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CASE REPORT

Finding on brain MRI mimicking focal cortical dysplasia in early Rasmussen's encephalitis: a case report and review

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Abstract
Introduction Rasmussen's encephalitis (RE) is one of the important causes of refractory seizure. The most impressive clinical manifestation of RE is epilepsia partialis continua (EPC). Others include progressive hemiparesis and neuropsychological deterioration. Currently, the best approach to RE is hemispherectomy.
Case histories We describe a patient whose clinical manifestations were compatible with RE; however, the initial brain MRI was interpreted as focal cortical dysplasia over right parietal region.
Discussion The follow-up brain MRI 1 year later showed diffuse atrophy of the brain with more atrophic change in right hemisphere, and the EPC disappeared after right hemispherectomy.

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Introduction

Chronic-encephalitis-related focal seizure was first reported by Rasmussen and his colleagues in 1958 [12]. Twenty years later, Rasmussen [13] reported 27 children; most of them appeared to have a syndrome which we would now term Rasmussen's encephalitis (RE). It usually affects children under the age of 10 and more rarely in adolescents and adults. Patients with RE usually have intractable focal motor seizures, often evolving into epilepsia partialis continua (EPC), progressive hemiparesis, and neuropsychological deterioration, and even results in homonymous hemianopia and loss of language skills [4, 13].

Here, we present a 4-year-old boy whose clinical manifestations were compatible with RE; however, the initial brain MRI was interpreted to be focal cortical dysplasia over right parietal region.

Case histories

This 4-year-old boy, the first child of healthy parents, was quite well both developmentally and neurologically until 2 years of age when he started to have episodic vomiting. The episodic vomiting occurred for three times in 2 months, and each episode would persist for 1 day. In that particular day, he would vomit repeatedly with large amount of secretion of saliva.

EPC developed since 2.5 years old, with the clinical manifestations of persistent involuntary twitches of left side

of face, left shoulder, and left hand, with or without blinks of left eye, in both wakeful state and sleep state. Progressive weakness of left-side limbs was noticed since then. There was no past history of trauma, CNS infection, or exposure to drugs, radiation, or chemicals. Anti-epileptic agents for his seizure were ineffective (sodium valproate, clonazepam, levetiracetam, phenobarbital, topiramate).

Physical examination at age of 3 revealed his height, weight, and head size were all within the normal range. Neurological examinations revealed intact high cortical function and cranial nerves. Visual field and acuity were normal. Muscle strength was slightly decreased in the left side extremities, grade 3+/5 in upper and 4+/5 in lower limb on the Medical Research Council Scale. Deep tendon reflexes were increased in left side limbs but there was absence of Babinski's reflex. The sensory examinations were normal.

Workups for genetic, metabolic, infectious, and autoimmune disorders were all normal. EEG showed intermittent spikes over the right fronto-central and right anterior temporal areas and there were continuous slow waves at the same areas (Fig. 1). SPECT and PET both showed extensive hypometabolism over right frontal-parietal-temporal region. However, there was focal hypermetabolism over right parietal region, for which ictal focus was suspected (Fig. 2). The T2 FLAIR MRI of brain at 3 years of age revealed focal hyperintense lesion over right parietal area, and the interpretation was focal cortical dysplasia (Fig. 3). Excision of the focal lesion was recommended, but the family refused.

One year later, the EPC still persisted, and his cognition and left hemiparesis got worse. He could not walk anymore. EEG showed diffuse background slow and frequent multifocal spikes over right hemisphere. In addition, frequent spikes were also noted in the left hemisphere (Fig. 4). PET showed hypometabolism over right frontal-parietal and bilateral mesial temporal region (Fig. 5). The follow-up brain MRI at 4 years of age revealed diffuse atrophic change of the brain, which is more prominent in right hemisphere (Fig. 6).

Hence, RE was highly suspected and right hemispherectomy was performed. The pathological report was compatible with RE. The boy's EPC disappeared, and his cognitive function and left-side motor function improved markedly, and he was able to walk without assistance after right hemispherectomy.

Discussion

EPC, the most impressive clinical manifestation of RE, is characterized by continuous clonic contractions of a muscle or a muscle group [16]. Though the causes of EPC include a variety of conditions such as brain tumors, vascular lesions, trauma, infections, neuronal migration anomalies, autoimmune, genetic, and metabolic disorders, RE is still the leading etiology of EPC so far [5, 15, 16]. In addition to EPC, there is concomitant neuropsychological deterioration in RE.

