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Delayed transhemispheric propagation of electrographic seizures following functional hemispherectomy

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1. Introduction

Functional hemispherectomy is a procedure in which one cerebral hemisphere is functionally disconnected from the contralateral hemisphere by means of surgical disconnection of neuronal fibers between the hemispheres with preservation of frontal and occipital poles [1]. In hemimegalencephaly with pharmacoresistant epilepsy goal of such a procedure is to isolate seizures to the disconnected megalencephalic cerebral hemisphere and thus render seizures clinically silent.

We report on a case of a child with particularly demonstrative electroencephalography of delayed transhemispheric propagation of seizures following functional hemispherectomy for hemimegalencephaly. Additionally, we review related concepts including epilepsy outcomes of functional hemispherectomy for hemimegalencephaly, kindling effect, and our practice regarding the treatment of similar cases.

2. Case report

Our patient is a 4 years and 9 months old male whose past medical history includes congenital right hemimegalencephaly complicated by pharmacoresistant epilepsy with onset on day of life 5 (treated with lacosamide 9 mg/kg/day, phenobarbital 2 mg/kg/day, oxcarbazepine 18 mg/kg/day, levetiracetam 47 mg/kg/day, clobazam 1 mg/kg/day). Patient underwent right functional hemispherectomy with temporal lobectomy at age 1 year and 9 months by transsylvian approach with corpus callosotomy, temporal lobectomy, subfrontal disconnection, and insular disconnection. Delay in referral to surgery occurred due to a complex social situation of the family immigrating from a developing country. The procedure was complicated by perioperative intraventricular hemorrhage with associated hydrocephalus requiring temporary external ventricular drain and infarction of right middle cerebral artery territory and left putamen. Postoperative MRI demonstrated a very small residual callosal connection (Fig. 1). Patient remained on multiple antiepileptic drugs but was without clinical seizures since shortly after hemispherectomy.

On day of presentation to our hospital (three years after functional hemispherectomy) patient had developed an upper viral respiratory infection with low grade fever, nasal congestion and cough followed by a generalized clonic convulsion lasting about 60 s with subsequent drowsiness and decreased spontaneous movements. The patient was found to have positive Respiratory Syncytial Virus B by nasopharyngeal swab and diagnosed with viral bronchiolitis and breakthrough seizure. Video-Electroencephalogram (VEEG) was obtained to evaluate for nonconvulsive status epilepticus and demonstrated frequent electrographic seizures originating from the disconnected right hemisphere, at times briefly propagating to central and left frontal electrodes (Fig. 2), all without observed clinical correlate. Patient was administered 20 mg/kg of IV fosphenytoin without appreciable change on VEEG.

Previous VEEG in our epilepsy monitoring unit at age 2 years and 9 months (12 months after right functional hemispherectomy) had demonstrated frequent electrographic seizures from right hemisphere

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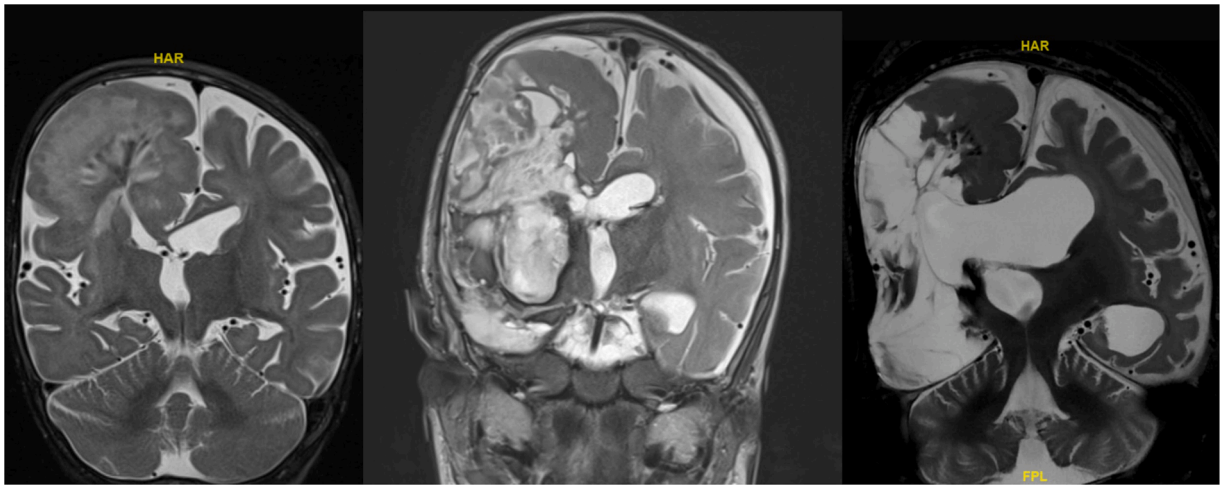

Fig. 1. Coronal T2 MRI, before functional hemispherectomy (left panel), 4 weeks (central panel) and 3 years after surgery (right panel) demonstrating temporal lobectomy and residual callosal connection.

