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Case Report

Epilepsy surgery in bifrontal injury from prior craniopharyngioma resections☆,☆☆

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ABSTRACT

Epilepsy surgery in frontal lobe epilepsy (FLE) has less favorable seizure-free outcomes than temporal lobe epilepsies. Possible contributing factors include fast propagation patterns and large clinically silent areas which are characteristics of the frontal lobes. Bilateral frontal lobe abnormalities on MRI are another relative contraindication to epilepsy surgery. For example, bilateral encephalomalacia may be a presupposition to bilateral or multifocal epilepsy. The possibility of potential disinhibition with already poor reserves may be another deterrent to consideration for resective epilepsy surgery. As such, conventional surgical approaches to intractable epilepsy with bilateral frontal injury may be limited to palliative procedures like vagus nerve stimulation and corpus callosotomy. We present a case in which the epileptogenic zone was a subset of the acquired, bilateral, cystic encephalomalacia. This iatrogenic injury resulted from two prior craniotomies for excision of craniopharyngioma and its recurrence.

Following the initial bilateral and subsequent unilateral, subdural grid- and depth electrode-based localization and resection, our patient has remained seizure-free 2 years after epilepsy surgery with marked improvement in her quality of life, as corroborated by her neuropsychological test scores. Our patient's clinical course is testament to the potential role for resective strategies in selected cases of intractable epilepsy associated with bifrontal injury. Reversal of behavioral deficits with frontal lobe epilepsy surgery such as in this patient provides a unique opportunity to further our understanding of the complex nature of frontal lobe function.

1. Introduction

Despite being the second largest group of potentially operable epilepsies, FLE is more challenging both in its diagnosis and localization than other localization-related epilepsies. Scalp EEG and diverse seizure semiology often reflect rapid and varied, either simultaneous or successive, propagation patterns. A lateralized lesion on MRI can help guide the location of the hypothetical epileptogenic zone. However, bilateral lesions may lead to further ambiguity, and with the increased potential for frontal lobe disinhibition, surgical therapy may not be considered a viable option.

1.1. Case

An 18-year-old female was first diagnosed with craniopharyngioma at 7 years of age when she presented with headaches. The suprasellar mass was resected via a right subfrontal craniotomy which resulted in panhypopituitarism. Subsequent serial imaging showed tumor recurrence at age 11, and the intrasellar mass was circumferentially dissected via a bilateral subfrontal craniotomy.

Seizures were diagnosed 5 years later at age 17 and persisted despite optimized doses of multiple antiseizure medications. Seizure semiology included staring with right-hand automatisms and frequent giggling. For the last six months, she also saw a "little green man" in the bathroom and felt a pressure to laugh. These daily events lasted up to 10 to 15 min. Postictally, she occasionally had slurred speech and right-sided weakness. Every 3–4 months, she also had a secondarily generalized seizure. More recently, she began having frequent astatic seizures, resulting in a compound fracture of the left humerus.

Her birth history was unremarkable, and her development was normal. However, after the second tumor resection surgery, she had a flat affect and increased latency in speech. Neuropsychological testing revealed diffuse cognitive deficits, predominantly involving attention, executive function, and psychomotor speed (see preoperative scores

Abbreviations: FLE, frontal lobe epilepsy; FSPGR, fast spoiled gradient-recalled echo; 3-D, 3-dimensional; RCI, reliable change index; SISCOM, subtraction ictal SPECT coregistered on MRI.

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in Fig. 3). She graduated from high school but stayed at home, with little motivation or interest in interacting with her environment.

Interictal EEG showed frontal 1- to 8-Hz spike-and-wave complexes, in isolation or long trains, maximal left, occasionally followed by generalized paroxysmal fast activity for 2–4 s. Recorded seizure semiology included a blank facial expression during which she occasionally answered questions and subsequently smiled. On a few occasions, there were brief myoclonic head jerks and pursing of lips. On at least 2 occasions, these progressed to clonic movements of the right face (Figs. 1A–B). A blank facial expression and marked latency of response concomitant with continuous generalized spike-and-wave discharges were also consistent with episodic nonconvulsive status. A brain MRI showed bilateral frontal encephalomalacia, maximal right (Figs. 1C–D), while patchy areas of bilateral frontoparietal uptake were seen on SISCOM (Figs. 1E–F).

