Resection of focal cortical dysplasia located in the upper pre-central gyrus

Samer Serag Eldin [1], Masaki Iwasaki [1], Yoshiyuki Nishio [2], Kazutaka Jin [3], Nobukazu Nakasato [3], Teiji Tominaga [1]

[1] Department of Neurosurgery,
[2] Department of Behavioral Neurology and Cognitive Neuroscience,
[3] Department of Epileptology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

ABSTRACT – The primary motor cortex of the oro-facial level can be removed without permanent deficits, because of the bilateral representation of the innate functions. In contrast, resective surgery of the hand motor cortex or higher levels presents more challenges. We treated two adult patients with intractable epilepsy caused by small focal cortical dysplasia in the pre-central gyrus located between the foot and hand primary motor cortices. Focal cortical resection was guided by cortical EEG and intra-operative motor evoked potential, resulting in seizure freedom without neurological deficits in both cases. These cases illustrate that resective surgery can be safely performed in the primary motor cortex even dorsal to the oro-facial level, as long as the critical regions of the hand and foot motor cortices remain intact. Accurate delineation of the anatomical lesion and functional areas using intra-operative neurophysiological monitoring is crucial for successful outcome of the surgery.

Key words: focal cortical dysplasia, epilepsy surgery, multimodal imaging, primary motor cortex, seizure outcome

Surgical removal of epileptogenic tissue may be prevented by the presence of eloquent cortex, resulting in reduced seizure control. Other surgical techniques, such as multiple subpial transection, have been developed for the treatment of epileptic lesions overlapping the functional cortex, but have lower efficacy compared to surgical removal. Therefore, surgical removal should be attempted if the epileptogenic region is demarcated from the functionally eloquent cortex. The primary motor cortex at the oro-facial level can be safely removed without permanent deficit (Pondal-Sordo *et al.*, 2006), but resection is not usually considered in the higher (dorsal) levels. Limited resection under the guidance of careful pre- and intra-operative functional mapping has been achieved in rare cases (Mikuni *et al.*, 2005). However, the co-location of epileptogenicity and functionality greatly increase the challenges of surgical intervention. We report two successful cases of resective epilepsy surgery for small focal cortical dysplasia (FCD) located in the upper pre-central gyrus between the hand and foot motor representations.

Correspondence:
Masaki Iwasaki
Department of Neurosurgery,
Tohoku University Graduate School of Medicine,
Seiryo-machi, Aoba-ku, Sendai,
Miyagi 980-8574, Japan
<iwa@nsg.med.tohoku.ac.jp>

Case studies

Case 1

A 35-year-old, right-handed woman with no known previous history of perinatal and developmental problems began suffering seizures at age 23 years. The seizures started with heaviness in the left side of the body, followed by stiffness of the left leg and arm lasting for 10 to 20 seconds without loss of awareness. She had one to two seizures a day despite administration of multiple antiepileptic medications including carbamazepine, valproate, phenytoin, zonisamide, phenobarbital, gabapentin, topiramate, levetiracetam, and clobazam. She experienced secondary generalized convulsion only once at the onset of epilepsy. She had normal intelligence and no neurological deficits. Long-term video-EEG monitoring revealed focal tonic seizures of the left foot and leg, associated with low-voltage fast rhythms over the mid-central region at the onset. Interictal EEG showed intermittent rhythmic slow waves at the same region.

Case 2

An 18-year-old, right-handed woman with a previous history of viral encephalitis at age 13 years and severe scoliosis had suffered from epileptic seizures since the age of 5 years. The seizures started with painful sensation in the left side of the body, followed by left arm and leg clonic seizures, and bilateral limb tonic seizures lasting for less than one minute without loss of awareness. The patient also suffered from psychiatric symptoms. She had three to five seizures a day despite administration of multiple antiepileptic medications including carbamazepine, phenytoin, valproate, phenobarbital, clobazam, gabapentin, and levetiracetam. On neurological examination, mild motor weakness in the left leg was identified. She had low intelligence (full-scale intelligence quotient of 64 on Wechsler Intelligence Scales for Children, 3rd Edition). Long-term video-EEG monitoring revealed focal clonic seizures of the left arm and leg, associated with ictal low-voltage fast waves over the vertex region at the onset. Interictal EEG showed semi-continuous repetitive spikes at the midline vertex region.

Imaging studies and surgery

MR imaging revealed small lesions in the right pre-central gyrus posterior to the superior frontal gyrus in Case 1 (*figure 1*) and in the right pre-central and superior frontal gyri in Case 2 (*figure 2*). The lesions appeared hyperintense on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images, and isointense on T1-weighted images with no enhancement by gadolinium. The abnormal area included a wedge-shaped extension into the deep white matter. Morphological analysis based on 3D FLAIR and 3D magnetization-prepared rapid gradient echo (MPRAGE) imaging indicated that the lesions were located at the bottom of an abnormal indentation of the pre-central gyrus in Case 1 and at the bottom of an abnormal "blind alley" sulcus in the superior frontal gyrus in Case 2. Magnetoencephalography revealed equivalent current dipole sources clustered around the lesion in both cases. Focal glucose hypometabolism was identified at the lesion on fusion images of fluorodeoxyglucose positron emission tomography and 3D-MPRAGE imaging.