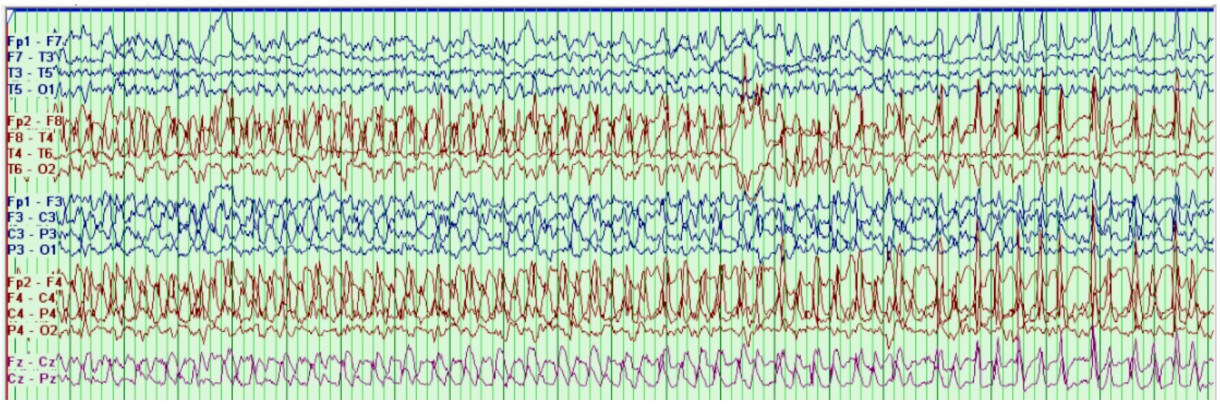

Fig. 2. Longitudinal bipolar montage at 1 s per bar demonstrating right hemispheric electrographic seizure with evolution to include central then left frontal electrodes.

without observable clinical correlate and specifically without propagation to contralateral hemisphere (Fig. 3A), as would be expected with a disconnected right hemisphere. VEEG 6 months prior to hemispherectomy revealed frequent, diffuse, right-hemispheric epileptiform discharges (Fig. 3B).

MRI brain without contrast (Fig. 1) obtained during admission revealed residual interhemispheric callosal body communication 8 mm in length in addition to expected anatomic and surgical changes.

Hospital course was notable for improvement in the respiratory status and level of alertness following treatment with stress-dose steroids and supportive oxygen treatment. No recurrence of clinical seizures was observed. Home doses of oxcarbazepine and clobazam were increased to 40 mg/Kg/day and 2 mg/Kg/day respectively, and the patient was discharged on the day following admission and has remained without clinical seizures in the intervening several months. Family declined further surgical procedures to address the callosal body communication.

3. Discussion

While total hemispherectomy as a treatment for intractable epilepsy was first performed in humans by McKenzie in 1938 [2], it fell out of favor in the 1960s as it was described that in about one-third of patients the large subdural cavity created following resection led to delayed development of persistent intracranial hemorrhage evidenced by superficial siderosis and obstructive hydrocephalus on autopsy [1].

In 1983 Rasmussen revisited hemispherectomy for medically-refractory epilepsy with premorbid hemiparesis with the modification that the frontal and occipital lobes were retained in the cranium with their blood supply while neuronally disconnecting them from the contralateral hemisphere [1]. This resulted in significant improvement in morbidity of the operation while coming at the cost of somewhat decreased effectiveness in seizure reduction compared to anatomic hemispherectomy and was termed “functional hemispherectomy” [1].

Failure of functional hemispherectomy may occur in up to 20 % of cases, and reasons can include incomplete disconnection, persistent epileptogenic activity in the ipsilateral insular cortex or bilateral independent epileptiform discharges. After this procedure, discharges often persist in the disconnected hemisphere but are usually not clinically relevant because they cannot propagate to the contralateral hemisphere [3,4].

In a review by Bulteau et al. of 10 publications describing >10 patients with hemimegalencephaly or hemicortical dysplasia undergoing functional hemispherectomy seizure freedom was quite variable ranging between 45–90 %, but at least some improvement in seizure burden was achieved in the vast majority [5]. Seizure freedom in these cases was overall lower than other groups such as Rasmussen’s encephalitis or vascular sequelae [5]. However it is admittedly difficult to directly compare studies that display much variance in patient populations, surgical techniques, and length of follow-up.