EEG findings of RE are variable. Most often, EEG shows impoverishment of background activity and polymorphic delta waves over the affected hemisphere, mainly over the central and temporal regions, and the continuous spike discharges may originate in one portion of the cortex. The contralateral EEG abnormalities are common and may be attributable either to secondarily generalized epilepsy, which may improve and even disappear postoperatively, or

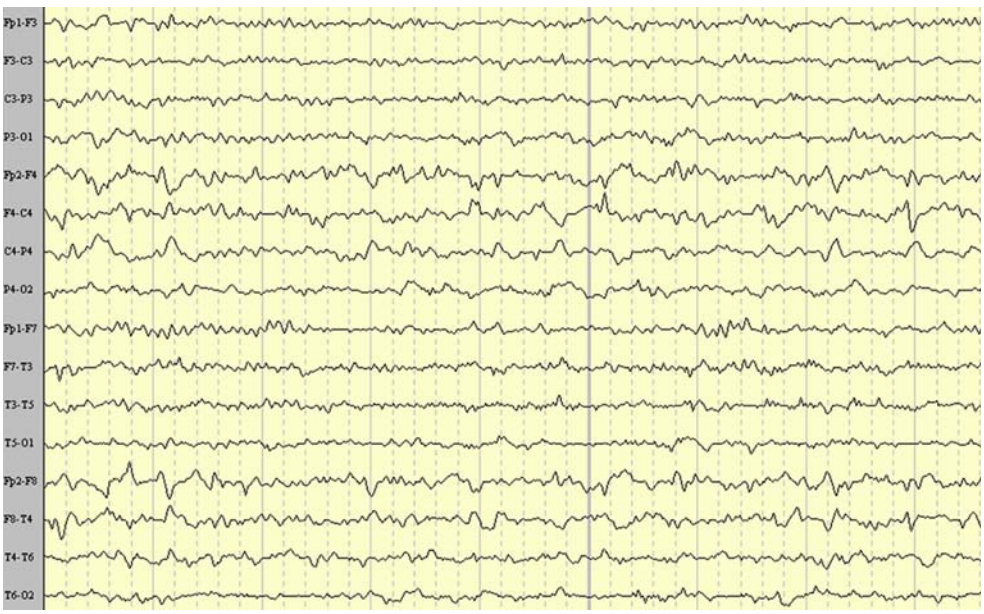

Fig. 1 EEG at age of 3 years showed intermittent spikes over right fronto-central and right anterior temporal areas and there were continuous slow waves at the same areas

