The presence of central nervous system (CNS) tissue outside the cranium is often referred to as “heterotopia,” although technically this should be termed “ectopia,” according to the dictionary definition. Glioneuronal heterotopia (GH) is a rare, mass-forming, malformative lesion. Ectopic glioneuronal tissue of the head and neck has been detected in the nasopharynx, oropharynx, tongue, palate, tonsils, soft tissue, eye, and orbit, and intracranial extracerebral glioneuronal heterotopia (IEGH) has also been reported, although less frequently. Since the first description of neuroglial heterotopia in the dorsal meninges of the cervical spinal cord by Wolbach in 1907, fewer than 20 cases of IEGH have been reported. Glioependymal cysts are rare, ependyma-lined, cystic lesions of the subarachnoid space, which have been referred to as epithelial or ependymal cysts. Histopathologically, they are lined with ependymal cells abutted on the glial layer and are commonly detected in the posterior fossa. The origin of glioependymal cysts of the posterior fossa is not clear, but these cysts may represent neuroglial heterotopia, persistent Blake’s pouch (diverticulum of the roof of the fourth ventricle), or remnants of a tela chorioidea. We report here a case of IEGH that was predominantly composed of cerebellar tissue with some fat tissue and a large glioependymal cyst, and was initially misdiagnosed as a teratoma with a glioependymal cyst.

CASE REPORT

The patient was a 4-month-old female infant who was delivered spontaneously at 37 weeks of gestation. An atrial septal defect and patent foramen ovale of the heart were detected after birth. The patient also showed a low nasal bridge, a right-sided deviated nasal septum, ptosis of the left eye, and limited extraocular movement of the left eye.

Brain magnetic resonance imaging (MRI) revealed a 5-cm mass in the left frontotemporal and suprasellar areas, with cystic changes at both the center and on the left side of the mass (Fig. 1). The peripheral portion of the mass had a component of fat tissue. A 5.6-cm arachnoid cyst was observed in the left middle cranial fossa (MCF). In addition, through the anterior skull base defect, we observed left paramedian herniation of the mass into 3 areas: the left nasal cavity, ethmoid sinus, and left medial extraconal orbital space.

Following left temporal craniotomy and dural incision, an arachnoid cyst was found in the left sphenoid ridge. This arachnoid cyst was penetrated during surgery, and another cyst was detected under this arachnoid cyst. This second cyst was located in the middle of the mass, and pathological examination showed it to be a glioependymal cyst. Low vascular masses, which had a component of fat tissue, were present in the MCF and ethmoid sinus. All of these abnormal tissues were removed.

Follow-up MRI at 18 months after the operation, at the age of 25 months, revealed subdural fluid collection and a persistent enlarged left lateral ventricle. However, the patient’s attainment of motor milestones was fair with no evident neurological deficit.

Histopathologically, the mass was composed of an admixture of well and poorly organized cerebellar and cerebral tissue, adi-
pose tissue, and cysts lined with ciliated ependymal cells abutted on the glial and fibrous tissue (Fig. 2). The well-organized cerebellar tissue consisted of a molecular layer, a Purkinje cell layer, and inner and outer granule cell layers with well-formed white matter. However, in the poorly organized areas, these 3 layers were intermixed irregularly. In some areas, cerebellar deep gray-like organization was noted. Dilated vessels were observed in the fat and cerebral tissues. There were 2 types of cysts: an arachnoid cyst and a glioependymal cyst. The glioependymal cyst wall was also partly surrounded by atrophic cerebellar tissue. The glioependymal lining cells were positive for S-100 protein, and the glial tissue underlying these cells was positive for glial fibrillary acidic protein.

**DISCUSSION**

GH has been referred to as glioneuronal choristoma, glioneuronal hamartoma, brain heterotopia, and neuroglial heterotopia.\(^{1,4,5}\) It is a rare malformative lesion, and its precise incidence is unknown. Gyure et al.\(^{6}\) classified GH according to location and putative pathogenic mechanism as follows: intraparenchymal GH, dural and leptomeningeal GH, IEGH, distal GH of...
Table 1. Summary of reported cases of intracranial extracerebral glioneuronal heterotopia

| Location                        | Histologic composition (other than glioneuronal tissue) | Accompanying congenital anomalies |
|--------------------------------|--------------------------------------------------------|--------------------------------|
| MCF, Lt. (n = 5), ACF, Lt. (n = 2), suprasellar region (n = 2), retroorbital region (n = 1), subfrontal region (n = 1), occipital region (n = 1), frontotemporal region, Rt. (n = 1), cerebellomedullary cistern (n = 1) | Ependymal cell (n = 7), choroid plexus (n = 7), cyst(s) (n = 6), adipose tissue (n = 5), microcalcification (n = 4), cerebellar tissue (n = 2), dilated vessels (n = 2), other components: fibrous tissue, muscle fascicle, peripheral nerve, ocular pigmented epithelium, dyslaminated gray matter, etc. | Cleft palate (n = 2), cleft lip (n = 1), hemifacial hypoplasia with anophthalmia of orbit, Rt. (n = 1), other: low-set ear and microgenia (n = 1) |
| Frontotemporal and suprasellar region, Lt. | Cerebellar tissue, disorganized, large cyst, adipose tissue, Dilated vessels | Anirial septal defect |

