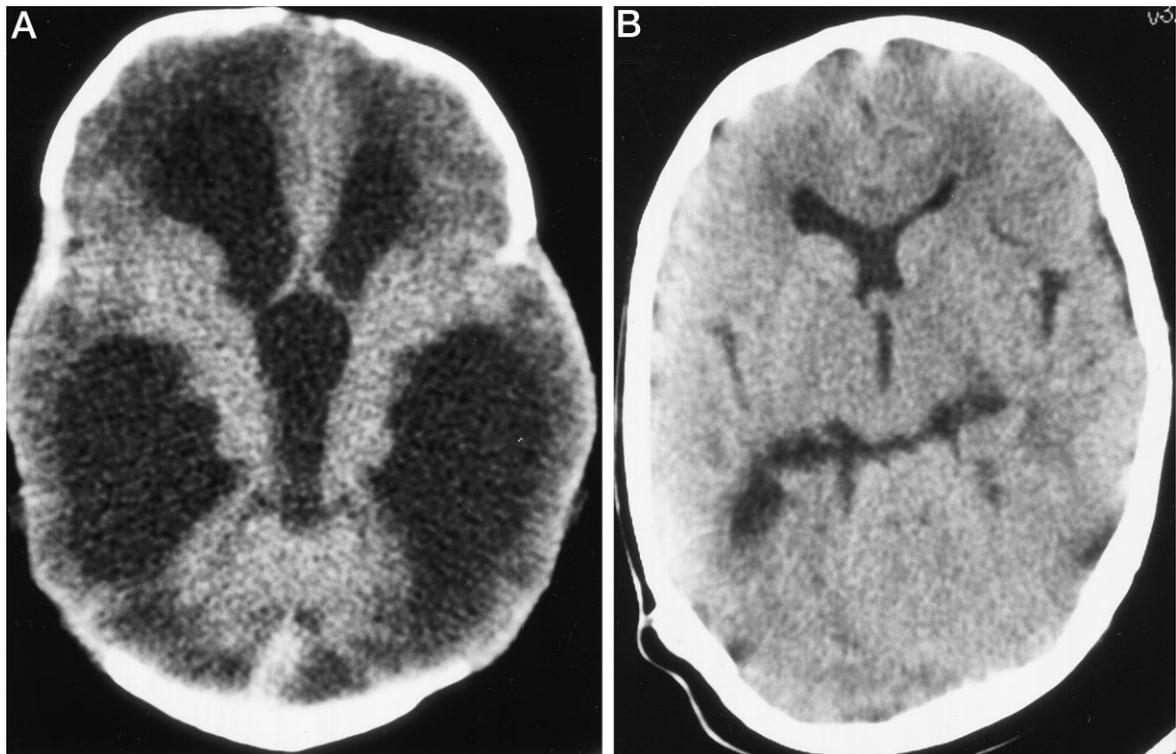


Fig 1. CT of Case 1. A, The scan obtained on the first day of life shows massive hydrocephalus. B, Subsequent scan shows adequate decompression of the ventricular system after placement of a ventriculoperitoneal shunt.

TABLE 1. Results of Laboratory Studies for Lymphocytic Choriomeningitis Virus Infection*

Case	Date	LCM Virus-specific IgM	LCM Virus-specific IgG
1 (Date of birth 7/1/94)	7/6/94	<1/100	≥1/6400
	8/20/94	<1/100	≥1/6400
	1/10/95	<1/100	≥1/6400
2 (Date of birth 5/27/95)	6/9/95	1/400	1/1600
	8/3/95	<1/100	1/6400
Mother	8/3/95	<1/100	1/6400
3 (Date of birth 9/29/95)	10/10/95	<1/100	1/1600
	10/17/95	<1/100	1/1600
	Cerebrospinal fluid	10/07/95	>1/256
	Mother	10/17/95	<1/100

* Serologic studies conducted at the Centers for Disease Control and Prevention using an LCM virus-specific enzyme-linked immunosorbent assay method.

