Interhemispheric Glioependymal Cyst Associated With Agenesis of the Corpus Callosum
—Case Report—

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Abstract
A male neonate was admitted because prenatal ultrasonography indicated central nervous system abnormalities. Neurological examination showed no abnormality except for electroencephalographic spike activities. Magnetic resonance imaging revealed a cystic lesion in the left interhemispheric fissure, agenesis of the corpus callosum, and microgyria in the left frontotemporal lobes. Cerebral blood flow (CBF) was diffusely reduced. The cyst wall was partially removed and a cyst-peritoneal shunt procedure was performed. The histological diagnosis was glioependymal cyst. The spike activity disappeared and CBF dramatically improved after the operation.

Key words: glioependymal cyst, agenesis of the corpus callosum, microgyria

Introduction
Cysts lined by epithelial cells are generally termed epithelial or neuroepithelial cysts.3,7,17 Epithelial cysts of the neuraxis can be further classified by the elements of neural structure into ependymal cyst, glioependymal cyst, choroidal epithelial cyst, neurenteric cyst, colloid cyst, Rathke’s cleft cyst, epidermoid cyst, and dermoid cyst. Therefore, a cyst lined with the wall composed of ependymal cells and glial cells is defined as a glioependymal cyst.9
Glioependymal cysts are considered to originate in developmental anomalies resulting from ependymal rests (diverticula of the developing neural tube isolated during embryogenesis) or cyst formation within the subarachnoid glial heterotopia with an ependymal element.1,3 Most glioependymal cysts occur in the subarachnoid space, usually over the cerebral hemisphere and occasionally in the intracerebral parenchyme.3,7,17

We describe a case of glioependymal cyst located in the interhemispheric fissure associated with total agenesis of the corpus callosum.

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Case Report
A male neonate was born to a 25-year-old female who was pregnant for the first time. She had visited the obstetrical-gynecological clinic for a regular prenatal check up at 30 weeks of gestation. Ultrasonography indicated congenital hydrocephalus of the fetus and the mother was transferred to our institution. She had no history of medication, alcoholism, or illicit drug abuse, and there was no individual or familial history of neurological illness. The fetal biparietal diameter was 91 mm at 37 weeks of gestation. The male infant was delivered at 38 weeks of gestation by cesarean section because of arrest of fetal descent and decreased fetal heart beat (100 bpm) during labor. He had an Apgar score of 9 at 5 minutes. The infant weighed 2780 g and his head circumference was 34.5 cm. The anterior fontanel was normal. The general condition was good with no irritability. No focal neurological deficits were found. Routine laboratory examinations and detailed cardiac evaluation were within normal limits.

Skull radiography showed no separation of the cranial sutures and no other abnormalities. Computed tomography (CT) showed a large cystic lesion in the frontoparietal interhemispheric area located
mainly on the left side and compressing the medial surface of the frontoparietal lobes (Fig. 1). The cyst content was isodense to the lateral ventricle. The bilateral lateral ventricles were colpocephalic shaped and compressed by the cystic lesion. Magnetic resonance (MR) imaging revealed that the cystic lesion had double compartments separated by a septum formation. The cystic lesion was mainly located in the left interhemispheric space and extended to the right side under the falk and compressed the third ventricle downward. $T_1$-weighted MR imaging showed the cyst content as slightly hypointense to the cerebrospinal fluid (CSF) in the lateral ventricle (Fig. 2). Gadolinium administration showed partial enhancement of the cyst wall. MR imaging also showed complete agenesis of the corpus callosum. Preoperative MR imaging showed no

Fig. 2 A: Axial magnetic resonance (MR) images showing the multilobulated cystic lesion divided by the septum. The cyst content is slightly hypointense to the cerebrospinal fluid in the lateral ventricle. B, C: Coronal (B) and sagittal (C) MR images showing the cystic lesion mainly located in the left interhemispheric area and extending into the right side, complete agenesis of the corpus callosum, and compression of the third ventricle.
neocortical maldevelopments such as heterotopic gray matter and microgyria, but postoperative MR imaging indicated polymicrogyria in the left frontal and temporal lobes.

Carotid angiography demonstrated marked separation of the bilateral anterior cerebral arteries and an avascular area in the frontoparietal region. Cerebral blood flow (CBF) measurement by single photon emission computed tomography (SPECT) with N-isopropyl-p-\(^{123}\)I]iodoamphetamine (\(^{123}\)I-IMP) showed severely reduced CBF in the cortex (Fig. 3). Semiquantitative analysis used regions of interest (ROIs) selected in the bilateral frontal, parietal, and occipital areas and the mean counts per voxel were estimated in each ROI. Cerebellar counts were used for semiquantification of the results and the cortical-to-cerebellar ratios were calculated (right frontal 0.77, left frontal 0.88, right temporal 1.07, left temporal 1.08, right parietal 0.79, left parietal 0.87, right occipital 0.60, left occipital 0.57). Electroencephalography showed spike activity over the bilateral frontal regions. Repeat CT at 16 days of age showed slight enlargement of the cystic region.

