Congenital Cytomegalovirus Infection of the Brain: MR Imaging and Ultrasonographic Findings of Paraventricular Cysts

Woo Mok Byun, M.D., Mi Soo Hwang, M.D.

Purpose: Although the neuroradiological findings of congenital cytomegalovirus (CMV) infection are well known, little has been reported concerning the imaging findings of paraventricular cysts occurring in patients with cytomegalovirus infection involving the brain. The purpose of this study is to describe the features of paraventricular cysts observed at MRI and ultrasonography.

Materials and Methods: MR and ultrasonographic studies of ten patients with congenital cytomegalovirus infections involving the brain were retrospectively reviewed. Diagnosis was confirmed by positive culture of the virus in urine (n = 4), the presence of CMV Ig G antibody (n = 4), or positive CMV Ig M antibody (n = 2), and on the basis of characteristic MR imaging findings. Initial MRI in all patients and initial ultrasonography in four of five with paraventricular cysts were performed. Three patients underwent follow-up MRI and ultrasonography for the evaluation of cystic change, and the size, location, bilaterality and morphology of the cysts were evaluated.

Results: Bilateral paraventricular cysts averaging 15 (range, 10–23) mm in size were found in five of the ten patients (50%). They were adjacent to the foramen of Monro in three cases, the occipital horn in one, and the temporal horn in one. MR imaging showed that the fluid content of all cysts was of similar signal intensity to cerebrospinal fluid (T1-WI, hypointense; T2-WI, hyperintense). The ultrasonographic findings varied: there was one pure cyst and one with a thick wall and septations, and two contained complex fluid. In three patients, follow up MRI and ultrasonography showed that the cysts disappeared after 4–23 months.

Conclusion: Although paraventricular cysts may appear at MRI to be purely cystic, ultrasonography may indicate that their contents are more complex, or that septations are present.

Index words: Infant, newborn, central nervous system
Brain, infection
Brain, MR
Brain, US
Cytomegalovirus (CMV), which causes transplacental infection, is a ubiquitous agent, and is the most common cause of congenital viral infections. In newborns, the reported incidence is 0.2-2.2%, and approximately 10% of such cases are postnatally symptomatic (1-2). CMV infection has widespread manifestations, including those found in the central nervous system, namely microcephaly, deafness, mental retardation, hypotonia, spastic quadriplegia, and varying degrees of perceptual, neurologic, psychomotor, and behavioral disturbances (3-4). Several reports have described the imaging findings of congenital CMV infection; these include periventricular calcification, ventriculomegaly, delayed myelination, oligo/pachygyria, periventricular and subcortical signal intensity change, cerebellar atrophy, and paraventricular cysts. The inflammatory process and necrosis caused by congenital CMV infection involving the brain can lead to paraventricular cystic lesions. Radiological studies have shown the presence of these in 36-60% of affected children (5-8).

Although a number of radiological findings have been reported in patients with congenital CMV infection, little has been written concerning the imaging findings of paraventricular cysts at MRI and ultrasonography. In this report, we describe the MRI and ultrasonographic findings of paraventricular cysts in patients with congenital CMV infection.

**Materials and Methods**

MRI and ultrasonographic studies of ten patients with congenital CMV infections involving the brain were retrospectively reviewed. There were six females and four males, who at the time of initial cranial MR imaging studies were aged between 7 days and 23 months (mean, 5 months). Three of the infants were born prematurely and seven were born at term. All cases were diagnosed on the basis of characteristic clinical and imaging findings in conjunction with positive serologic testing for CMV or culture of the virus from the urine of the child. Diagnosis was confirmed by positive culture of the virus \(n=4\), the presence of positive CMV Ig G antibody \(n=4\), or positive CMV Ig M antibody \(n=2\), and on the basis of typical MR findings. The diagnostic imaging findings were periventricular high signal intensity at T2-weighted imaging \(n=8\), cortical dysplasia \(n=4\), cerebellar atrophy \(n=1\) and noncommunicating hydrocephalus \(n=6\). The clinical signs for CMV infection were microcephaly \(n=6\), thrombocytopenia \(n=2\), seizure \(n=6\), and sensory neural hearing loss \(n=2\).

For MR examinations, a 0.5T (Gyroscope T5; Philips, Netherlands) and a 1.5T unit (Vision; Siemens, Erlangen, Germany) were employed. Axial and coronal T1-weighted images (repetition time msec/echo time msec: 400-600/25-30) were obtained before and after the administration of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany; 0.1mmol per kilogram of body weight), and axial T2-weighted (2000-2500/100-120) or turbo-T2-weighted images (3000-4000/90-100) were obtained before the administration of gadopentetate dimeglumine. Four patients were scanned through the anterior fontanel using real-time ultrasound (Ultrasound 9; ATL, Bothell, Washington, U.S.A.) with a 7-MHz sector transducer. Initial MRI in all patients and initial ultrasonography in four with paraventricular cysts were performed. Three patients underwent both second follow-up MR and ultrasonography for the evaluation of cystic change, and using these same modalities, one of the three was followed up a third time.