Since the seizure semiology only infrequently indicated left frontal involvement (right-face clonic seizure) and no imaging modality was definitively discordant, invasive evaluation with bilateral subdural electrode implantation was recommended at our institution's epilepsy management conference. Bilateral frontal subdural electrodes were implanted over the encephalomalacic region, along with the interhemispheric fissure (yellow) and orbitofrontal (red) and lateral frontal regions (green) (Fig. 2A). Four 6-contact depth electrodes (3 left, 1 right) were implanted in the frontal lobes (purple) (Fig. 2A). On the left, one electrode was placed with the long axis parallel to the middle frontal gyrus, with distal contacts corresponding to the anterior cingulate cortex (Figs. 2B–C), and the other two were aimed mesially and laterally from the lateral convexity.

With a lead time of 200 ms, all seizures (>15) arose from the left frontal electrodes before contralateral recruitment. No seizure had onset from the depth electrode contacts. The patient was taken back to the OR, and left-sided grid and strips were placed over the lateral convexity and the interhemispheric fissure (Fig. 2D). The second invasive recording showed seizure onset from the anterior grid and the interhemispheric strip. The captured seizures were predominantly electrographic with occasional right facial clonic activity. The patient underwent resection of the left mesial frontal region and an anterior corpus callosotomy.

She has remained seizure-free more than 3 years since epilepsy surgery. Pathology showed gliosis. Neuropsychological testing one year later showed significant improvement in nearly all cognitive domains, with most test scores improving to the normal range. Postoperative MRI and neuropsychological test scores one year after surgery are shown in Fig. 3. She now shows interest in her environment, has rekindled old friendships, and aspires to go to college. She reports no further visual hallucinations.

2. Discussion

As slow growing extra-axial tumors, craniopharyngiomas account for 5–15% of all intracranial tumors in childhood [1]. Typical presenting symptoms include headache and growth failure from pressure effects on the hypothalamic–pituitary axis. Seizures and psychiatric symptoms are uncommon presenting symptoms, but subsequent seizure prevalence rates of 28% and neurocognitive deficits (full-scale IQ < 80) in up to 20% of children are described [1,2]. Surgery with or without adjuvant external beam radiation is the most common first-line treatment. Despite gross total removal, recurrence rates of up to 62% are reported at 10-year follow-up [1]. The optimum surgical strategy for management of pediatric craniopharyngioma remains an area of active debate. Some groups advocate gross total resection, while others favor a more limited subtotal resection (if the tumor is adherent to adjacent structures) and supplementary local external beam radiotherapy. In the last decade, our own hospital experience includes 31 children with craniopharyngiomas, none of whom presented with seizures. Tumor recurrence was seen in 30%. Ten developed frontal encephalomalacia after surgery (7 bilateral, 3 unilateral). Although seven patients have had EEGs for paroxysmal events or altered mental status, only the patient presented here has developed seizures to date (3%). Our patient's course highlights the need for consideration of surgical strategies to minimize iatrogenic encephalomalacic injury with tumor resection such as craniopharyngiomas.

Identifying the epileptogenic zone in the frontal lobes is a challenge. Both rapid ipsilateral and contralateral propagation and large clinically silent regions may indicate clinical onset only after the seizure propagates to an eloquent region. Diverse seizure semiologies imply multifocal disease or differing propagation patterns. In our patient, gelastic seizures and frontal absence semiologies implicated the mesial frontal region including the anterior cingulate cortex, while the facial motor seizures illustrated motor cortex involvement [3]. The basal frontal regions were implicated by visual hallucinations [4]. Although MRI was more

