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CASE REPORT

A case of focal cortical dysplasia type Ib atypically showing reversible intensity changes on magnetic resonance imaging which could be affected by epileptic discharge activity

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Abstract
Focal cortical dysplasia (FCD) was first described as a distinct neuropathological entity in 1971 by Taylor and colleagues. FCD is thought to be an embryological migration disorder and is thus considered a non-progressive, unchangeable disease throughout life. A 9-year-old right-handed boy was referred from a local hospital for medically intractable epileptic seizures. Serial magnetic resonance images (MRI) showed intensity changes that indicated exacerbation and remission. After presurgical evaluations including intracranial video-electroencephalogram monitoring, we performed a lesionectomy aided by MRI and epileptic focus resection. He has been free from seizures for more than 3 years. Neuropathological findings showed FCD type Ib. We surgically treated a patient with FCD, which showed MRI intensity changes indicating exacerbation and remission. Although FCD type Ib is generally invisible on MRI, in this patient, changes in intensity on MRI made FCD type Ib visible.

Keywords Focal cortical dysplasia · MRI intensity change · FCD type Ib · MRI visibility · Histopathological change

Introduction

Focal cortical dysplasia (FCD) is one of the most common neuropathological findings in the tissue resected from patients with medically intractable epilepsy [1, 2]. Sixty-two percent of patients with FCD are seizure free after surgery to remove the epileptic focus [1, 2]. The best predictor of becoming seizure free after surgery is whether the entire FCD lesion was removed [1]. The epileptogenic zone is often larger than the lesion identified with magnetic resonance imaging (MRI) [1].

We, herein, report a patient with an FCD lesion in whom the intensity on MRI changed during the disease course.

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Case summary

Clinical course

A 9-year-old right-handed boy was referred from a local hospital. At 2 years old, he experienced the first focal onset seizure, which consisted of unresponsiveness and staring. T2-weighted and fluid-attenuated inversion recovery (FLAIR) MRI showed a left temporo-occipital high-intensity lesion. Diffusion-weighted imaging (DWI) showed no changes in intensity on MRI (Fig. 1). His seizures had been controlled for several years. However, the seizures recurred at 6 years of age and were refractory to medications. He was referred to our facility at the age of 9 years.

His first MRI at 9 years and 8 months old showed a left temporo-occipital high-intensity lesion on FLAIR. At a time when he had been seizure free, a second MRI showed that the high-intensity lesion had decreased in intensity, despite frequent interictal epileptiform discharges seen on an electroencephalogram (EEG). We defined that the "occasional discharge" had less than six spikes per minute; the "intermittent discharge" had more than or equal to six but less than 20 spikes per minute; the "frequent discharge" had 20 or more spikes per minute