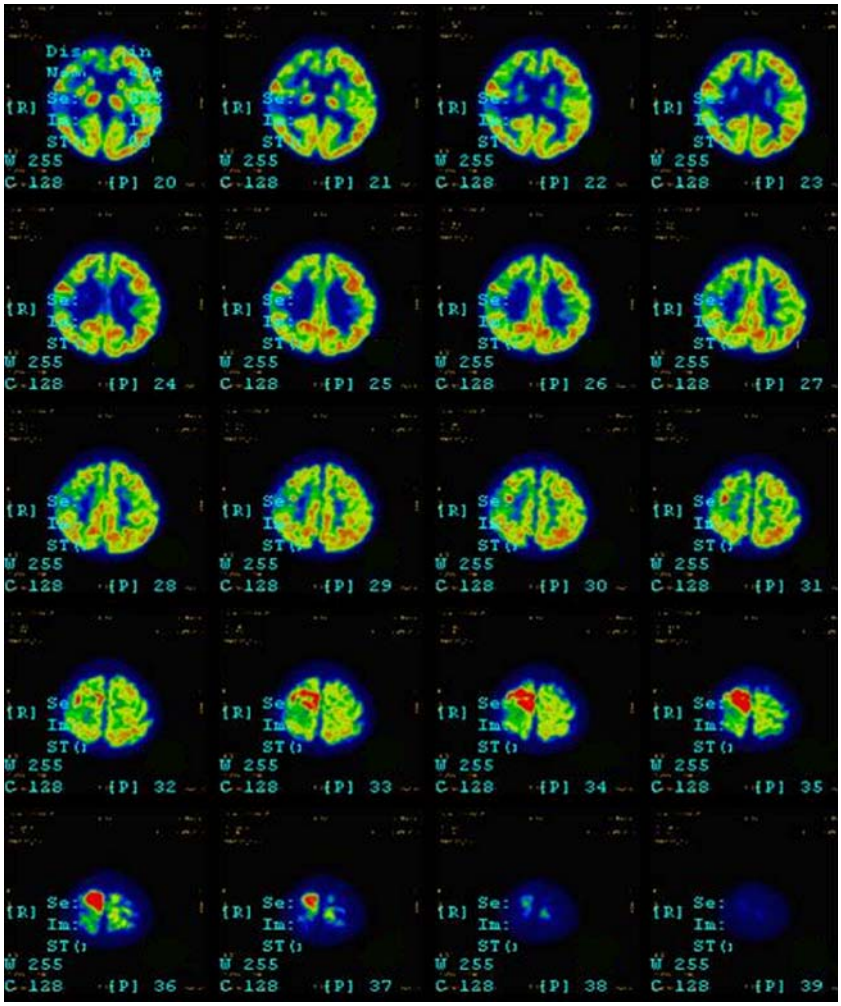

Fig. 2 FDG-PET at age of 3 years showed extensive hypometabolism over right frontal-parietal-temporal region, and there was focal hypermetabolism over right parietal region, for which ictal focus was suspected

to independent contralateral epileptogenic abnormality, for which prognosis is more guarded [7]. In our case, the disappearance of the left fronto-polar spikes after right hemispherectomy may indicate that the spike focus in left fronto-polar region is not an independent one but secondary to RE in right hemisphere.

The initial brain MRI findings in most patients with RE are usually normal. When the disease progresses, diffuse cortical atrophy in the affected hemisphere will be shown on brain MRI. Some studies suggest that early RE should be considered when there is any of the following finding on brain MRI: (1) focal cortical atrophy, especially the insular

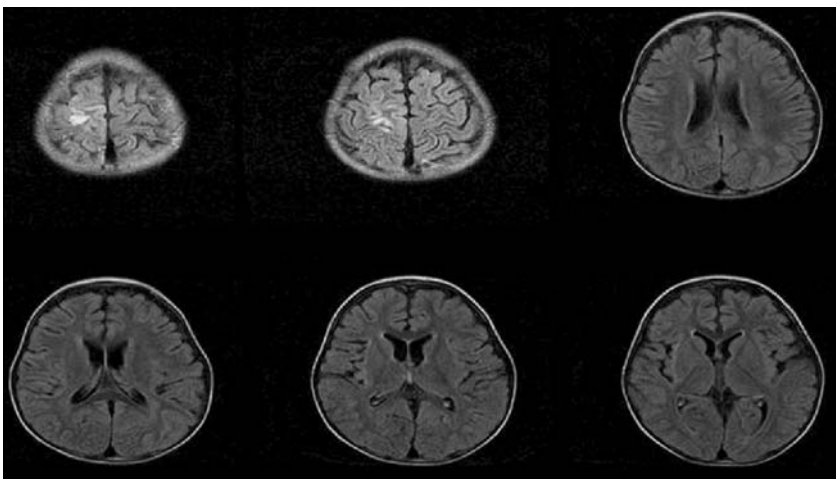

Fig. 3 T2 FLAIR MRI of brain at age of 3 years. The brain was symmetric, and there was no atrophic change but a focal hyperintense lesion over right parietal area, and the interpretation was focal cortical dysplasia