Invasive video-EEG study was performed in Case 1. A 4-contact depth electrode was inserted stereotactically to the depth of the lesion, and a total of 72 subdural contacts were placed on the lateral and medial surfaces of the fronto-parietal cortex over the lesion. Extraoperative video-EEG monitoring revealed that her seizures were associated with epileptiform discharges starting in the lesion and spreading to the medial frontal cortex. The epileptiform activities were limited to near the MR imaging lesion and were separated from the areas of critical motor functions of the upper and lower extremities determined with electrical cortical stimulation. Invasive video-EEG study was not performed in Case 2 due to her psychological problems.

Surgical removal of the lesion was performed in both cases. The arachnoid membrane of the fissure over the lesion was sharply cut to expose the indented surface of the dysplastic cortex (*figure* 1D). Intra-operative electrocorticography revealed frequent epileptiform spikes from the exposed cortex. After a histological sample was obtained, the lesion was aspirated with the cavitron ultrasonic surgical aspirator (*figure* 1E) under guidance from a neuronavigation system and motor evoked potential (MEP) monitoring. Surface electromyography of the left flexor pollicis brevis and plantar muscles was recorded after stimulation of the primary motor areas of the hand and foot, respectively, with platinum disc electrodes. At the final stage of removal, the leg MEP was monitored with subcortical stimulation from the resection cavity using a hand-held silver-ball electrode. Lesion removal was stopped when the MEP was evoked with a stimulus intensity as low as 5 mA, which suggested a distance to the pyramidal tract of 2 mm (Kamada *et al.*, 2009). The cortical MEP was preserved throughout the surgery in both cases. Post-operatively, Case 1 showed mild weakness (manual muscle testing [MMT]: 4/5) of the left leg, which had fully recovered within two days. She experienced very mild weakness in the left lower body axis during walking, which was difficult to confirm objectively and resolved completely in two weeks. Case 2 had