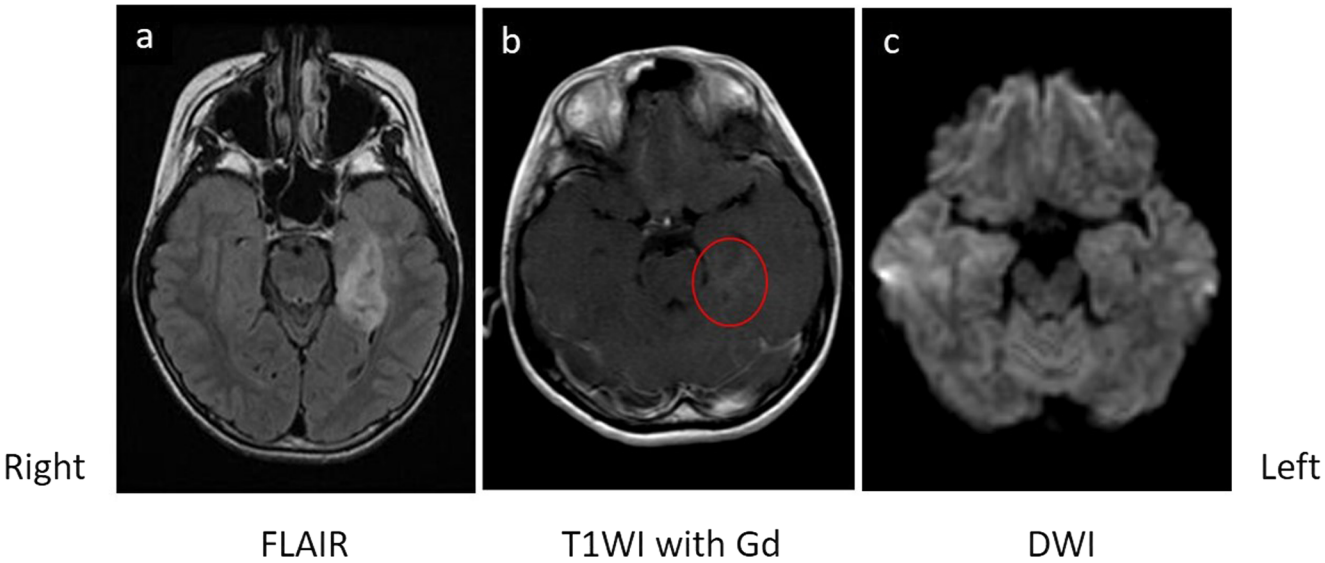

Fig. 1 The first MRI study at 9 years 8 months old. **a** Fluid-attenuated inversion recovery (FLAIR) MRI (left side) revealed a high-intensity cortico-subcortical area in the left temporo-occipital area and involved the medial temporal region and the hippocampus. **b** T1-weighted imaging with gadolinium contrast showed slight enhancement in the left hippocampal body and tail area. **c** This area showed no intensity changes on diffusion-weighted image (DWI) MRI

[3]. The third MRI, at a time when he was seizure free, showed a slight increase in intensity. After being seizure free for about 1 year, his seizures recurred monthly with clear exacerbation seen on the fourth MRI. Seizures continued to occur monthly, but the fifth MRI showed remission again. Despite an increase in medications, seizures became weekly, and exacerbation was seen on the sixth MRI (Fig. 2).

Intracranial EEG showed that epileptic seizures arose from the left temporo-occipital region of the ventral side adjacent to the lesion seen on MRI. Fluorodeoxyglucose-positron emission tomography (FDG-PET) showed decreased accumulation at the left mesial temporal lobe. Iomazenil (IMZ) or technetium-99m ethyl cysteinate dimer (99mTc-; ECD) single-photon emission computed tomography (SPECT) showed no abnormality.

As the Wada test was suggestive of left language dominance, we performed functional language mapping, which showed no overlap between language area and estimated resection area. We performed an MRI-guided lesionectomy as well as resection of the basal temporo-occipital epileptogenic focus. He exhibited no post-operative neurological deficits. He has been seizure free for more than 3 years.

Pathological findings

Histological examination of the resected cortex showed increased neurons and glial cells as well as dyslamination, irregular orientation of dendrites, and immature neurons. These abnormalities were consistent with FCD type Ib. We did not observe dysmorphic neurons, cytomegalic neurons, balloon cells, or grotesque cells. In the resected occipital lobe cortex, the lesion showed mild malformation of cortical development and remnants of the columnar pattern.

In the lesion in the subcortical region and the parasubiculum of the hippocampus, many Olig2-positive glial cells and glial fibrillary acidic protein-positive cells were present that may have indicated overgrowth of glial cells such as oligodendroglia and astrocytes. Few MIB-1-positive cells were seen. The hippocampus itself showed no findings of hippocampal sclerosis or a brain tumor.

Overall, the pathological diagnosis was FCD type Ib (Fig. 3). We did not find malignancy, other tumors, autoimmune encephalitis, multiple sclerosis, demyelination, or vasculitis upon pathological examination.

Discussion

In our case with FCD type Ib, exacerbation and remission were seen as changes in intensity on MRI, which was performed with the same MRI machine.