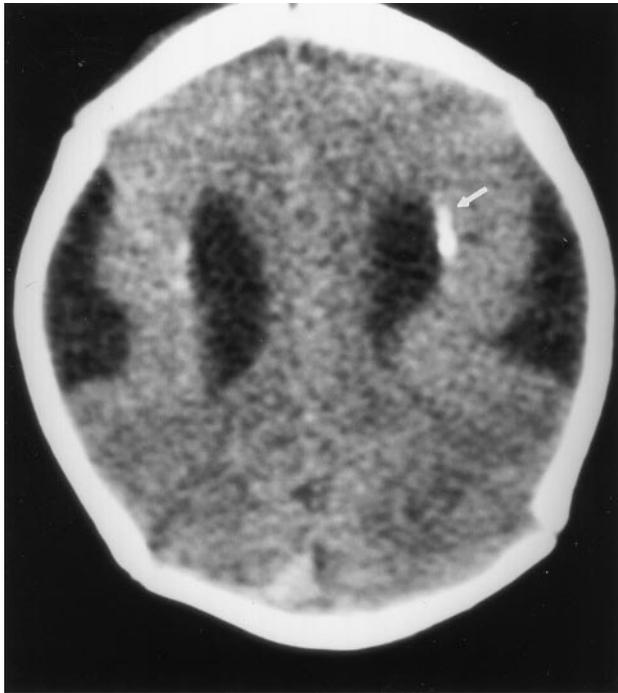


Fig 2. CT of Case 2. The scan shows periventricular calcifications (arrow) and an abnormal gyral pattern suggestive of a disorder of neuronal migration.

nema pallidum and *Toxoplasma gondii*. Histologic examination of the skin lesions was compatible with Staphylococcus scalded skin syndrome.

Serologic studies for LCM virus were consistent with congenital LCM virus infection (Table 1). The infant's mother indicated that she lived in a house where mice were present during the first few months of her pregnancy (August to November), but she did not recall having direct physical contact with the mice. At 8 months of age, the infant had spastic quadriplegia, microcephaly, severe developmental delay, and intermittent seizure activity.

Case 3

This male infant was the 3520-g product of a full-term pregnancy of a 17-year-old primigravida whose pregnancy had been complicated by a week-long illness with severe headache and fever during the fifth month. These symptoms resolved spontaneously. An antenatal uterine ultrasound study suggested the possibility of fetal heart block and holoprosencephaly. The infant was born vaginally and had Apgar scores of 8 at 1 minute and 9 at 5 minutes.

He was an alert, active infant who had normal facial features. His head circumference was 32 cm (15th percentile). He had no heart murmurs, no skin lesions, and no enlargement of the liver or spleen. His extremities were normal. An ophthalmologic exami-

nation revealed pale optic disks and bilateral retinal atrophic changes.

His CSF had a glucose of 33 mg/dL, protein of 197 mg/dL, 140 erythrocytes/ μ L, and 1 WBC/ μ L. His platelet count was 259 000/ μ L. Studies for etiologic agents included negative serologies for syphilis and toxoplasmosis, negative urine culture for CMV; the rubella titer was 1:32, and the mumps titer was 1:28. Serologic studies of blood and CSF were consistent with intrauterine infection with LCM virus (Table 1).

REVIEW OF THE LITERATURE AND SUMMARY OF CASES

Study Population

Reports regarding 23 published cases of congenital or transplacental LCM virus infection were identified by computer-assisted review of the medical literature.⁹⁻¹⁴ The majority were case reports.^{9,11-13} Sheinbergas' report consisted of 16 infants identified retrospectively by serologic surveys of 833 newborn infants, 40 infants under 1 year of age with hydrocephalus, and 110 infants under 2 years of age with various neurologic conditions.¹⁰ A single infant reported by Chastel et al¹⁴ was also identified retrospectively from a serologic survey of 452 infants with major medical conditions (jaundice, hepatosplenomegaly, prematurity, neurologic problems, and so forth) or congenital malformations.

