

A Surgical Case of Frontal Lobe Epilepsy Due to Focal Cortical Dysplasia Accompanied by Olfactory Nerve Enlargement: Case Report

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Abstract

A 45-year-old man came to our clinic due to refractory general tonic seizure and an attack of unintended yelling. Magnetic resonance imaging (MRI) demonstrated mild cortical hyperintensity on fluid attenuated inversion recovery (FLAIR) image in the left basal frontal area. Enlargement of the left olfactory nerve was also detected below the affected gyrus. Subtotal resection of the MRI-visible epileptogenic lesion was performed without any neurological deficit. The final pathological diagnosis was focal cortical dysplasia (FCD) type IIa. Seizures and yelling attacks subsided after surgery. Extracerebral abnormalities, including cranial nerve enlargement, are common in patients with hemimegalencephaly. However, such abnormalities are rare with FCD.

Key words: epilepsy, olfactory nerve, focal cortical dysplasia, hemimegalencephaly

Introduction

Focal cortical dysplasia (FCD) is one of the major cause of frontal lobe epilepsy. Extracerebral abnormalities, such as enlargement of the cranial nerves, cerebral vascular dilatation, and cerebellar deformity, are common in patients with hemimegalencephaly. However, such abnormalities are rare in patients with FCD. In addition, such abnormalities are generally thought to be helpful in differentiating between hemimegalencephaly and cortical dysplasia.¹⁾ Here, the authors present a rare surgical case with frontal lobe epilepsy due to FCD accompanied by ipsilateral olfactory nerve enlargement.

Case Report

I. History and examination

A 45-year-old man came to our outpatient clinic due to intractable tonic seizure and yelling. For him, the unintended yelling attack was the most bothersome symptom. The first epileptic event occurred when he was 10 years old, and was a tonic seizure after loss of consciousness. He was diagnosed with epilepsy at a pediatric clinic and started to take antiepileptic drugs. The medication was initiated with phenytoin, but carbamazepine, gabapentin,

and clobazam were added because the seizures were intractable.

The symptoms were resistant to such drugs and seizures occurred two or three times a week. Psychiatric symptoms, such as auditory hallucinations and yelling, which was a protective response against offensive voices in his head, developed gradually. These psychiatric symptoms initially responded to aripiprazole, but gradually became refractory to drugs. An extraordinary lesion was detected on magnetic resonance imaging (MRI), and a diagnosis of frontal lobe epilepsy due to FCD was made. He was referred to our clinic to investigate surgical indications for refractory seizures. Before surgical treatment, generalized tonic seizures continued for 5–10 s and occurred once or twice a week, with yelling attacks occurring many times a day. He also complained of an olfactory aura described as unpleasant. The patient had no past medical history, including the perinatal period, except epileptic events. He showed no neurological deficits including olfaction.

Psychological testing, including Wechsler Adult Intelligence Scale (WAIS-III), Wechsler Memory Scale (WMS-R), Ray Auditory Verbal Learning Test (RAVLT), and frontal lobe testing, such as Wisconsin Card Sorting Test (WCST), showed almost normal results and no specific abnormalities were detected. On fluid-attenuated inversion recovery (FLAIR) and short T₁ inversion recovery (STIR) imaging, mild cortical hyperintensity was observed with obscured

sulci around the left orbital gyrus (Fig. 1). The enlarged ipsilateral olfactory nerve was also detected (Fig. 1). The affected nerve ranged from the olfactory trigone to the olfactory bulb. Moreover, the enlarged olfactory nerve was connected to the affected basal frontal lobe including the anterior perforated substance (Fig. 1). The authors also performed WADA test to determine the dominant side of the hemispheres especially regarding language, and the left was found to be the dominant hemisphere.

II. Operation and findings

General anesthesia was induced by inhalation of 5% sevoflurane, and the trachea was intubated with rocuronium. A curvilinear incision was made and a left frontal craniotomy was performed. The dura was opened and intraoperative electrocorticography was performed. During electrocorticography, the end-tidal sevoflurane concentration was continued at 2.8% and end-tidal CO₂ was maintained at 30 mmHg. An abnormal sharp wave originating from the orbitofrontal cortex was found (Fig. 2).