As FCD is thought to be an embryological migration disorder, FCD is considered a non-progressive, unchangeable disease [1, 2, 4–7]. Exacerbation or remission is rarely seen with neuroimaging in patients with FCD. Lesions that show changes on MRI may indicate malignant transformation of a benign tumor, autoimmune

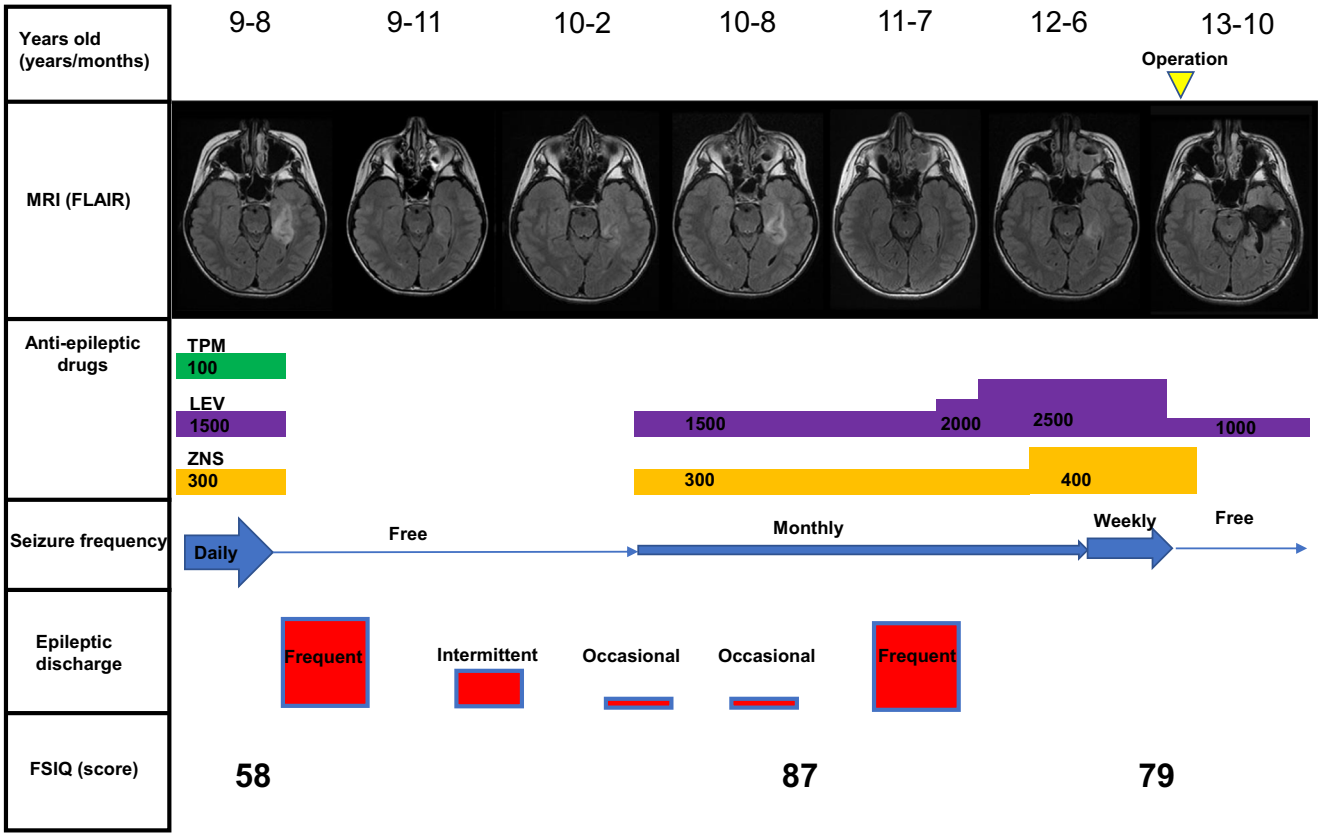

Fig. 2 Period, seizure frequency, medications, and MRI intensity changes. We observed a high-intensity area in the left medial temporal lobe with fluid-attenuated inversion recovery (FLAIR) at the age of 9 years 8 months. The high-intensity lesion improved on FLAIR at the age of 9 years 11 months. However, the high-intensity area appeared again at the age of 10 years and disappeared at 11 years. Re-exacerbation was seen at the age of 12 years. FSIQ, full-scale intelligence quotient; TPM, topiramate; LEV, levetiracetam; ZNS, zonisamide