In the majority of cases, including those reported here, LCM virus infection was established serologically by assay of the infant's serum and/or CSF and, in some instances, maternal serum. The serologic methods included: complement fixation and neutralization test;^{9,14} indirect immunofluorescent assay for LCM virus antibody (class unspecified);¹⁰ immunofluorescent assay of LCM virus-specific IgM and IgG;^{11,12} and enzyme-linked immunosorbent assay for LCM virus-specific IgM and IgG.^{11,12} LCM virus infection was established in one case by inoculating mice intracerebrally with a sample of the infant's CSF and neutralization of murine material with LCM virus-specific immune serum.¹³

Neonatal Systemic Manifestations

Twenty-two infants were products of term gestations (≥ 37 weeks) (gestational age was not reported for four infants), and birth weights were appropriate or large for gestational age, ranging from 2384 g (37-week gestation) to 4400 g. Median birth weight was 3520 g. Systemic signs suggesting congenital infection were infrequent, although information re-

garding the 16 infants reported by Sheinbergas was incomplete.¹⁰ None of the remaining infants had hepatosplenomegaly or petechial rash, but an infant reported by Ackermann⁹ had hyperbilirubinemia (total bilirubin of 17 mg/dL). The infant reported by Chastel had a valgus deformity of one foot.¹⁴

The infant reported by Komrower et al¹³ had clinical signs compatible with acute neonatal meningitis, consisting of a fever, poor feeding, dehydration, bulging fontanel, seizures, and opisthotonic posturing. The CSF contained 54 white blood cells/ μ L. One of our patients had cutaneous abnormalities compatible with staphylococcal scalded-skin syndrome.

Neonatal Neurologic Manifestations

Because Sheinbergas¹⁰ used hydrocephalus as a selection criteria for assaying serum samples for LCM virus, the neonatal neurologic features of congenital LCM virus infection were biased toward macrocephaly. Birth head circumferences for 23 infants ranged from 29 cm (<10th percentile) to 44.5 cm (>97th percentile), and 10 (43%) of these infants had abnormally large head circumferences (≥ 37 cm; 90th percentile). Three were considered microcephalic at birth, and in one of these, progressive hydrocephalus developed postnatally. Information regarding the remainder of the neonatal neurologic examination, although incomplete, suggested that some infants seemed normal initially, whereas others had clinical signs compatible with progressive hydrocephalus.

Ophthalmologic Features

Chorioretinopathy was a major clinical feature of congenital LCM virus infection, affecting 21 (88%) of

the 24 infants for whom ophthalmologic examinations were described. In most instances, the chorioretinopathy was bilateral (16 of 21), and in some cases resembled the lacunar retinopathy of Aicardi syndrome. Only three infants with congenital LCM virus infection were apparently free of chorioretinitis. Several other abnormal ophthalmologic features were reported, including optic atrophy, microphthalmia, vitreitis, leukokoria, and cataract. Optic atrophy was present in 11 infants.

Audiologic Studies

The hearing status, reported for only three infants (including two in the current report), was normal in each infant.

Neurodiagnostic Studies

CSF results, available for 18 infants, were variable, with nearly one half showing a mild pleocytosis of up to 64 WBC/ μ L. CSF protein content was mildly elevated in several cases (median: 67 mg/dL; range: 9 to 477 mg/dL; N = 17), and the CSF glucose content was normal or mildly low (median: 53 mg/dL; range: 28 to 78 mg/dL; N = 13). One infant's CSF (Case 19) became markedly abnormal coincident with progressive hydrocephalus, with the cell count and protein increasing from 10 to 2080 WBC/ μ L and 46 to 1840 mg/dL, respectively, during a two-month period.¹⁰

Five infants underwent neuroimaging studies (Cases 21 to 25; Table 2); five by CT and three by magnetic resonance imaging. Four infants had calcifications adjacent to the lateral ventricles or in the periventricular white matter. Two of these infants

TABLE 2. Summary of Cases of Congenital Lymphocytic Choriomeningitis Virus Infection*