Subpial removal of the affected left orbitofrontal lesion was completed using microdissection scissors, bipolar electrodes, and a cavitron ultrasonic surgical aspirator (CUSA; Vallelab, Boulder, Colorado, USA). The affected frontal lobe was moderately hard, but the macroscopic appearance was almost normal. A definitely enlarged olfactory nerve was also detected (Fig. 3). To preserve olfaction, the surgeon did not resect any part of the enlarged olfactory nerve. The

olfactory enlarged trigone was identified and the affected anterior perforated substance, which was located just behind it, was preserved. The abnormal sharp waves subsided after resection. The final pathological diagnosis of resected basal frontal area was FCD type IIa (Fig. 3).

III. Postoperative course

The patient had a stable postoperative course without any complications. Postoperative MRI indicated successful resection of the lesion affected with FCD (Fig. 4). There were no morphological changes in the residual olfactory nerve. The patient left the hospital and went home on postoperative day 12. The patient's seizures and yelling subsided soon after the operation. The frequency of tonic seizures reduced to once a month and the duration also reduced to 2 s or 3 s. Although the number of auditory hallucination did not get reduced, the frequency of yelling was reduced to once a week. He now routinely visits the outpatient clinic.

Discussion

Extracerebral abnormalities, such as enlargement of the cranial nerves, cerebral vascular dilatation, and cerebellar deformity, are common in patients with hemimegalencephaly. The most commonly affected cranial nerve is the olfactory nerve. Previously, it was reported that ipsilateral olfactory nerve enlargement was detected in 26.7% of patients with

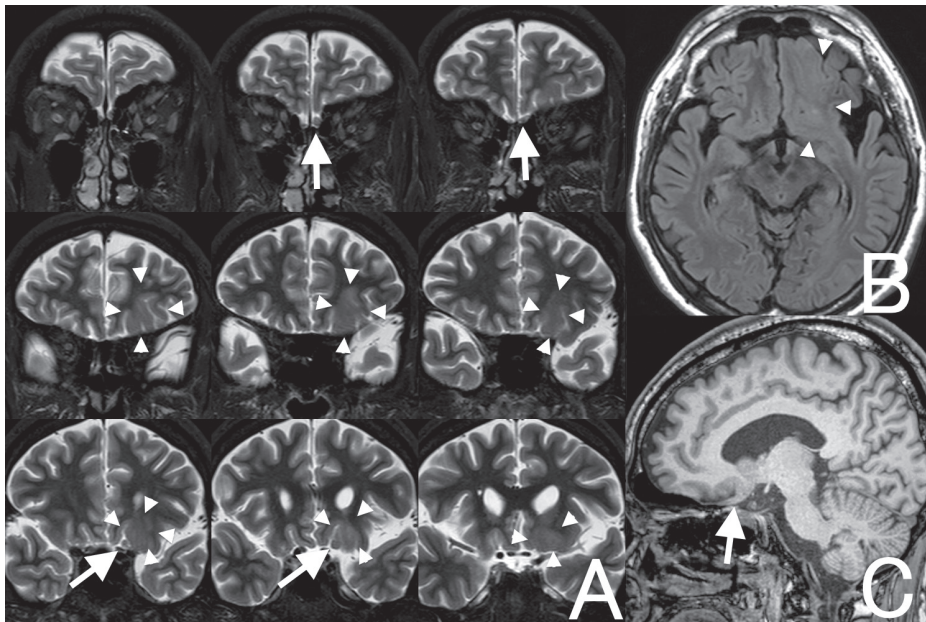


Fig. 1 A: Coronal short T₁ inversion recovery (STIR) images revealed an isointense mass below the left frontal lobe (arrows) and mild cortical hyperintensity that extended to the left anterior perforated substance (arrowheads). B: Axial fluid attenuated inversion recovery (FLAIR) image showing the area of hyperintensity in the left basal frontal area (arrowheads). C: Sagittal T₁ weighted image showing the definitely enlarged olfactory nerve under the anterior perforated substance (arrow).