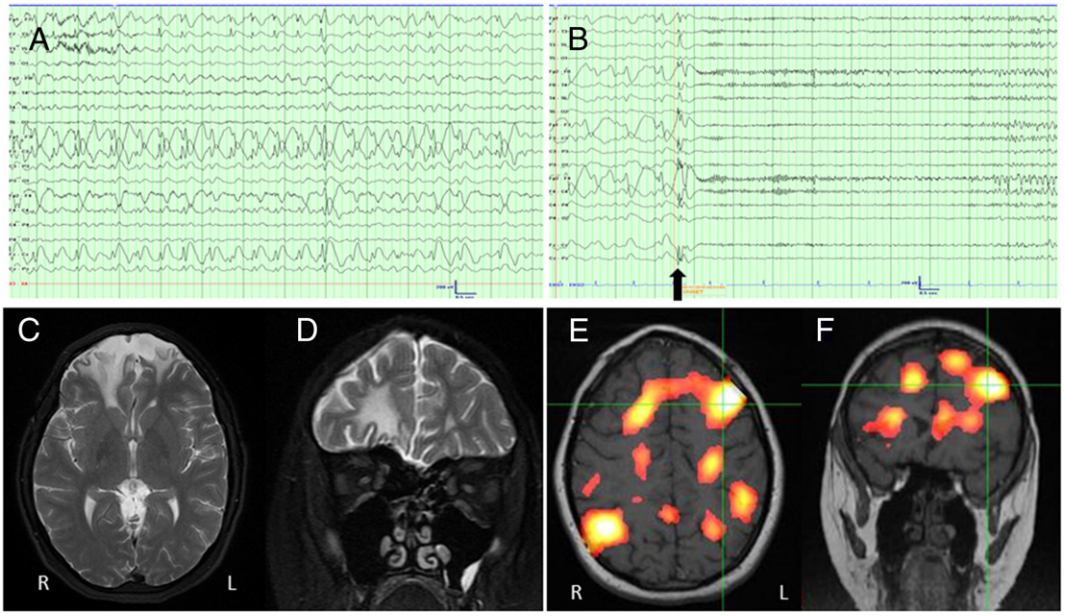


Fig. 1. Ictal EEG with both left frontal spike and wave discharges (A), and generalized attenuation with superimposed beta, maximal right frontal (B); MRI with bifrontal encephalomalacia, Right > Left (C, D); SISCOM with patchy frontoparietal uptake (E, F).

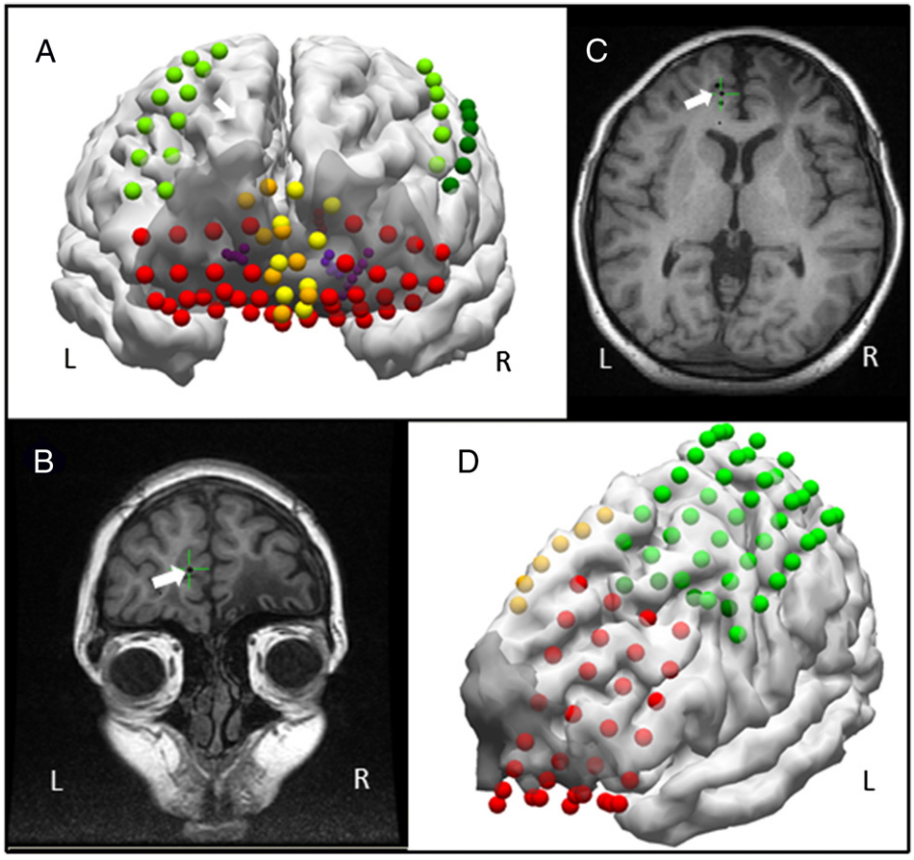
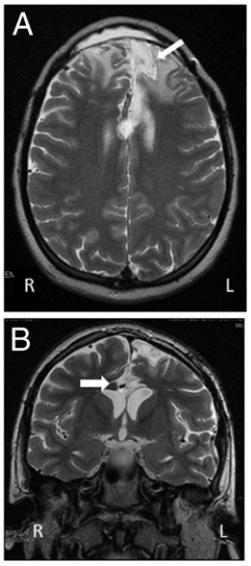