In our patient, expected electrographic seizures emanating from the disconnected right hemisphere were observed on VEEG 12 months

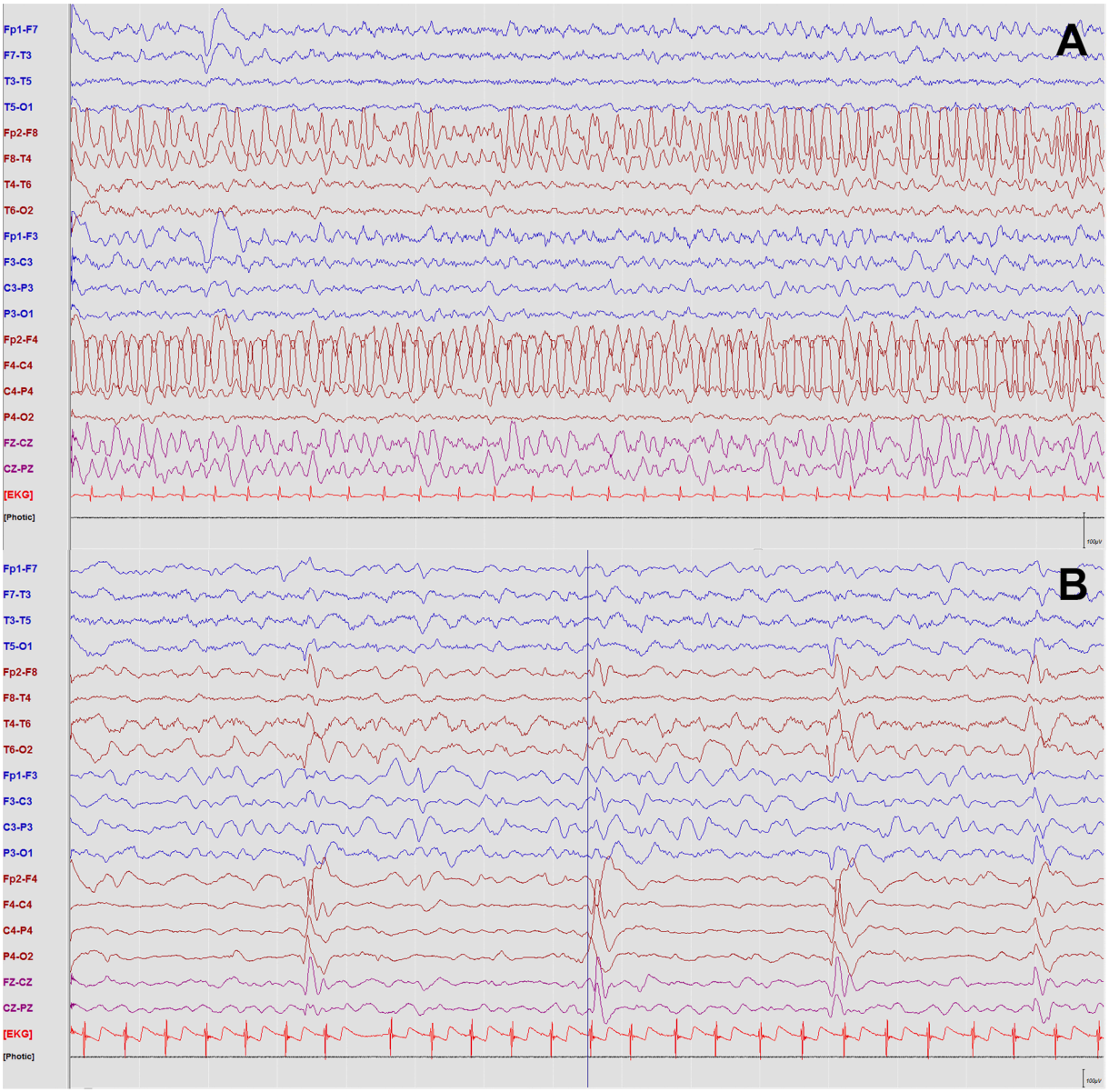

Fig. 3. Video EEG obtained 12 months after right functional hemispherectomy (A, top panel) demonstrating a typical electrographic seizure from right hemisphere without propagation to contralateral hemisphere. Video EEG obtained 6 months prior to surgery (B, bottom panel) showed frequent, diffuse, high-amplitude right-hemispheric epileptiform discharges. Longitudinal bipolar montage at 1 s per bar.

following functional hemispherectomy without observable semiology and without propagation to the left hemisphere despite the small residual callosal connection. Three years after surgery however, this tiny residual tract allowed propagation of electrographic seizures into the left hemisphere, as documented by VEEG (Fig. 2), in the setting of decreased seizure threshold from viral illness.

Furthermore, this may also implicate a "kindling effect." This refers to the concept that repetitive electrical stimulation, such as electrographic seizures, may sensitize the cortex to have further seizures [6]. In our case we believe that repetitive electrographic seizures of the right hemisphere resulted in increased predilection to seizures of the left hemisphere cortex adjacent to the residual callosal connection, ultimately generalizing into the clinical seizure leading to presentation.

We continued use of anti-epileptic drugs at increased levels in our patient, with the goal to suppress right hemispheric electrographic seizure propagation into the left hemisphere so as to avoid future clinical seizures and minimize a kindling effect in that region.

4. Conclusion

This report explores pharmacoresistant hemimegalencephaly treated with functional hemispherectomy with delayed recurrence of clinical seizures linked to transhemispheric propagation by retained callosal tissue. Our case is informative in its instructive electroencephalography, description of challenging treatment determinations based on our practice, and review of associated literature.

Declaration of Competing Interest

The authors report no declarations of interest.

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