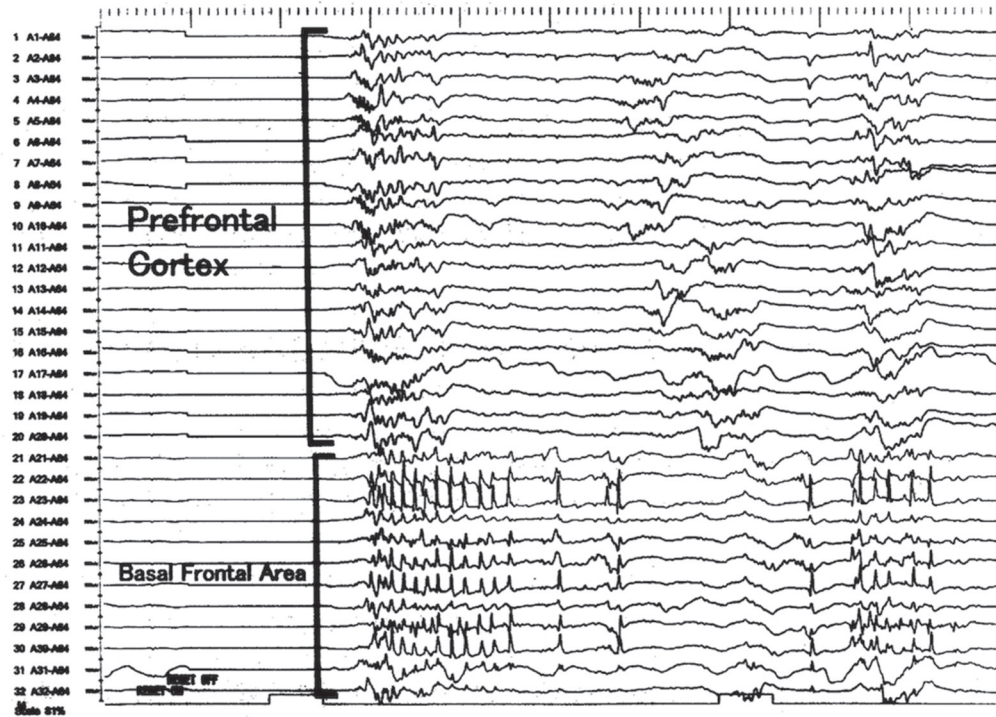


Fig. 2 Intraoperative electrocorticography demonstrating abnormal sharp waves originating from the basal frontal area. This was performed using a 5 × 4 grid of electrodes placed on the prefrontal cortex and three sets of 4 × 1 electrodes on the basal frontal area. During the procedure, the end-tidal sevoflurane concentration was continued at 2.8% and end-tidal CO₂ was maintained at 30 mmHg.

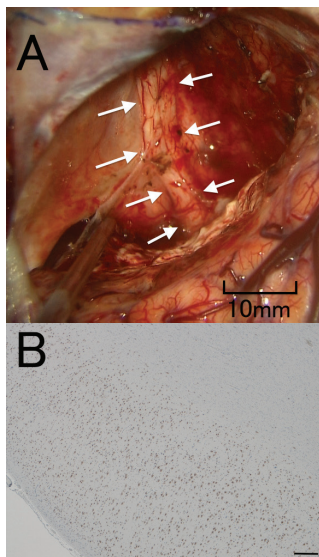


Fig. 3 A: Intraoperative view through a left frontal craniotomy. *White arrows* indicate the left enlarged olfactory nerve adjacent to the left optic nerve under the partially resected basal frontal area. B: Neuronal Nuclei (NeuN) staining of resected left orbital gyri. The columnar organization of the enlarged dysmorphic neurons can be seen in the lower right portion of the figure. Scale bar: 300 μm.

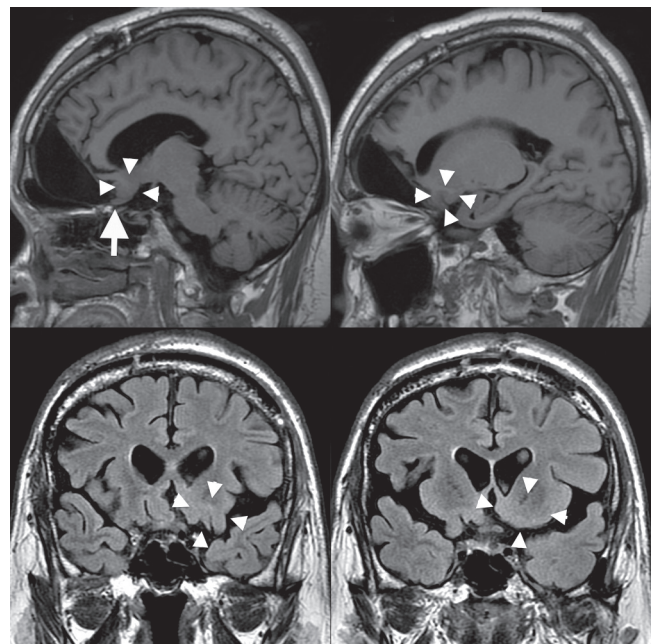


Fig. 4 Postoperative magnetic resonance imaging (MRI) showing subtotal resection of the affected left basal frontal area. The *arrow* indicates the preserved left olfactory nerve, and the *arrowheads* indicate the preserved anterior perforated substance.