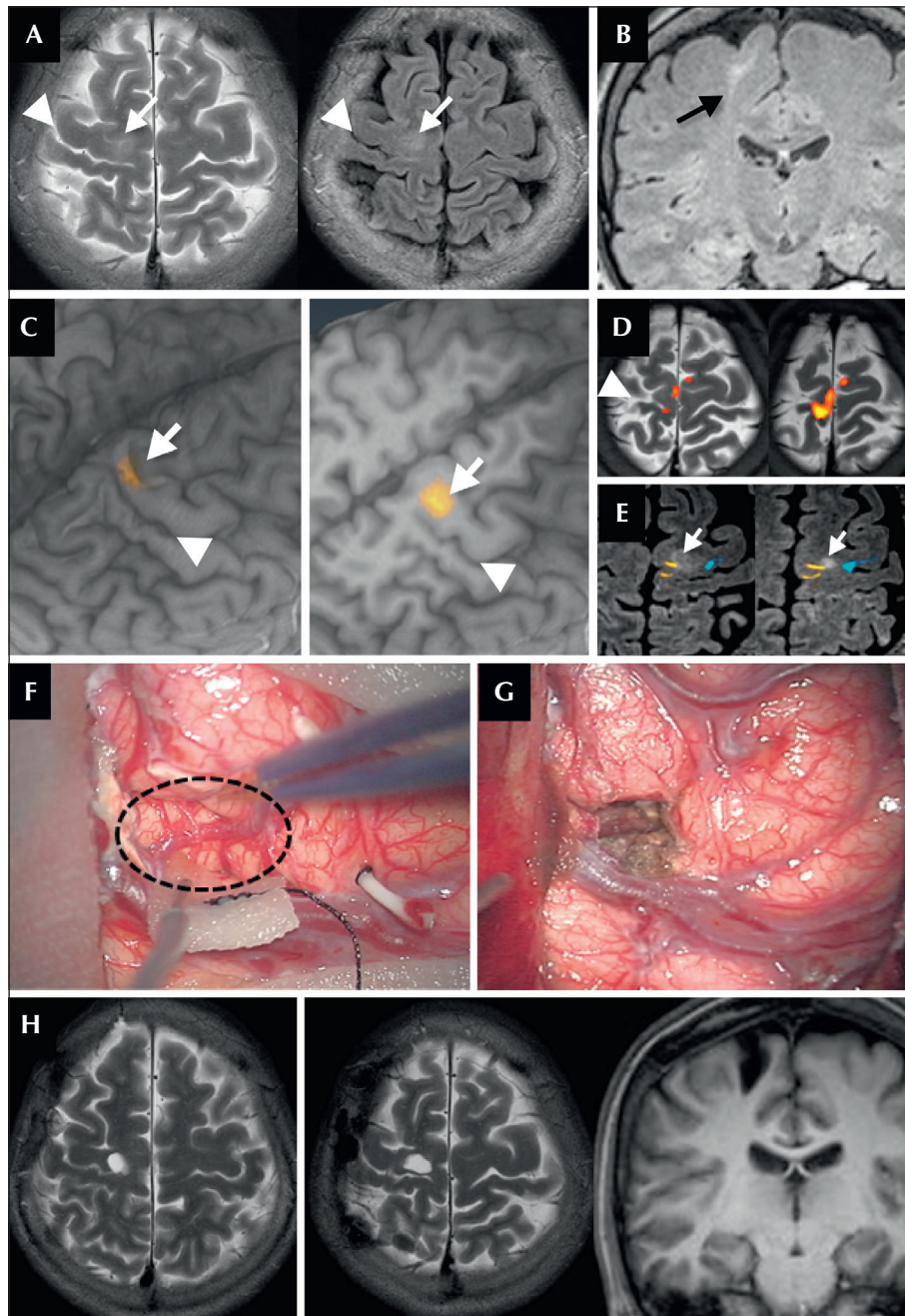
Figure 1. Case 1. (A-E) Pre-operative images showing the lesion (arrow) and the central sulcus (arrowhead). Axial T2-weighted (A, left) and FLAIR (A, right) MR images showing a small hyperintense lesion in the right pre-central gyrus. Coronal FLAIR image (B) showing a transmantle sign (black arrow). 3D brain images (C) showing the anatomical relationship of the lesion (highlighted with orange) to the pre-central gyrus. The lesion is located at the bottom of an abnormal indentation of the pre-central gyrus. Functional MR images during a left foot motor task (D) revealed significant BOLD signal change in the pre-central gyrus medial to the lesion. Fibre tracking from the leg and hand motor cortices viewed from above and overlaid on the axial FLAIR images (E) showed that the foot (yellow) and hand (blue) motor fibres coursed down immediately medial and lateral to the lesion, respectively. (F) Intra-operative view before resection. The arachnoid was dissected to reveal the "indented" pre-central gyrus including the lesion (dotted circle). Lesion resection was guided by a neuronavigation system and continuous MEP monitoring with cortical and subcortical stimulation. (G) Intra-operative view after resection. (H) Post-operative axial T2-weighted and coronal T1-weighted images. Focal resection had spared the foot and hand motor pyramidal tracts.
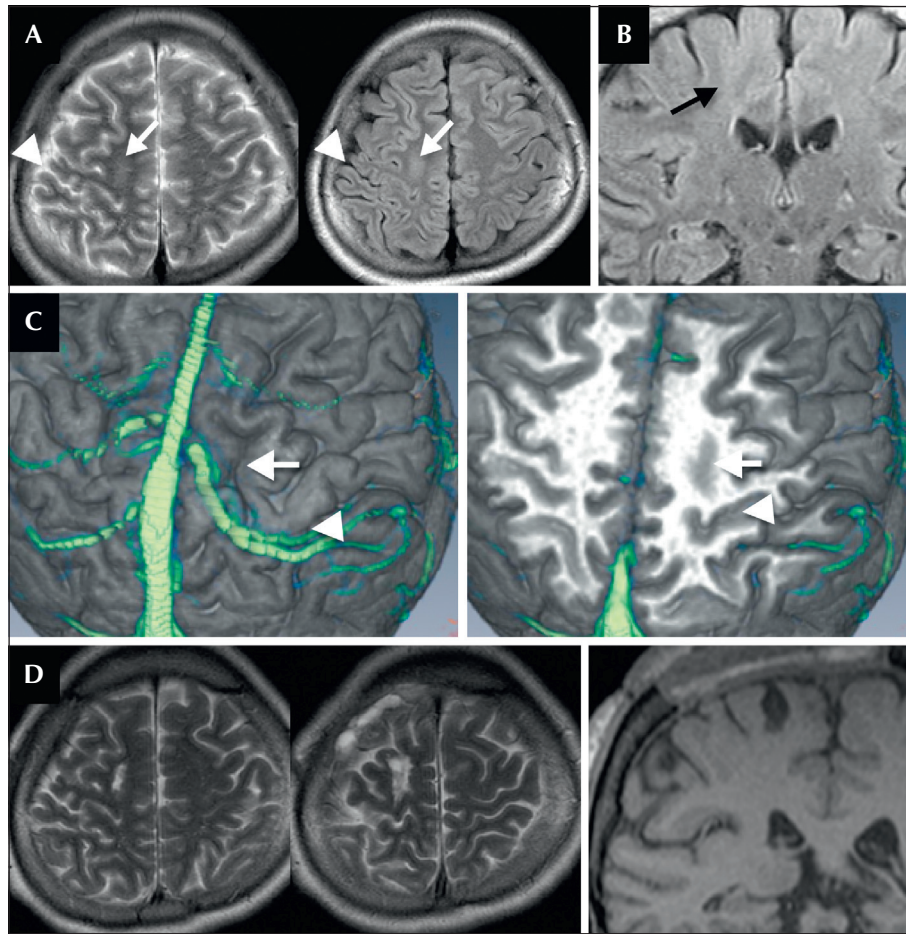
Figure 2. Case 2. (A-C) Pre-operative images showing the lesion (arrow) and the central sulcus (arrowhead). Axial T2-weighted (A, left) and FLAIR (A, right) images showing a small hyperintense lesion in the right pre-central gyrus and superior frontal gyrus. Coronal FLAIR image (B) showing a transmantle sign (black arrow). 3D brain images (C) showing that the lesion is located at the bottom of an abnormal "blind alley" sulcus in the pre-central and superior frontal gyri. (D) Post-operative axial T2-weighted and coronal T1-weighted images. Focal resection had spared the foot and hand motor pyramidal tracts.