inflammation such as Rasmussen encephalitis [8], demyelination, or edema related to status epilepticus [9]. In our case, *N*-methyl-D-aspartic acid antibody staining was negative, and no cells were present in his cerebrospinal fluid.

Only two reports of FCD with lesions with alternating intensity on MRI have been published [6, 7]. According to Owens et al. [7], the neuroimaging change in FCD is due to edema after an epileptic seizure. In that case, the seizure frequency increased drastically while showing high-intensity changes on MRI. Status epilepticus or frequent seizures induce cytotoxic edema, which mimics the growth of the lesion [9]. Another paper described MRI intensity alterations in FCD without status epilepticus or frequent seizures [6]. In this case, the patient also had increased seizure frequency and increased interictal discharges. The authors speculated that alterations in MRI intensity in our case were related to ongoing subclinical seizures from a deep-seated focus that was inaccessible by the scalp EEG. These two cases of FCD were reported as FCD type IIb. However, the neuropathological diagnosis of our case was FCD type Ib. The lesions in FCD type Ib are generally thought to be invisible on MRI. Therefore, the MRIs at ages 9 years 11 months and 11 years 7 months, which showed negative findings, were considered his baseline MRI findings.

Seizure activity can produce pathological changes, and pathological changes can worsen seizure activity. This theory is considered the mechanism of hippocampus sclerosis, which is the state of acquired irreversible pathological changes resulting from this vicious cycle following an initial disease or injuries such as trauma, FCD, or infection [10].

This theory may explain the mechanism of the changes in our case. According to this theory, changes in the lesion are considered to be induced by latent epileptic discharge. However, anti-seizure medications may stop the vicious cycle in the latent stage while it is still reversible, and thus, the lesion may show exacerbation and remission on MRI. It is well known that status epilepticus is shown as high intensity on DWI [11]. On the one hand, changes in DWI intensity were