Case	Author	Birth Weight (g)	OFC at Birth (cm)	Chorioretinitis	Hydrocephalus	Alive or dead	Sequelae
1	Komrower	2755	ND	ND	Yes	D	...
2	Ackermann	3100	37	Yes (?)	Yes	A	DD
3	Ackermann	3080	39	Yes (?)	Yes	A	DD
4	Sheinbergas	2580	30	Yes (B)	Yes	A	SQ, SZ
5	Sheinbergas	4000	36	Yes (B)	Yes	D	SQ
6	Sheinbergas	3700	40	Yes (B)	Yes	D	SQ
7	Sheinbergas	2550	34	Yes (B)	Yes	D	SQ
8	Sheinbergas	3600	35	Yes (U)	Yes	A	Slight delay
9	Sheinbergas	3240	36	No	No	A	Normal
10	Sheinbergas	3100	37	Yes (B)	Yes	A	SQ, MR
11	Sheinbergas	4400	37	Yes (U)	Yes	D	SQ
12	Sheinbergas	3800	35	Yes (B)	Yes	D	SQ
13	Sheinbergas	4000	36	No	Yes	A	SQ
14	Sheinbergas	3600	37	Yes (B)	Yes	A	SQ, SZ
15	Sheinbergas	4100	37	Yes (B)	ND	A	SQ
16	Sheinbergas	2850	35	Yes (B)	Yes	A	SQ
17	Sheinbergas	4100	42	Yes (B)	Yes	D	SQ
18	Sheinbergas	4000	ND†	ND	ND	D	ND
19	Sheinbergas	3700	40	Yes (B)	Yes	D	SQ
20	Chastel	ND	ND	Yes (B)	Yes	A	Normal
21	Larsen	2898	34.5	Yes (U)	Yes	A	DD, B
22	Barton	2420	29	Yes (B)	No	A	DD, MC
23	Barton	2384	33.3	Yes (B)	No	A	Near normal
24	Current report	3660	44.5	Yes (B)	Yes	A	DD
25	Current report	3210	29.5	No	No	A	DD, MC
26	Current report	3520	32	Yes (B)	No	A	ND

Abbreviations: OFC, occipital frontal head circumference; U, unilateral; B, bilateral; ?, unknown; A, alive; D, dead; ND, no data; DD, developmental delay; SQ, spastic quadriplegia or cerebral palsy; SZ, seizures; MR, mental retardation; B, blindness; MC, microcephaly. * The table indicates the status of the child at the time of the author's report.

† Cephalotomy was performed.

also had ventricular enlargement, and in one of these infants the white matter was described as hypodense. The remaining infant's CT showed massive hydrocephalus without intracranial calcification. The three magnetic resonance imaging scans were also abnormal, showing ventriculomegaly or patchy abnormalities of white matter on T2-weighted images. One infant's gyral pattern was described as flattened, suggesting a migrational disorder.¹²

Maternal Illnesses

Thirteen (52%) of the 25 mothers (one mother had LCM virus-infected twins; Cases 22 and 23) reported illnesses compatible with LCM virus infection during their pregnancies. In nine cases the illness consisted of a flu-like syndrome between the second and sixth months of gestation, and four mothers, including two in this report, had illnesses compatible with aseptic meningitis. Symptoms in the latter cases included fever, headache, vomiting, and/or malaise. Six (24%) of the 25 mothers reported exposure to rodents during their pregnancies (three with mice, two with hamsters, and one with hamsters, mice, and gerbils).

Outcome

Information regarding outcome was available for 25 infants. There were nine deaths among the reported cases, corresponding to an overall mortality of 35%. Deaths occurred between birth and 21 months of age. Ten (63%) of the 16 surviving children had severe neurologic sequelae, consisting of spastic quadriparesis, seizures, visual loss, developmental delay, or mental retardation. One had slight motor delay, whereas only three children, ages 9, 30, and 50 months^{10,12,14} were described as normal at the time of reporting. Data were incomplete for the two remaining infants, although they were reported as retarded.⁹

DISCUSSION

The Arenaviridae family includes several viruses causing LCM or hemorrhagic fever in humans. Among the Old World arenaviruses, the most important human pathogens are the LCM virus (found also in the New World) and the Lassa fever virus of West Africa. Numerous New World viruses have been described, including Junin (the agent of Argentine hemorrhagic fever), Machupo (the agent of Bolivian hemorrhagic fever), and Guanarito (the agent of Venezuelan hemorrhagic fever).^{7,15} Rodents, the primary reservoirs of the arenaviruses (the house mouse, *Mus musculus*, for LCM virus), harbor chronic infections and excrete the viruses for life.

Human infection is presumed to occur by contact with infected rodents or their excreta.¹⁵ LCM virus-infected colonies of mice or hamsters can sustain virus transmission without evidence of disease and become sources of human infection.^{7,16-19} In temperate climates, such as in Iowa and Illinois, natural human exposure often occurs during the winter months, when mice move indoors into heated areas.