severe motor weakness in the left arm (MMT: 1/5) and in the left leg (MMT: 2/5), which fully recovered in seven days. Post-operative MR imaging showed complete removal of the lesion and no associated injury in the surrounding cortex. Case 1 has been completely free from seizures for four years and Case 2 for 12 months with continuing antiepileptic medication. Histological examination showed findings compatible with FCD type IIa in both cases (Blümcke *et al.*, 2011).

Discussion

Our case study illustrates that resective surgery is possible in the primary motor cortex, even dorsal to the oro-facial level, as long as the critical regions of the hand and foot motor areas are left intact. The classical Penfield map assigns the primary motor area between the upper and lower limb motor representations to the

body trunk, although somatomotor responses of the trunk were detected on very rare occasions (Penfield and Rasmussen, 1950). To our knowledge, the neurological consequences of removal of this area have not been studied. However, control of the axial and girdle muscles is mediated by the anterior corticospinal tract, which innervates the bilateral muscles. Therefore, resection of the trunk motor area would be functionally compensated by the other hemisphere.

In our two cases, small FCD caused intractable epilepsy, and removal of the neuroimaging lesion resulted in seizure freedom. Careful diagnosis with high-field MR imaging is important because such small dysplasia may be very subtle in appearance and might not be detected by conventional imaging. Small FCD is often located at the bottom of the sulcus (Besson *et al.*, 2008; Hofman *et al.*, 2011). In our two cases, the lesions were located at an unusual indentation of the pre-central gyrus and at the bottom of an abnormal sul-

cus in the superior frontal gyrus. We believe that our cases had type IIb FCD because of characteristic MR imaging features. Only a part of the lesion was given for histopathological study, and balloon cells were likely missed in the specimen.

Functional recovery after cortical resection is determined either by the absence of function in the cortex removed or by functional compensation by the cortex left intact. Regions with histological evidence of FCD with balloon cells (type IIb) and increased intensity on FLAIR MR imaging are not co-localized with function (Marusic *et al.*, 2002). Resection of rolandic type II FCD based on neurophysiological and imaging results is followed only by transient sensori-motor deficits (Chassoux *et al.*, 2010). Larger resection potentially carries significant risks for permanent neurological deficits (Sarkis *et al.*, 2010), but meaningful functional recovery can be expected even in adults (Chamoun *et al.*, 2007). A functional MR imaging study demonstrated reorganization of primary motor function in children after removal of rolandic type II FCD (Barba *et al.*, 2012). Complete resection of the lesion is correlated with post-operative seizure freedom in the surgical treatment of type IIb FCD. Accumulating experiences obviated the need for invasive monitoring in selected cases (Chassoux *et al.*, 2012). High-quality anatomical imaging and functional studies, including functional MR imaging and tractography, are important for accurate and safe approach to the anatomical lesion. Additionally, intra-operative functional monitoring of the pyramidal tract with MEP is useful for maximizing resection of the epileptogenic tissue and minimizing surgical morbidity. Proximal parts of extremities, *i.e.* the arm and leg, would have been additionally monitored in our cases for more appropriate localization of critical motor function, because these parts were somatotopically closer to the lesion and at higher risk than the distal parts. □

Supplementary data.

Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.

None of the authors have any conflict of interest to disclose.

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TEST YOURSELF

(1) Why is surgical removal indicated for the circumscribed lesion, suggestive of type IIb FCD, within proximity of eloquent cortex?

(2) Is chronic intracranial EEG study mandatory for type IIb FCD located in the primary motor cortex?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".