Coexistence of Ganglioglioma and Cortical Dysplasia in a Patient with Intractable Epilepsy
—Case Report—

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Abstract
An 8-year-old girl presented with coexistence of ganglioglioma and cortical dysplasia manifesting as intractable epilepsy. Preoperative computed tomography demonstrated a small calcified lesion in the left frontal lobe which was not diagnosed as ganglioglioma. Magnetic resonance imaging also failed to demonstrate positive evidence of ganglioglioma or cortical dysplasia. A calcified tumor and the surrounding epileptogenic areas were resected under electrocorticography (ECoG) guidance. Histological examination revealed coexistence of ganglioglioma and cortical dysplasia. The patient became seizure-free after surgery. Resection of the ganglioglioma together with the adjacent epileptogenic area under intraoperative ECoG guidance is important to achieve a successful surgical result in patients with ganglioglioma.

Key words: ganglioglioma, cortical dysplasia, epilepsy

Introduction
Ganglioglioma is one of the rarest of all intracranial neoplasms.3) Ganglioglioma frequently occurs in the temporal lobe and sometimes in the frontal lobe,14,17) with a relatively high incidence in children and young adults.4,13,17) Most patients with ganglioglioma have a favorable prognosis, but a few malignant cases have been reported.3,4,14,15,17) The incidence of accompanying epileptic seizures is 90%14) to 92%.17) Long-standing seizure is the most characteristic clinical feature of ganglioglioma.14,17) Only about half of all ganglioglioma patients become seizure-free after removal of the tumor.5,13) However, 11 of 12 patients became seizure-free after additional resection of the adjacent brain tissue under electrocorticography (ECoG) guidance.12) This result implies that the brain tissue surrounding a ganglioglioma is very important in epileptogenesis. However, the histological basis of such epileptic brain has not been studied thoroughly.

We present an epilepsy patient with a frontal lobe ganglioglioma and adjacent cortical dysplasia in which strong epileptiform discharges were detected by intraoperative ECoG.

Case Report
An 8-year-old girl had suffered seizures since the age of 3 months. Her seizures began with blank staring with the eyes in a fixed position and often developed to tonic flexion of the extremities. Generalized tonic-clonic seizures sometimes followed. Despite treatment with various antiepileptic drugs, her seizures became progressively more intractable. Her mental state gradually deteriorated with increased hyperactivity and emotional numbness. When she visited our hospital, she could not speak a word and was attending a center for the disabled. Her seizures consisted of drop attacks, complex partial seizures, and generalized tonic seizures.

Computed tomography (CT) demonstrated a small calcification in the left frontal lobe and extreme atrophy of the left temporal lobe (Fig. 1 left). Magnetic resonance (MR) imaging was performed on a 0.5 tesla unit. T1-weighted images (repetition time/echo
time [TR/TE] 600/26 msec) depicted the calcified area as an isointense mass with a hypointense center (Fig. 1 center). T2-weighted images (TR/TE 2000/100 msec) revealed the lesion as a hypointense mass (Fig. 1 right). The area was not enhanced with gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA). T2-weighted images of the left frontal lobe clearly demonstrated the medullary branch, which becomes blurred in most patients with cortical dysplasia.6,16) Preoperative neuroradiological examinations could not detect the coexistence of ganglioglioma and cortical dysplasia. Repeat electroencephalography (EEG) showed epileptic discharges in the left temporal and right frontal areas, but not in the left frontal region.

Based upon the preoperative evaluation, she underwent left temporal lobectomy for the complex partial seizures, and anterior two-thirds corpus callosotomy for the drop attacks. Histological examination of the surgical specimen from the left temporal lobe showed marked astrocytosis in the hippocampus. She was completely relieved from the drop attacks and complex partial seizures immediately after the operation, but generalized tonic seizures still oc-
curred once or twice per day.

Postoperative EEGs showed the epileptic discharges had shifted to the left frontal lobe where the calcified mass had been detected. After one-year observation of clinical seizures and scalp EEGs, we decided to perform a second operation for resection of the left frontal lobe. Intraoperative ECoG demonstrated strong epileptic discharges in the anterior part of the left frontal lobe indicating the calcified mass (Fig. 2). Under ECoG guidance, the most active epileptic region in the left frontal pole was resected. However, residual epileptic discharges were observed in the anterior stump of the frontal lobe. Additional resection of this area disclosed a well-defined hard mass (Fig. 3 left) that may have corresponded to the calcified area. Epileptic discharges disappeared after additional resection. ECoG with sevoflurane anesthesia was important in determining the epileptogenic area. Sevoflurane has a proconvulsant effect in epileptic cortex, but does not cause any proconvulsant effect in non-epileptic cortex. Based on the ECoG data, the epileptogenic areas were resected until the spike activities were totally eliminated under sevoflurane anesthesia.