Seroprevalence studies performed during the 1940s suggested that as many as 10% of the popula-

tion had been infected with LCM virus.¹⁸ A more recent report indicated that 4.7% of adults attending a sexually transmitted disease clinic in Baltimore had antibodies to LCM virus, indicating prior infection.¹⁹ Infection likely goes unrecognized in most LCM virus-infected humans, with symptoms often being attributed to a flu syndrome.¹⁶ No data suggest that humans become infected chronically.¹⁵

LCM virus can be isolated from blood or CSF during the acute illness,¹⁵ but most human infections are established serologically. Because of the relatively low prevalence of antibodies to LCM virus, positive serologic results for this agent have more diagnostic importance than serologic studies for CMV or toxoplasmosis. Congenital infection in these three infants, although not confirmed by virus isolation, was supported by detection of LCM virus-specific IgM in serum or CSF in Cases 2 and 3 and by persisting high titers of LCM virus-specific IgG in case 1. Given that a related arenavirus, Lassa virus, can be detected by reverse transcription polymerase chain reaction,²⁰ studies using LCM virus-specific oligonucleotide primers could be considered in future cases of suspected congenital LCM virus infection.

The pathogenesis of human congenital LCM virus infection probably resembles that of congenital CMV infection.^{7,21} Given the predominant location of the CNS lesions in LCM virus-infected infants,¹³ the virus seems to enter the CNS via the choroid plexus and replicate in cells of the ependyma and periventricular germinal matrix zones. In contrast to CMV, however, LCM virus replication more commonly produces a necrotizing ependymitis that leads to aqueductal obstruction. In this regard congenital LCM virus infection resembles the potential CNS effects of acquired mumps virus infection.²²

In experimental murine infection LCM virus replicates primarily in the choroid plexus and meninges, and T-cell mediated acute inflammatory responses are responsible for clearing virus-infected cells.¹⁵ Both ependymal and meningeal inflammation have been observed in a fatal, human LCM virus encephalitis.²³ These observations may explain the periventricular calcifications and obstructive hydrocephalus in human congenital LCM virus infection.

Chorioretinitis, a nearly uniform feature of human congenital LCM virus infections, has been observed in the offspring of female rats inoculated with LCM virus.²⁴ This experimental retinitis can be prevented or ameliorated by immunosuppression, suggesting that immunopathologic mechanisms mediate the ocular damage. The lacunar character of the LCM virus-associated chorioretinopathy in the human newborn resembles the eye lesion of Aicardi syndrome, a chromosomal disorder, but the infant with congenital LCM virus infection lacks vertebral anomalies and has an intact corpus callosum.²⁵

Infants with congenital LCM virus infection seem to have a poor prognosis. More than one-third of the reported infants died, and the majority of survivors had severe neurodevelopmental sequelae. Case selection, however, could impart bias toward a more severe syndrome and outcome, especially for the

infants described by Sheinbergas.¹⁰ Because prospective epidemiologic and clinical studies of congenital LCM virus infection have not been performed, it is not known if infected infants can be less severely affected or asymptomatic at birth.

In summary, LCM virus infection should be recognized as a potential cause of congenital viral infection among infants born in the United States. This infection should be considered among infants who have chorioretinitis and congenital hydrocephalus or microcephaly, lack hepatosplenomegaly, and have negative microbiologic studies for CMV, *T gondii*, and other more common pathogens. Prospective studies are needed, however, to determine precisely the epidemiology and clinical spectrum of congenital LCM virus infection among infants born in the United States.