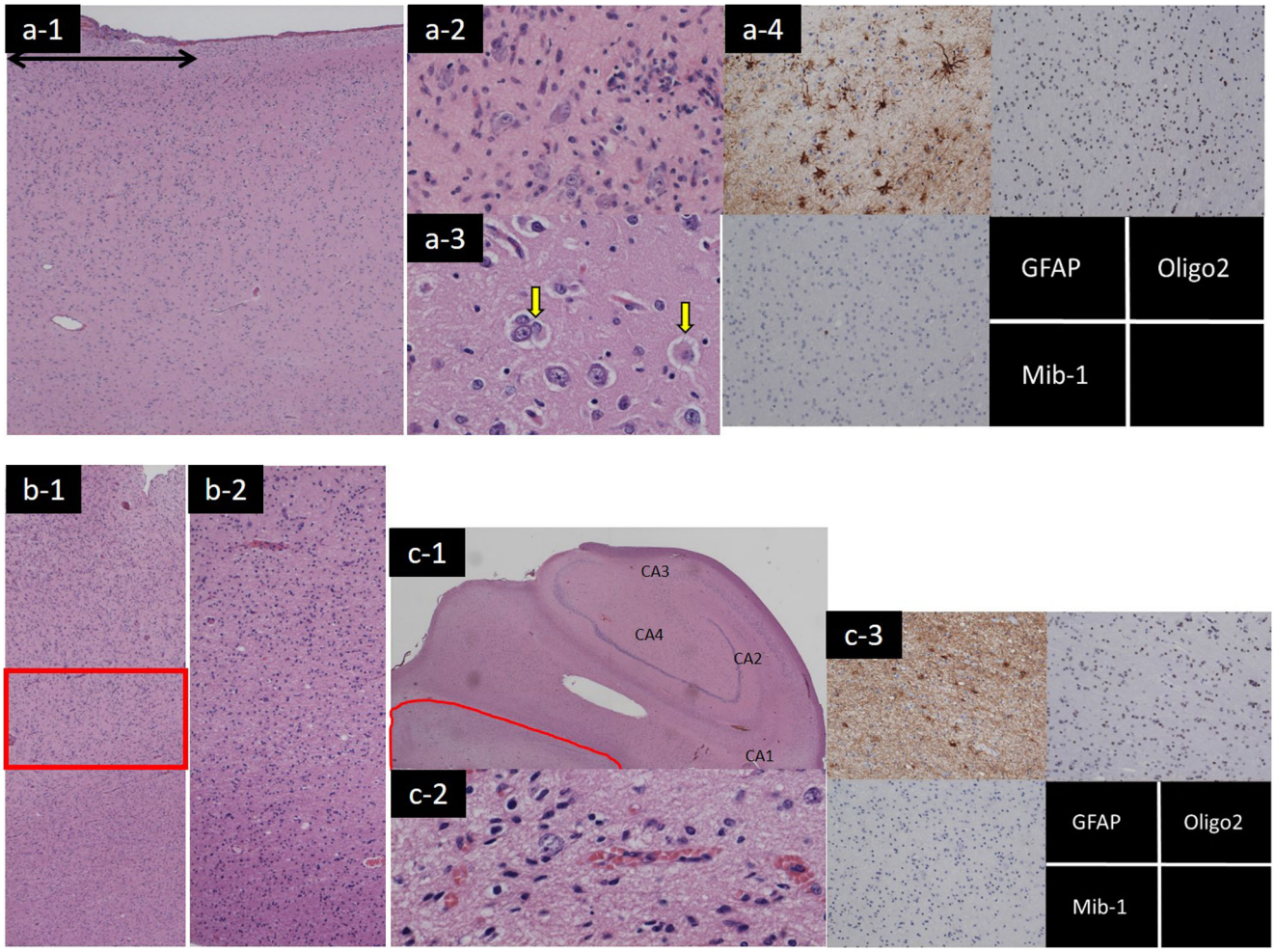

Fig. 3 Neuropathological findings. Temporal lobe cortex (**a**); the correct arrangement of layers was maintained. However, on the left (black arrow), appropriate layer arrangement is not seen (a-1). Dyslamination and irregular orientation of the dendrites were seen in the cortex (a-2). Large atypical glial cells were seen in the cortex (a-3, yellow arrow). Immunohistochemical staining showed glial fibrillary acidic protein-positive cells, Oligo2-positive cells, and very few MIB-1-positive cells (a-4). The neuropathology indicated FCD type Ib. Temporal lobe subcortex (**b**); the borderline of the cortex and subcortex was unclear due to increased numbers of neuronal and glial cells (b-1). High-power field of the red line area in b-1 (b-2). Hippocampus (**c**); increased numbers of glial cells and heterotopic neural cells are seen in the red line area (c-1). High-power field of the red line area of c-1 (c-2). Immunohistochemical staining was similar to that in the temporal lobe (c-3)

found in 19% of patients with status epilepticus. On the other hand, single seizure was found in 2.5–3% of patients [12]. This could explain why DWI in our case did not show a change in intensity.

We found slight enhancement in the left mesial temporal lesion and the fronto-basal lobe on MRI. This could be explained by peri-ictal dysfunction of the blood-brain barrier due to subclinical epileptic state [13].

Our case represents a lesion of FCD type Ib with a high-intensity area on MRI. Latent epileptic activity may cause a signal change in the lesion that is usually invisible on MRI.