Histological examination showed the calcified mass was a ganglioglioma consisting of both large polymorphic ganglion cells and bizarre cells (Fig. 4 upper left). The ganglion cells in the tumor occasionally showed binucleation and hydropic change, and immunostaining with antibodies against synaptophysin, neurofilament-200 kd, and neuron-specific enolase showed positive reactions in some areas. The bizarre cells were relatively weakly positive for glial fibrillary acidic protein, and strongly positive for vimentin (Fig. 4 upper right), an intermediate filament expressed in immature astrocytes, suggesting that the bizarre cells originated from astrocytes. The frontal pole where epileptic discharges were active included components of cortical dysplasia (Fig. 4 lower) including laminar abnormality of the cortex, increased neuronal density in the molecular layer, and single heterotopic neurons in the white matter. The histological diagnosis of the resected epileptogenic areas adjacent to ganglioglioma was cortical dysplasia (Fig. 3 right).

The patient has remained seizure-free for 2 years after the operation and her behavioral problems showed gradual improvement.

**Discussion**

Neuroradiological diagnosis of ganglioglioma is not always easy. In our patient, the small calcified lesion without Gd-DTPA enhancement was postoperatively diagnosed as ganglioglioma based on histological examination. Unexpected diagnosis of ganglioglioma of surgical specimens resected during epilepsy surgery has been reported previously. Calcification, cystic formation, and a solid lesion are infrequently observed on CT or MR images in ganglioglioma. Calc-DTPA enhancement was found in only 44% of cases. Based on the previous data, the specific neuroradiological features of ganglioglioma are difficult to characterize. Therefore, ganglioglioma...
Fig. 4 Photomicrograph showing a ganglioglioma consisting of both large polymorphic ganglion cells and bizarre cells (upper left: HE stain, × 200). The bizarre cells were immunostained with vimentin (upper right: streptavidin biotin method, × 100). Specimen from the frontal lobe (1 to 3 layers of gray matter) showing irregularity of neuronal architecture and increase of neuronal density (lower: Klüver-Barrera stain, × 150).

ganglioglioma should always be considered in an epileptic patient with an isolated calcified mass lesion.

Recently, the histological definition and classification of cortical dysplasia have been widely discussed. Our case showed architectural disorganization consisting of clustering neurons in the gray matter and heterotopic neurons in the white matter. Cellular abnormalities such as bizarre glial cells or neuronal cytomegaly were not detected. Therefore, this type of cortical dysplasia could be classified as microdysgenesis. In contrast, the histological findings of the ganglioglioma included definite cellular abnormalities including bizarre cells containing vimentin and synaptophysin.

The exact etiology and epileptogenic mechanism of ganglioglioma are still poorly understood. The coexistence of cortical dysplasia and congenital tumors such as ganglioglioma, dysembryoplastic neuroepithelial tumor, and low-grade glioma has recently been reported. A proposed neuroradiological classification describes these tumors as neoplasms associated with disordered cortex. In our case, the epileptogenic area as detected by intraoperative ECoG was composed of cortical dysplasia and ganglioglioma. The patient became seizure-free after resection of both lesions. Adjacent cortical architectural abnormalities occurred in 50% of patients with ganglioglioma, suggesting that as half of all gangliogliomas coexist with a dysplastic lesion, tumor resection alone is unlikely to achieve seizure control.

Tumor resection followed by anticonvulsant therapy is the conventional treatment for ganglioglioma. However, as shown in our case, intractable epilepsy is caused not only by the tumor but also by surrounding cortical dysplasia in most patients with ganglioglioma. Associated cortical dysplasia should always be considered in planning resection of ganglioglioma, even if preoperative neuroimaging provides no evidence. Epilepsy originating from cortical dysplasia is notoriously medication-resistant. Since patients with ganglioglioma are generally young, residual seizures often compromise their daily activity for a long time after surgery. Therefore, the importance of resection of the ganglioglioma together with the adjacent epileptogenic area based on intraoperative ECoG cannot be overemphasized.

References

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