Diagnosis was established on the basis of MR imaging findings such as fluid signal intensity with a thin wall. The size, location, bilateralization and morphology of the cysts were evaluated by MRI and ultrasonography, and the former was also used to determine whether wall enhancement was present.

<table>
<thead>
<tr>
<th>Cases</th>
<th>Ages</th>
<th>Term [GA]</th>
<th>Location</th>
<th>Size [Cm]</th>
<th>Disappearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 weeks</td>
<td>Full [40w]</td>
<td>Foramen of Monro</td>
<td>1.5</td>
<td>6 months</td>
</tr>
<tr>
<td>2</td>
<td>5 months</td>
<td>Full [39w]</td>
<td>Temporal horn</td>
<td>2.3</td>
<td>4 months</td>
</tr>
<tr>
<td>3</td>
<td>8 days</td>
<td>Premature [36w]</td>
<td>Occipital horn</td>
<td>1.5</td>
<td>23 months</td>
</tr>
<tr>
<td>4</td>
<td>10 days</td>
<td>Premature [36w]</td>
<td>Foramen of Monro</td>
<td>1.0</td>
<td>No follow up</td>
</tr>
<tr>
<td>5</td>
<td>7 days</td>
<td>Full [39w]</td>
<td>Foramen of Monro</td>
<td>1.3</td>
<td>No follow up</td>
</tr>
</tbody>
</table>

GA: Gestational age, w: weeks
Results

Bilateral paraventricular cysts averaging 15 [range, 10-23] mm in size were found in five patients (50%). They were adjacent to the foramen of Monro in three cases, the occipital horn in one case, and the temporal horn in one case (see Table). MR imaging showed that the fluid content of all cysts was of similar signal intensity to cerebrospinal fluid (T1-WI, hypointense; T2-WI, hyperintense) (Fig. 1A, B). For the four cysts examined ultrasonographically, the findings varied: there was one pure cyst and one with a thick wall and septations, and two contained complex fluid (Fig. 1, 2, 3). The pure cyst was situated adjacent to the occipital horns, and the remaining three, located adjacent to the foramen of Monro, had a sonographic appearance which mimicked hematoma of the germinal matrix (Fig. 3A). Follow up MR imaging and ultrasonography indicated that the cysts of the three patients disappeared after 4, 6, and 23 months respectively. Two cysts adjacent to the foramen of Monro disappeared after four and six months, respectively, while the one adjacent to the occipital horn became smaller after four months and disappeared after 23 months (Fig. 1E). At follow-up MR imaging, we found no evidence of hematoma in cysts adjacent to the foramen of Monro. Contrast T1-weighted images revealed that in all cases, the cystic wall was unenhanced. At the time a cyst disappeared, initial and follow-up MRI revealed no abnormal signal intensity caused by gliosis in surrounding brain parenchyma.

Discussion

In most infants with intrauterine CMV infection, clinical manifestations are not apparent at birth, while about 10% of neonates exhibit findings suggestive of congenital infection [9-10]. The diagnosis of CMV infection ultimately rests on the recovery of the infectious virus from tissue or body fluid. Demonstration of seroconver-
sion or a fourfold change in CMV antibody titers strongly suggests recent CMV infection, while other techniques such as immunofluorescence, and light and electron microscopic examination of tissue, may have diagnostic utility in selected cases (11). The neuroradiological imaging of infants with congenital CMV infection is important, and several reports have described the findings. It is well known that intracerebral calcification is the most common abnormality revealed by neuroradiological imaging in infants with congenital CMV infection: it has been found in up to 40% of affected children, either at plain radiography of the skull, or at CT (6, 12). In our study, however, it was detected by neither ultrasonography nor MRI. Radiological studies have demonstrated the presence of paraventricular cysts, not uncommonly in the brain, in 36–60% of CMV-infected children (5, 6, 8). Boesch et al. (6) reported that cranial MR imaging of ten children with congenital cytomegalovirus infection showed a dilated lateral ventricle (n = 10) and subarachnoid space (n = 8), oligo/pachygyria (n = 8), delayed/ pathological myelination (n = 7), paraventricular cysts, (n = 6) and intracerebral calcification (n = 1). They mentioned that six patients had characteristic paraventricular cysts; these were bilateral and adjacent to the occipital horns of the lateral ventricles. Barkovich et al. (8) reported that in MRI and CT studies of 11 patients with congenital CMV infection involving the brain, four had paraventricular cysts adjacent to the

![Fig. 2. Full term 2-week-old patient with delayed myelination. Paraventricular cysts with thick wall and septations.](image)