Surgery was planned because of the mass effect to the surrounding brain parenchyma with the spike activity and the reduced CBF at 30 days of age. A small left frontoparietal craniotomy was performed. Opening of the dura mater over the cysts found no adhesion between the dura and the cyst wall. Reflection of the dura mater encountered the dome of the cyst between the falx and the brain. The cyst wall was composed of thin semitranslucent membrane and cortical veins on the surface of the cyst wall. Prominent tortuous fine blood vessels coursed over the cyst. The cyst wall was partially resected and fenestrated. The cyst contained slightly xanthochromic, protein-rich fluid (protein 257 mg/dl, sugar 91 mg). Communication between the two lobulated cyst compartments was established by tearing the septum under the operating microscope and implanting a cyst-peritoneal (CP) shunt.

The postoperative course was uneventful and spike activity disappeared without anticonvulsant administration. CT showed remarkable reduction in the cyst size (Fig. 4) and postoperative \(^{123}\)I-IMP SPECT showed dramatic improvement in CBF over the whole brain (Fig. 5). The cortical cerebellar ratios were also calculated (right frontal 1.32, left frontal 1.11, right temporal 1.64, left temporal 1.53, right parietal 1.53, left parietal 1.56, right occipital 1.39, left occipital 1.21).

Histological examination of the cyst specimen showed that the inner surface of the wall consisted of

Fig. 4 Postoperative computed tomography scans showing the reduced cystic lesion with the cyst-peritoneal shunt tube.
of an inner layer of flattened and low cuboidal epithelial cells and an outer layer of fibrous connective tissue and dark glia-like cells which were stained positively for glial fibrillary acidic protein (Fig. 6). Electron microscopy showed the luminal surface cells possessed microvilli. The histological diagnosis was glioependymal cyst.

Follow-up CT detected no subdural fluid collection. Eleven months following surgery, the patient showed normal development without neurological deficits.

Discussion

Table 1 summarizes the clinical, radiological, and combined central nervous system (CNS) anomalies of six previous cases and the present case of glioependymal cyst associated with agenesis of the corpus callosum.\textsuperscript{1,2,12,13,18,19} The descriptions of the glial tissue component within the cyst wall in Cases 2 and 4 are inconsistent with the diagnosis of ependymal cyst, and indicate glioependymal cysts. The patients were aged from neonate to 5 years with apparent male dominance (6 males and 1 female). The most common initial symptoms were macrocephalus and seizure, sometimes accompanied by mild motor weakness. CT and MR imaging showed the mass lesions as isodense to slightly hyperdense or isointense to hyperintense to the CSF in the interhemispheric fissure (5), intra-lateral ventricle (1), and paraventricular region (1).

Associated agenesis of the corpus callosum was complete in five cases and partial in two cases. Interestingly, glioependymal cysts associated with agenesis of the corpus callosum were also associated with other CNS anomalies such as microgyria (4/7 patients), heterotopic gray matter (2/7 patients), and cerebellar hypoplasia (2/7 patients). Agenesis of the corpus callosum may also be associated with other epithelial cysts including ependymal cyst,\textsuperscript{17} choroidal epithelial cyst,\textsuperscript{4} and arachnoid cyst\textsuperscript{20} in
Table 1  Cases of gliopendymal cyst associated with agenesis of the corpus callosum