hemimegalencephaly, while optic nerve enlargement was detected in 3.3% of these cases.²⁾ A diagnosis of multilobar cortical dysplasia is made when the dysplastic cortices extend over multiple gyri or multiple lobes.³⁾ Nakahashi et al. performed a retrospective review of the MRI findings in 43 patients with hemimegalencephaly and 10 patients with multilobar cortical dysplasia.¹⁾ In their series, there were no cases with extracerebral abnormalities, such as olfactory nerve enlargement, among patients with multilobar cortical dysplasia, and they concluded that such abnormalities would be helpful in differentiating between hemimegalencephaly and cortical dysplasia.¹⁾ Thus, olfactory nerve enlargement with FCD is extremely rare. In hemimegalencephaly, the affected hemisphere may occasionally become atrophic if seizures are not well controlled.⁴⁾ In such cases, it may be difficult to distinguish between hemimegalencephaly and cortical dysplasia. In our case, almost all brain structures except the left olfactory nerve and inferior part of the frontal lobe were symmetrical and localized hemimegalencephaly was unlikely (Fig. 1). Therefore, we made a diagnosis of FCD with unilateral olfactory nerve enlargement. Another study indicated ipsilateral olfactory nerve enlargement with hemimegalencephaly, although little comment was made regarding these findings.⁵⁾ To our knowledge, the reports mentioned above are the only articles referring to an association between olfactory nerve enlargement and hemimegalencephaly or cortical dysplasia. Extracerebral abnormalities may be useful for differentiating between hemimegalencephaly and cortical dysplasia, but the present case indicated that the possibility of cortical dysplasia could not be excluded even if olfactory nerve enlargement is detected. There have been no reports of an embryological relationship between hemimegalencephaly and olfactory nerve enlargement. However, Antonelli et al. demonstrated increased levels of nerve growth factor (NGF) and numerous high-affinity NGF-receptor-positive cells in hemimegalencephaly tissues compared with control brain tissues.⁶⁾ NGF is produced and released by brain cells and is highly expressed in the central nervous system innervated by the magnocellular cholinergic neurons of the basal forebrain, including the hippocampus, olfactory bulb, and neocortex.⁷⁾ Moreover, not only neurons but also small blood vessels and nerve fibers displayed high-affinity NGF receptor positivity. In our patient, the affected olfactory nerve seemed to be connected to the abnormal orbitofrontal gyrus. The enlargement of the olfactory nerve may have been due to the high levels of NGF and NGF-receptor expression, but, further examinations regarding NGF were not done.

In surgery for frontal lobe epilepsy, the probability of becoming seizure-free is 55.7% at 1 year, 45.1% at 3 years, and 30.1% at 5 years.⁸⁾ MRI-visible frontal lobe lesions are correlated with a seizure-free postoperative course. However, the rate of recurrence ranges from 28% to 45%.⁸⁻¹⁰⁾ In addition, patients with FCD type II tend to have larger foci compared to patients with FCD type I. Indeed the most

important prognostic factor is total resection of the affected area. However, it is impossible to remove it completely when the affected area includes vital and neurologically important structures, such as those related to sensorimotor activity or speech.¹¹⁾ In this case, the affected area extended to the anterior perforating substance, which was unresectable. Hence there may be residual FCD. The postoperative image showed subtotal resection of the visible area on MRI. However, the symptoms persist although they have been partially relieved after surgery.

Yelling or shouting is sometimes observed in frontal lobe epilepsy patients. However, in this patient, it was considered to be related to the auditory hallucinations accompanied with psychosis due to refractory epilepsy. Hence, it may have been different from typical frontal lobe epilepsy yelling and it was considered to be a self-protective reaction against the offensive auditory hallucination, e.g., "you must die!" The primary purpose of the surgical resection was only the seizure control. However, it alleviated not only the general tonic seizures but also yelling attacks. To our knowledge, there have been no previous reports that surgery relieves such symptoms. Our case suggests the potential effectiveness of such surgery for frontal lobe epilepsy, and further studies are required.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in the article. All authors who are members of The Japan Neurological Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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