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REFERENCES

1. Bale JF Jr., Murph JR. Congenital infections and the nervous system. *Pediatr Clin North Am.* 1992;39:669–690
2. Nahmias AJ, Walls KW, Stewart JA, et al. The TORCH complex: perinatal infections associated with toxoplasma and rubella, cytomegalovirus and herpes simplex virus infections. *Pediatr Res.* 1971;5:405
3. Centers for Disease Control and Prevention. Rubella prevention. *MMWR.* 1990;39:1
4. Demmler GJ. Summary of a workshop on surveillance for congenital cytomegalovirus disease. *Rev Infect Dis.* 1991;13:315–329
5. Hutto C, Arvin A, Jacobs R, et al. Intrauterine herpes simplex virus infections. *J Pediatr.* 1987;110:97–101
6. Grose C. Congenital infections caused by varicella zoster virus and herpes simplex virus. *Semin Pediatr Neurol.* 1994;1:43–49
7. Lehman-Grube F. Portraits of viruses: arenaviruses. *Intervirology.* 1984; 22:121–145
8. Hirsch MS, Moellerling RC, Pope HC, Poskanzer DC. Lymphocytic choriomeningitis infection traced to a pet hamster. *N Engl J Med.* 1974; 291:610–612
9. Ackermann R, Körver G, Turss T, Wönne R, Hochgesand R. Pränatale Infektion mit dem virus der lymphozytären choriomeningitis. *Dusch Med Wschr.* 1974;99:629–632
10. Sheinbergas M. Hydrocephalus due to prenatal infection with the lymphocytic choriomeningitis virus. *Infection.* 1976;4:185–191
11. Larsen PD, Chartrand SA, Tomashek KM, Hauser LG, Ksiazek TG. Hydrocephalus complicating lymphocytic choriomeningitis virus infection. *Pediatr Infect Dis J.* 1993;12:528–531
12. Barton LL, Budd SC, Morfitt WS, et al. Congenital lymphocytic choriomeningitis virus infection in twins. *Pediatr Infect Dis J.* 1993;12:942–946
13. Komrower GM, Williams BL, Stones PB. Lymphocytic choriomeningitis in the newborn. Probable transplacental infection. *Lancet.* 1955;1: 697–698
14. Chastel C, Bosshard S, Le Goff F, Quillien M-C, Gilly R, Aymard M. Transplacental infection by lymphocytic choriomeningitis virus. *Nouv Press Méd.* 1978;7:1089–1092
15. Peters CJ, Buchmeier M, Rollin PE, Ksiazek TG. Arenaviruses. In: Fields BN, Knipe DM, Howley PM, et al, eds. *Fields Virology.* 3rd ed. Philadelphia, PA: Lippincott-Raven Publishers; 1996:1521–1551
16. Biggar RJ, Woodall JP, Walter PD, Haughie GE. Lymphocytic choriomeningitis outbreak associated with pet hamsters. Fifty-seven cases from New York State. *JAMA.* 1975;232:494–500
17. Dykewicz CA, Dato VM, Fisher-Hoch SP, et al. Lymphocytic choriomeningitis outbreak associated with nude mice in a research institute. *JAMA.* 1992;267:1349–1353
18. Armstrong C. Studies on choriomeningitis and poliomyelitis. *The Harvey Lectures.* 1941;36:39–65
19. Childs JE, Glass GE, Ksiazek TG, Rossi CA, Oror JGB, Leduc JW. Human-rodent contact and infection with lymphocytic choriomeningitis and Seoul viruses in an inner city population. *Am J Trop Med Hyg.* 1991;41:117–121
20. Lukenheimer K, Hufert FT, Schmitz H. Detection of Lassa virus RNA in specimens from patients with Lassa fever by using the polymerase chain reaction. *J Clin Microbiol.* 1990;28:2689–2692
21. Bale JF Jr. Human cytomegalovirus infection and disorders of the nervous system. *Arch Neurol.* 1984;41:310–320
22. Bray PF. Mumps. A cause of hydrocephalus. *Pediatrics.* 1972;49:446–447
23. Warkel RL, Rinaldi CF, Bancroft WH, Cardiff RD, Holmes GE, Wilsnack RE. Fatal acute meningoencephalitis due to lymphocytic choriomeningitis virus. *Neurology.* 1973;23:198–203
24. Cerro MD, Grover D, Monan A, Pfau C, Dematte J. Congenital retinitis in the rat following maternal exposure to lymphocytic choriomeningitis virus. *Exp Eye Res.* 1984;38:313–324
25. Willis J, Rosman NP. The Aicardi syndrome versus congenital infection. *J Pediatr.* 1980;96:235–239

Congenital Lymphocytic Choriomeningitis Virus Syndrome: A Disease That Mimics Congenital Toxoplasmosis or Cytomegalovirus Infection

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