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author (Year)</th>
<th>Age (Sex)</th>
<th>Symptoms</th>
<th>Site of cyst</th>
<th>CT</th>
<th>MR imaging</th>
<th>Cyst content</th>
<th>Type of agenesis</th>
<th>Other CNS anomalies</th>
<th>Operation</th>
<th>Outcome (complications)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Brihaye et al. (1956)</td>
<td>4 mos (F)</td>
<td>infantile spasm</td>
<td>inter-</td>
<td>---</td>
<td>---</td>
<td>ND</td>
<td>complete</td>
<td>microgyria, heterotopia, absence of pineal body, malformed cerebellum</td>
<td>none</td>
<td>dead</td>
</tr>
<tr>
<td>2</td>
<td>Takeshita et al. (1982)</td>
<td>1 mo (M)</td>
<td>macrocephalus</td>
<td>para-ventricular</td>
<td>CSF density</td>
<td>---</td>
<td>---</td>
<td>partial</td>
<td>xantho-chromic fluid</td>
<td>none</td>
<td>cyst removal</td>
</tr>
<tr>
<td>3</td>
<td>Barth et al. (1984)</td>
<td>neonate (M)</td>
<td>seizure</td>
<td>inter-hemispheric</td>
<td>---</td>
<td>---</td>
<td>ND</td>
<td>complete</td>
<td>microgyria, heterotopia, cerebellar hypoplasia</td>
<td>none</td>
<td>dead</td>
</tr>
<tr>
<td>4</td>
<td>Morimoto et al. (1986)</td>
<td>11 mos (M)</td>
<td>macrocerephalus, motor weakness</td>
<td>inter-hemispheric</td>
<td>CSF density</td>
<td>---</td>
<td>watery fluid</td>
<td>complete</td>
<td>none</td>
<td>cyst opening</td>
<td>good (subdural effusion)</td>
</tr>
<tr>
<td>5</td>
<td>Utsunomiya et al. (1987)</td>
<td>neonate (M)</td>
<td>none</td>
<td>inter-hemispheric</td>
<td>CSF density</td>
<td>---</td>
<td>watery and dark fluid</td>
<td>complete</td>
<td>microgyria</td>
<td>cyst opening, cyst removal</td>
<td>good (recurrence)</td>
</tr>
<tr>
<td>6</td>
<td>Niwa et al. (1991)</td>
<td>5 yrs (M)</td>
<td>seizure, motor weakness</td>
<td>lateral ventricle</td>
<td>hyperdense to CSF, cyst wall enhancement</td>
<td>hyperintense to CSF</td>
<td>hyperintense to CSF, cyst wall enhancement</td>
<td>partial</td>
<td>none</td>
<td>cyst opening</td>
<td>good</td>
</tr>
<tr>
<td>7</td>
<td>Present case</td>
<td>neonate (M)</td>
<td>EEG spikes</td>
<td>inter-hemispheric</td>
<td>CSF density</td>
<td>---</td>
<td>xantho-chromic fluid</td>
<td>complete</td>
<td>microgyria</td>
<td>cyst removal with CP shunt</td>
<td>good</td>
</tr>
</tbody>
</table>

Cases 2 and 4 were reported as ependymal cysts, but the cysts had glial tissue in the cyst wall, so the correct identification is gliopendymal cyst. CNS: central nervous system, CP: cyst-peritoneal, CSF: cerebrospinal fluid, CT: computed tomography, EEG: electroencephalography, MR: magnetic resonance, ND: not described.
the interhemispheric fissure. Any link between the pathogenesis of interhemispheric epithelial cyst and agenesis of the corpus callosum remains unclear. Agenesis of the corpus callosum is generally considered to result from a genetic, metabolic, or mechanical defect confined to the commissural plate early in development (6th week of gestation)." The pathogenesis could involve cystic lesions because a large interhemispheric cyst could mechanically impede the development of the interhemispheric association fibers. However, a very small cyst is sometimes found in the interhemispheric area associated with complete agenesis of the corpus callosum. Therefore, the association of gliopendymal cyst with various CNS anomalies is unlikely to be incidental. Heterotopia (ectopic gray matter) and microgyria are believed to result from disturbance of the neuronal migration that occurs at the 7th week of gestation. The wide variety of associated anomalies and origin in different periods of embryogenesis suggests that various pathogenic factors lead to formation of gliopendymal cyst. Gliopendymal cyst may be the result of inappropriate displacement and heterotopia of ventricular epithelium. Gliopendymal cyst and neocortical maldevelopments may both be caused by disturbance of normal cell migration. Agenesis of the corpus callosum is also associated with other CNS anomalies such as neuronal heterotopia and microgyria. However, this issue is still unclear and needs further investigation.

Gliopendymal cyst associated with agenesis of the corpus callosum should be differentiated from other CNS anomalies such as dorsal cyst caused by holoprosencephaly and cystic dilation (diencephalic cyst) associated with agenesis of the corpus callosum. Coronal MR imaging is helpful to elucidate the anatomical relationship between the cystic lesion and the third ventricle. Dorsal cyst and diencephalic cyst show anatomical continuity with the third ventricle but interhemispheric gliopendymal cyst is separate from and compresses the third ventricle. Midline lipoma should also be differentiated. Arachnoid cyst located in the interhemispheric fissure is also associated with agenesis of the corpus callosum. Arachnoid cyst is generally hard to differentiate radiologically from gliopendymal cyst. However, the fluid of gliopendymal cyst is protein rich. The diagnosis of gliopendymal cyst can be based on isointensity or slight hyperintensity on T2-weighted images because of the protein-rich fluid of the cyst. Four cases of gliopendymal cysts contained colored (xanthochromic) fluid. MR imaging findings showing that the cyst content of gliopendymal cyst is slightly hyperintense to CSF and the wall is partially enhanced by gadolinium may help to differentiate gliopendymal and arachnoid cyst.

The ideal treatment for gliopendymal cyst is complete removal. Fenestration was performed in four cases, resulting in cyst recurrence in one case and subdural effusion in another. We performed partial removal of the cyst wall with CP shunt because preoperative differential diagnosis from arachnoid cyst was difficult and less invasive treatment was advisable for this neonate. CP shunt may be useful to prevent recurrence or subdural effusion after partial removal of the cyst wall. We achieved a good outcome but the CP shunt should be monitored for malfunction because the fluid of gliopendymal cyst is protein rich.

References

11) Mori K: Giant interhemispheric cysts associated with

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