The third component was intraparenchymal adipose tissue, which was admixed with the heterotopic brain tissue. Because of the presence of adipose tissue, the major differential diagnosis was teratoma; however, this was also observed in 5 of the previously reported cases. Gyure et al. suggested that the adipose tissue was simply an admixture of soft tissue around the IEGH, but Nishio et al. interpreted this tissue as embryonic ectomesenchymal elements (derivatives of the neural crest) that matured after aberrant migration during the formation of the neural tube. Skeletal muscle and salivary gland tissue have also been reported adjacent to the IEGH.3,10

Detection of tissue components such as mature neuroectodermal tissue, including cerebrum and cerebellum tissue, admixed with adipose tissue can lead to misdiagnoses of teratoma. However, the absence of tissues derived from other germ layers is the clue to distinguishing GH from mature teratoma. It has already been highlighted that GH may easily be misdiagnosed as a teratoma or a CNS tumor.6 However, some cases of GH are actually accompanied by nasopharyngeal teratoma.

Variably sized cysts in IEGH are not a rare finding, since they have been reported in 6 (31.6%) of the 19 cases (Table 1).1,2,4,5,8,9 Notably, 2 cysts were present in our case: one occupying the MCF and the other presenting around the tumor. Since, in our case, the glioneuronal cyst was located inside the IEGH and some part of this cyst was surrounded by atrophic cerebellar tissue, the glioneuronal cyst itself was thought to be a main manifestation of the IEGH.

There are 3 major theories to explain the pathogenesis of
Glioneuronal Heterotopia Accompanying Fat Tissue

IEGH: protrusion theory, accessory brain theory, and outpouching theory. Although many investigators favor a common origin for IEGHs and leptomeningeal and dural heterotopia, the protrusion theory of the brain into the subarachnoid space offers only a limited explanation for IEGHs because it cannot explain the presence of normal cerebellum tissue in its unusual position in combination with heterotopic adipose tissue. The accessory brain theory was introduced by Harris et al. because of the relatively large size of IEGHs. In the cases reported by Harris et al., the sizes of the IEGHs were similar to the size of a normal brain. The authors therefore suggested the development of an accessory brain between the fifth and sixth weeks of embryogenesis. The third theory suggests that outpouching of CNS tissue may occur at the same time as outpouching of the developing telencephalon from the prosencephalon, at the base of the telencephalic vesicles. The outpouching theory would explain the reason that most IEGHs are located in an inferior position in the cranium, but it cannot explain the presence of cerebellar tissue. If the outpouching theory is applicable in our case, outpouching should occur from multiple brain vesicles, including telencephalic and metencephalic vesicles (cerebellar primordium), at the secondary 5-vesicle stage, or from the neural tube stage just before the primary 3-vesicle stage, and then differentiate into telencephalic and metencephalic brain tissues. Moreover, glioependymal cysts can also originate from the central canal (future ventricles) of the brain vesicles.

In addition to the 3 aforementioned major theories, the aberrant migration theory states that embryonic neuroepithelial tissue aberrantly migrates into the subarachnoid space and continues to grow, rather than undergoing degenerative changes, resulting in heterotopias. The aberrant migration theory can explain the histology of this GH, as it is composed of cerebral and cerebellar tissue in heterotopic loci. However, the mechanism by which this aberrantly migrated tissue becomes well organized in heterotopic loci is unknown.

In summary, we have described a rare case of IEGH that occurred as a congenital cystic mass in the MCF in a patient who presented with ptosis of the left eye and who had an atrial septal defect of the heart. Histologically, the IEGH was composed of well-formed cerebellar and cerebral tissue, adipose tissue, and a glioependymal cyst. The main differential diagnosis was mature teratoma. Further reports of IEGH cases would improve our comprehension of this lesion, and elucidation of the pathogenesis of IEGH may expand our understanding of the mal-development of the CNS.

Conflicts of Interest
No potential conflict of interest relevant to this article was reported.

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