Fig. 2. Initial surgical evaluation with bilateral subdural (A) and depth electrode placement, including the anterior cingulate gyrus, coronal (B), axial (C). Subsequent left hemispheric subdural electrode placement over the lateral and mesial frontal regions (D). 3-D (3-Dimensional) representations of the brain surface and electrodes were created with Freesurfer (surfer.nmr.mgh.harvard.edu) and Curry 6 (neuroscan.com/curry.cfm) software. The primary brain volume (light gray) was automatically segmented with Freesurfer using a pre-operative 1.5T T1-weighted 3-D Fast Spoiled Gradient-Recalled-Echo (FSPGR) sequence. Frontal lobe lesions not included by Freesurfer were manually segmented with Curry 6 (dark gray) from the 3-D FSPGR. Electrode locations were obtained from a post-operative CT and were coregistered with the above volumes using Curry 6.

skewed to the right frontal region, the EEG showed either generalized discharges or left lateralization with occasional right facial clonic activity; there was no indication of independent right frontal involvement either by EEG or by seizure semiology. We felt that this was enough to warrant a surgical approach, especially given the increasing severity of her epilepsy and its devastating impact on her quality of life. The first



Test	Preoperative	Postoperative
WAIS-III		
VIQ (Verbal IQ)	68	85[a]
PIQ (Performance IQ)	75	95[a]
FSIQ (Full Scale IQ)	69	89[a]
POI (Perceptual Organization Index)	76	91[a]
VCI(Verbal Comprehension Index)	82	91[a]
WMI (Working Memory Index)	61	78
PSI (Processing Speed Index)	60	81[a]
Token Test	80	100
Verbal fluency	58	76[a]
Grooved Pegboard		
Right	45	87
Left	22	88[a]
Rey Osterrieth Complex Figure (copy)	39	89[a]
Rey AVLT (20-minute delayed recall)	65	105[a]
WMS-III Logical Memory II	90	110
Rey Osterrieth Complex Figure (delay)	84	90
Stroop Color & Word Test (Color-Word)	70	88[a]
Trail Making Test (Part B)	< 30	109[a]

[a]Pre- and postoperative RCI score changes exceeding 90 percent confidence interval.

Fig. 3. Post-surgical MRI with resection in the left mesial frontal region (A) and anterior corpus callosotomy (B); Selected pre- and postoperative neuropsychological test scores (Table). Reliable Change Index (RCI) scores were generated, and postoperative test scores exceeding the critical 90 percent confidence interval are indicated. If available, data pertaining to test-retest reliability within a non-surgical epilepsy sample was utilized to generate RCI calculations [5-7]; otherwise, published normative data was utilized.

bilateral monitoring established lateralization, while the second provided coverage of the implicated region and enabled grid-based resection. The anterior callosotomy was performed to ensure prevention of any contralateral seizure spread. Not widely adopted in the United States, bilateral electrode implantation utilizing stereoelectroencephalography may be another methodology to lateralize and localize the epileptogenic zone in patients with poorly lateralized seizures [8].

While the literature of intractable epilepsy seldom mentions encephalomalacia as an etiology, gliosis has significant potential for epileptogenesis, whether from posttraumatic or iatrogenic injury such as may be with tumor resection. Bilateral encephalomalacia is discussed even less frequently [5]. This may in part be because completeness of resection of encephalomalacia as determined by MRI is felt to be necessary to achieve seizure freedom [9]. Our patient's course does not corroborate that prognostic indicator. Preoperative widespread interictal discharges also did not have an adverse effect on our patient's outcome [10], and all postoperative EEGs have not shown any epileptiform discharges [11].

The frontal lobe syndrome exhibited by our patient included dysfunction in all three behaviorally relevant circuits including executive dysfunction mediated by the dorsolateral prefrontal circuit, apathy mediated by the anterior cingulate circuit, and sensory disinhibition (visual hallucinations) involving the orbital frontal region [12,13]. With an anterior corpus callosotomy and resection confined to the left mesial region, well within the visible lesion, seizures resolved with no epileptogenicity as seen on subsequent EEGs. Additionally, there was marked improvement in all domains of the frontal lobe syndrome suggesting that large parts of the frontal lobe were involved as the irritative, symptomatogenic, and functional deficit zones, rather than as the epileptogenic zone [14] and that at least in some patients, these zones can be “reversed” with successful epilepsy surgery.

While the epileptogenic zone typically extends beyond the visible margins on MRI, it may also be confined to a smaller substrate well within the visible MRI lesion as in our patient. In spite of widespread EEG abnormalities, multiple seizure semiologies, and bilateral MRI involvement, successful surgery outcomes may be achieved in the frontal lobe. Successful frontal epilepsy surgery outcomes provide a unique opportunity to further our understanding of the frontal lobe syndrome and its risk factors. This, in turn, may translate to more patients being considered as candidates for resective rather than palliative epilepsy surgery.

Conflict of interest

All authors report no disclosures.

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