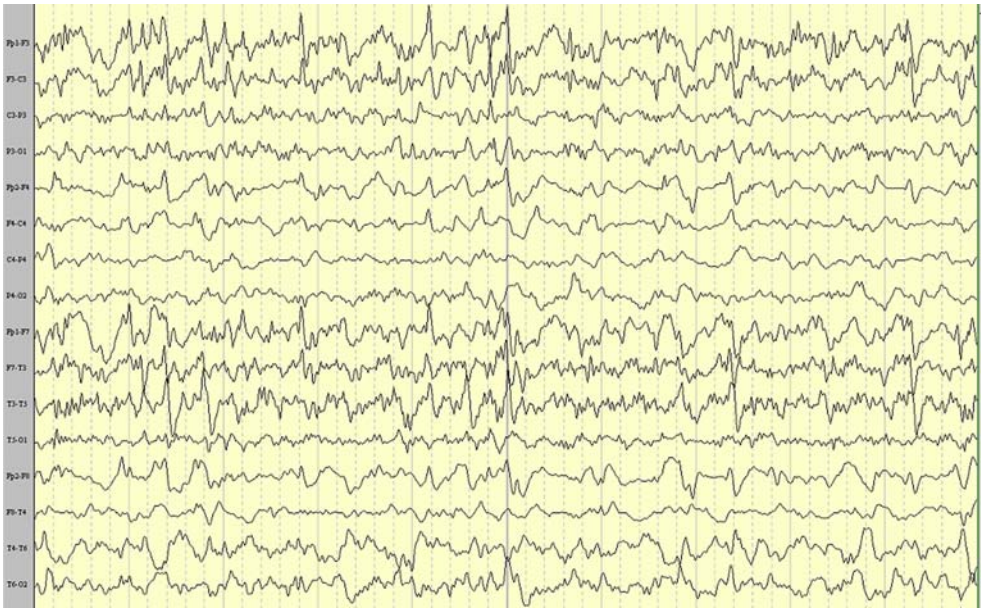

Fig. 4 EEG at age of 4 years showed multifocal epileptogenicity in right hemisphere (right centro-parietal, right fronto-central, and right anterior–midtemporal regions) and repetitive spikes arising from the left fronto-polar regions and left anterior-midtemporal regions

cortex; (2) white matter or cortical signal hyperintensity; and (3) atrophy of the head of the caudate nucleus [3, 7]. In this case, the initial brain MRI was suspected to have focal cortical dysplasia. If focal resection for focal cortical dysplasia was to be performed, the operation to cure the patient would be destined to fail. And fortunately, the family was reluctant to accept operation at that time. Retrospectively, the focal cortical change which was mistakenly interpreted as focal cortical dysplasia on initial brain MRI might be secondary to repetitive discharges of focal cortical neurons and so might be the brain PET study, which showed focal cortical hypermetabolism.

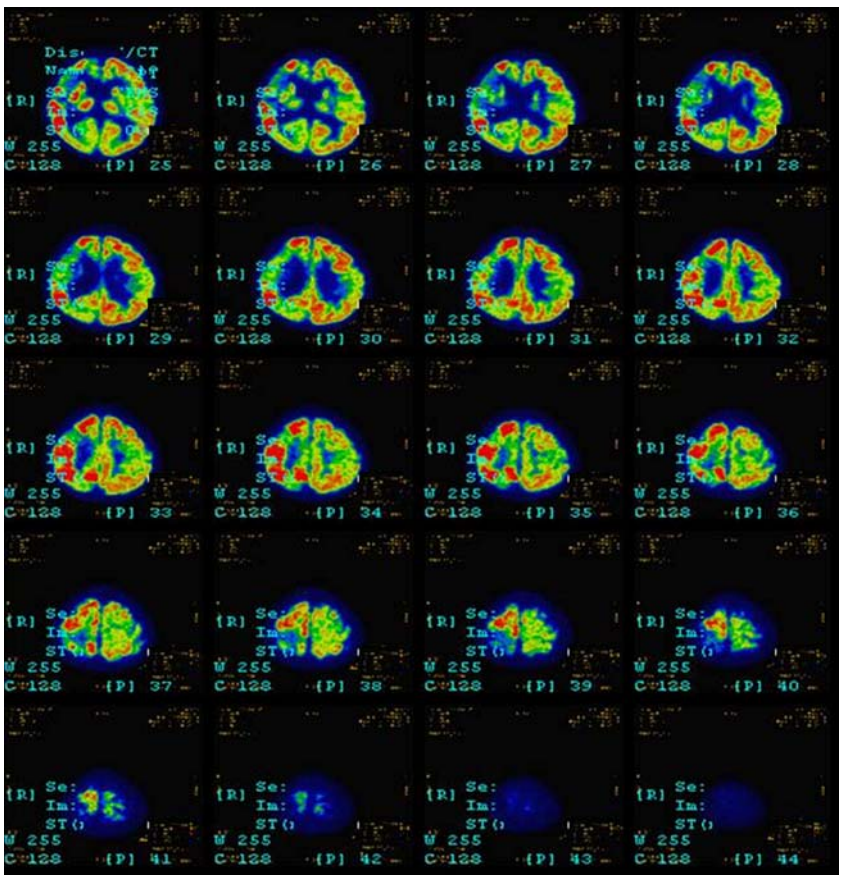

Fig. 5 FDG-PET at age of 4 years showed extensive hypometabolism over right fronto-parietal region and bilateral mesial temporal regions, and there was focal hypermetabolism over the right lateral temporal region extending to the right parietal region