Compliance with ethical standards

Written informed consent for publication of case details was obtained from the patient's parents. This study was approved by the ethics committee at the Seirei Hamamatsu General Hospital.

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Guerrini R, Duchowny M, Jayakar P, Krsek P, Kahane P, Tassi L, Melani F, Polster T, Andre VM, Cepeda C, Krueger DA, Cross JH, Spreafico R, Cosottini M, Gotman J, Chassoux F, Ryvlin P, Bartolomei F, Bernasconi A, Stefan H, Miller I, Devaux B, Najm I, Giordano F, Vonck K, Barba C, Blumcke I (2015) Diagnostic methods and treatment options for focal cortical dysplasia. Epilepsia 56:1669–1686
2. Hauptman JS, Mathern GW (2012) Surgical treatment of epilepsy associated with cortical dysplasia: 2012 update. Epilepsia 53(Suppl 4):98–104

3. Fujimoto A, Ochi A, Imai K, Chan D, Sharma R, Viljoen A, Chu B, Holowka S, Kemp SM, Chuang SH, Matsumura A, Ayuzawa S, Snead OC 3rd, Otsubo H (2009) Magnetoencephalography using total intravenous anesthesia in pediatric patients with intractable epilepsy: lesional vs nonlesional epilepsy. Brain Dev 31:34–41
4. Taylor DC, Falconer MA, Bruton CJ, Corsellis JA (1971) Focal dysplasia of the cerebral cortex in epilepsy. J Neurol Neurosurg Psychiatry 34:369–387
5. Blumcke I, Aronica E, Miyata H, Sarnat HB, Thom M, Roessler K, Rydenhag B, Jehi L, Krsek P, Wiebe S, Spreafico R (2016) International recommendation for a comprehensive neuropathologic workup of epilepsy surgery brain tissue: a consensus task force report from the ILAE commission on diagnostic methods. Epilepsia 57:348–358
6. Forgacs PB, Sarkis R, Folkerth R, Golby A, Hsu L, Bubrick EJ, Dworetzky BA (2014) Focal cortical dysplasia IIb presenting as slowly progressive aphasia mimicking a brain tumor. Seizure 23: 161–163
7. Owens C, Bradley L, Farrell M, O'Brien D, King MD, Ryan SP (2010) Seizure-induced inflammation in focal cortical dysplasia resulting in imaging progression that simulates neoplasia. J Neuroimaging 20:208–210
8. Wang D, Blumcke I, Gui Q, Zhou W, Zuo H, Lin J, Luo Y (2013) Clinico-pathological investigations of Rasmussen encephalitis suggest multifocal disease progression and associated focal cortical dysplasia. Epileptic Disord 15:32–43
9. Finn MA, Blumenthal DT, Salzman KL, Jensen RL (2007) Transient postictal MRI changes in patients with brain tumors may mimic disease progression. Surg Neurol 67:246–250
10. Yang T, Zhou D, Stefan H (2010) Why mesial temporal lobe epilepsy with hippocampal sclerosis is progressive: uncontrolled inflammation drives disease progression? J Neurol Sci 296:1–6
11. Kim JA, Chung JI, Yoon PH, Kim DI, Chung TS, Kim EJ, Jeong EK (2001) Transient MR signal changes in patients with generalized tonicoclonic seizure or status epilepticus: periictal diffusion-weighted imaging. AJNR Am J Neuroradiol 22:1149–1160
12. Hubers A, Thoma K, Schocke M, Fauser S, Ludolph AC, Kassubek J, Pinkhardt EH (2018) Acute DWI reductions in patients after single epileptic seizures - more common than assumed. Front Neurol 9:550
13. Ruber T, David B, Luchters G, Nass RD, Friedman A, Surges R, Stocker T, Weber B, Deichmann R, Schlaug G, Hattingen E, Elger CE (2018) Evidence for peri-ictal blood-brain barrier dysfunction in patients with epilepsy. Brain 141:2952–2965