Coronal (A) ultrasonographic scan shows cysts with thick wall (short arrows) and septations (long arrow) adjacent to foramen of Monro. Paraventricular cyst shows low signal intensity (arrows) similar to cerebrospinal fluid (CSF) signal intensity at postcontrast coronal T1-weighted image. No enhancement of the cyst wall is seen (B). Follow-up ultrasonography (C) after two months shows reduction (open arrow) in size of the paraventricular cysts. Noncommunicating hydrocephalus is seen on coronal ultrasonography (B, C). Bilateral cysts disappeared completely on follow-up ultrasonography after four months (D).
temporal horns. Butt et al. (5) stated that paraventricular cysts found in two of the four patients with congenital cytomegalovirus infection were observed at ultrasound examination. The prominent periventricular location of viral damage has been attributed to the predilection of CMV to infect rapidly-growing subependymal or germinal matrix cells (11). The necrotizing inflammatory process in CMV infection involving the brain reads to the growth of paraventricular or subependymal cysts (5). For the former, location and bilaterality may therefore be characteristic but nonspecific imaging features of congenital CMV infection involving the brain.

Our results showed that although all paraventricular cysts were bilateral and had a pure cyst-like appearance at MR imaging (T1-WI, hypointense; T2-WI, hyperintense), ultrasonographic examination revealed different and various patterns. The ultrasonographic findings of paraventricular cysts included a pure cysts, one with a thick wall and separations, and two with complex fluid. Three cysts with septation or complex fluid contents were situated adjacent to the foramen of Monro and their sonographic appearance mimicked hematoma of the germinal matrix. In our study, differentiation at ultrasonography between germinal matrix hemorrhage and cysts adjacent to the foramen of Monro was difficult, though at MRI, because a hematoma demonstrates varying signal intensities at different stages of resolution, differentiation between a hematoma and a cyst was not. At MRI, cysts adjacent to the foramen of Monro show no signal intensities characteristic of a hematoma.

Sofer et al. [13] reported the occurrence of congenital CMV periventriculitis mimicking the classical sonographic picture of periventricular hemorrhage. They stated that sonographic examination of a CMV-infected brain revealed periventricular echogenic clumps, main-
ly in the occipital region of the brain, that were isoechic with the choroid plexus. They also mentioned that at necropsy, examination of the brain revealed irregularity of the walls of the lateral ventricles accompanied by small irregular patches; at microscopic examination, these patches, containing CMV inclusion bodies, were shown to be foci of periventricular necrotizing encephalitis. Most reports have mentioned that the formation of paraventricular cysts or echogenic materials concurrent with congenital CMV infection involving the brain results from necrosis and an inflammatory process. Barkovich et al. (8) stated that the significance of paraventricular cysts is uncertain and that they are probably the result of localized tissue destruction. We suggest that necrotizing and inflammatory paraventricular cysts may be either purely cystic or complex, mimicking hematoma at ultrasonography. Complex contents in paraventricular cysts may be clumps or sludge caused by focal necrosis and inflammatory reaction. Recognition of the various appearances of these cysts at ultrasonography may be important for proper diagnosis of congenital CMV infection in the brain.

Boesch et al. (6) reported that in one of six patients with paraventricular cysts, a second MRI examination was performed seven months later, and at that time the cystic structure still persisted. In our study, three patients underwent follow-up MR and ultrasonography, and it was found that the cysts disappeared after four to 23 months.

Paraventricular cysts occur in other congenital viral infections of the brain. In newborns, their most common proven causes are rubella and CMV infections, and Beltinger et al. (14) stated that in two newborns with congenital rubella syndrome, cranial ultrasonography demonstrated bilateral cystic lesions in the subependymal germinal matrix. On the basis of our results and this report, we believe that congenital viral infections should be included in the differential diagnosis of neonates with various or characteristic paraventricular cysts. The sonographic detection of such cysts should prompt an intensive search for congenital viral infections.

In conclusion, we found that paraventricular cysts were most commonly located adjacent to the foramen of Monro. Although they may appear at MRI to be purely cystic in nature, ultrasonography may reveal that their contents are complex, or that septations are present. The recognition of these characteristics at neuroradiological imaging may be important for the proper diagnosis of congenital CMV infection. Further studies of paraventricular cysts in more patients are needed.

Acknowledgements

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References

Cytomegalovirus (CMV)

요약

요약: cytomegalovirus (CMV)에 의한 뇌의 염증과 질병의 웅적임을 포함한 CMV의 임상 및 MRI 소견을 조사하였다. 본 연구의 목적은 CMV에 의한 뇌의 염증과 질병의 진단과 치료를 개선하는 것이다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있었다. 본 연구의 결과는 CMV에 의한 뇌의 염증과 질병의 진단과 치료에 대한 지침을 제시할 수 있다.