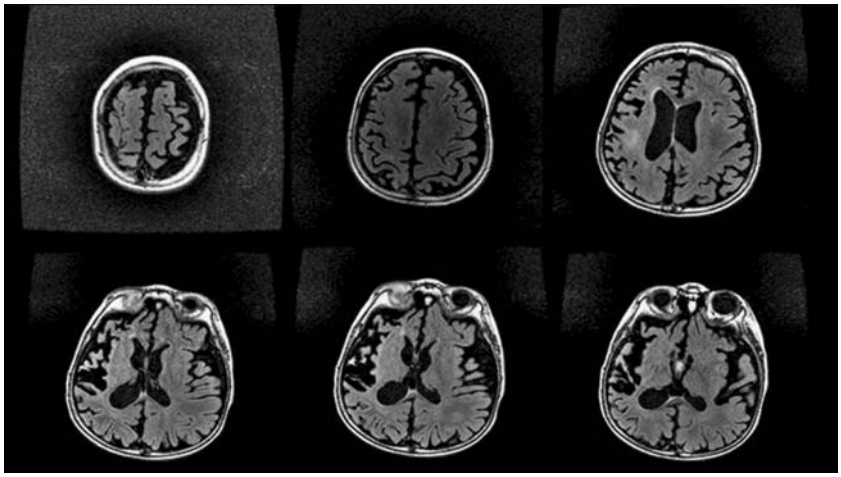

Fig. 6 T2 FLAIR MRI of brain at age of 4 years showed more severe atrophic change in right hemisphere, especially the right middle temporal and insular area. The previous hyperintense lesion over right parietal area could not be found anymore

Most of the patients with RE are sporadic, and there is no evidence of genetic component, though association with SCN1A mutation was reported [10]. However, two thirds of children do have an infectious or inflammatory illness before the onset of the EPC. RE was suspected to relate to virus infection process previously, but no virus has ever been detected by biopsy so far [12, 13]. Since 1994, glutamate receptor antibodies (GluR3) were suspected to be related to RE by animal model [14]. RE is now believed to be an ongoing and progressive immune-mediated process of neuronal damage that involves neuroglial and lymphocytic responses, leading to destruction of a single hemisphere [2, 11], and virus infection may be an important trigger factor, resembling acute disseminated encephalomyelitis or post-infectious encephalitis.

Based on the above evidences, intravenous immunoglobulin, steroid, and plasmapheresis have been tried on RE but long-term studies have not proven these measures to be effective [1, 6]. Currently, hemispherectomy is still the gold standard of treatment of RE. The effectiveness and prognosis of hemispherectomy in RE are generally very good. Of 111 hemispherectomies performed at Hopkins [8], 46 were for RE, 65% of these became seizure-free after surgery, and most were off medications. Most of those with residual seizures had mild episodes, which no longer interfered with their quality of life.

Hemispherectomy is an irreversible procedure and every effort must be made preoperatively to confirm the normality of the opposite side of the brain. Though the brain MRI showed diffuse cortical atrophy in both hemispheres, implying poor prognosis after hemispherectomy, good outcome was still obtained in this boy. The possible mechanisms that a child's motor function on contralateral limbs is still well preserved or is improving after hemispherectomy might include (1) strengthening of ipsilateral pathways already present due to functional demand, (2) axonal sprouting to allow a novel functional connection, and (3) the absence of transcallosal inhibitory influence [9].

Would the prognosis be good if focal cortical resection was done according to the initial brain MRI and PET finding in this case? There were reports that focal surgeries such as lobar and even multilobar resections, as originally demonstrated by Rasmussen, are ineffective in controlling either the seizures or the progressive nature of the disease. The condition inevitably recurs in other locations within the same hemisphere [4, 13]. "Focal cortical resection early in the course of the illness seldom reduced the seizure tendency significantly unless it was practicable to carry out extensive excision such as a complete or subtotal hemispherectomy." Rasmussen's aphorism [4]. Therefore, serial follow-up of brain MRI is indicated on a patient who has the clinical manifestations of RE and whose initial brain MRI could not provide adequate evidence which is compatible with RE.

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

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