

Surgery for encephalomalacias presenting with intractable epilepsy

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ABSTRACT

Background: Surgery for intractable epilepsy caused by encephalomalacia (especially post-traumatic) has been reported very scarcely in the literature. **Materials and Methods:** 21 cases are presented who underwent resections for encephalomalacias for medically intractable epilepsy are presented from a series of 632 cases. **Results:** Seizure duration pre-surgery ranged from 3 to 29 years (mean 7.8 years, median of 7 years). Seizure frequency ranged from 2 seizures/month to 7/day, with a median of 10 seizures/month. Causes included head trauma (9), encephalitis (2), peri natal ischemia (3) post abscess (3) and idiopathic (4). The postoperative follow-up was 21 months (ranging from 12 to 63 months). 17 had Engel's Class I seizure outcome. Four patients had poor seizure outcome (two Class IV and two Class III). All post traumatic encephalomalacias had excellent outcome, and post encephalitis the worst. **Conclusions:** Encephalomalacia with intractable epilepsy have a varied outcome and depends on the pathology.

Key words: Encephalomalacia, traumatic, abscess, epilepsy, surgery

INTRODUCTION

Wilder Penfield,^[1] working with Otfried Foerster in Breslau, Germany, studied a series of patients with post-traumatic frontal lesions and suggested that resection of frontal foci of encephalomalacia might relieve intractable post-traumatic epilepsy.

However, despite such early beginnings, surgery for intractable epilepsy caused by encephalomalacia (especially post-traumatic) has been reported very scarcely in the literature.^[2-4]

That encephalomalacia is an important cause of medically intractable epilepsy is evident from the fact that it represented as much as 8% of focal structural lesions in a large magnetic resonance imaging (MRI) series^[5] of patients with intractable epilepsy.

In our own series of 632 cases who underwent surgery

for intractable epilepsy, 21 cases had encephalomalacias (Unit I, Neurology and Neurosurgery) presenting with intractable epilepsy.

MATERIALS AND METHODS

Patient Material

This was a retrospective study of 21 patients (12 males) who underwent surgery for encephalomalacia (1998–2011) between April 1998 and May 2011.

Pre-operative Workup

All these patients were initially evaluated by the team epileptologist to confirm the medical intractability of seizures. All the patients were on at least two drugs with a range of two to five drugs. Pre-operative investigations included inter-ictal standard EEG, video EEG (VEEG), MRI (as per epilepsy protocol) and ictal single-photon emission tomography (SPECT) (SISCOS: ictal subtracted from inter-ictal SPECT; SISCOM: SISCOS superimposed on the MRI image). Positron emission tomography (PET) was performed in cases showing non-focal lesions.

The details of the pre-operative work up have been provided in the earlier publications.^[6-10]

Surgery

Pre-operative concordance strongly determined the

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type of surgery and the management paradigm. An awake craniotomy was performed if the focus was felt to be too close to an eloquent area. Intraoperative MRI with neuronavigation was utilized in four patients. Pre-operatively, if the encephalomalacia was seen to correspond with the localization of inter-ictal EEG, VEEG, SPECT, and/or PET, it was possible to perform resective surgery using electrocorticography.^[11] Frequency and severity of seizures also played an important role in proper delineation of epileptogenic focus.^[11]

Invasive EEG was performed in cases where MRI was non-focal or bilateral.^[12] All surgically removed specimens underwent a complete histopathologic examination.

Antiepileptic drugs were gradually tapered on follow-up with consultation of the epileptologist if the seizures remained controlled for more than 1 year. Seizure outcome assessment was done using Engel's grading.^[13]

RESULTS

The study included 21 patients (12 males; mean age 22 years, range 9–38 years) who had undergone focus resections for encephalomalacias as treatment for medically intractable epilepsy. Partial seizure with generalization was the commonest pattern of seizures,^[11] followed by complex partial^[3] and only partial seizures.^[13]

Seizure duration pre-surgery ranged from 3 to 29 years (mean 7.8 years, median of 7 years). Such a late referral reflects a tendency of holding on to medical treatment before recommending surgery in this group of patients, probably because surgical treatment for encephalomalacias is not as commonly recognized.

Seizure frequency ranged from 2 seizures/month to 7 seizures/day, with a median of 10 seizures/month.

MR revealed foci of encephalomalacia as shown in Table 1. The commonest cause of encephalomalacia leading to intractable epilepsy was head injury. Not surprisingly, all cases of post-traumatic encephalomalacia leading to intractable epilepsy were located in the frontal lobes. The mean interval between trauma and the onset of medically intractable epilepsy was 4 ± 3.87 years (range of <24 hours to 10 years). The median duration of epilepsy before surgery for post-traumatic encephalomalacia was 8 years (range of 3–29 years). This long duration may be due to a tendency by the referring physicians to recommend medical treatment for as long as possible. One of the patients operated for post-traumatic intractable epilepsy also had CSF rhinorrhea due to a cribriform plate defect, which had led to repeated episodes of meningitis. The

defect was repaired in the same operative procedure for post-traumatic epilepsy.

The duration of epilepsy before surgery for the two porencephalic cysts arising as sequelae of neonatal encephalitis was 6 and 15 years each.

The patients with hemiatrophy due to perinatal stroke included a 27-year-old male with seizure duration of 25 years and a 12-year-old male with seizure duration of 9 years. Both these patients were intellectually retarded and had hemiparesis.

Management

MRI revealed a single focus in 15 patients – 6 with a single frontal focus, 3 with a single temporal focus, 3 with a single parietal focus, and 3 with single porencephalic cysts. SPECT revealed the same focus in all these 15 patients. However, VEEG was inconclusive in 3 and revealed bilateral/discordant foci in 2 of these 12 patients. Both these patients with bilateral/discordant foci (to the MR-identified focus) on VEEG ultimately underwent focus resection of the MR-identified focus with good seizure outcome. EEG was inconclusive in 3 patients and revealed bilateral/discordant foci in 6 of these 12 patients. All these six patients with bilateral/discordant foci (to the MR-identified focus) on EEG ultimately underwent focus resection of the MR-identified focus with good seizure outcome.

In contrast to this, generally only additive value of SPECT/VEEG/EEG in patients with conclusively identified single foci on MRI, SPECT/VEEG/EEG had a far greater role to play in the three patients with bilateral frontal foci on MRI and the two patients with hemiatrophy on MRI. Both the patient groups with bilateral frontal foci had more signal changes on MR on the right side and that

Table 1: MR location of encephalomalacia (with probable cause)

Location	Number	Cause
Left frontal	3	Abscess in 1, head injury in 2
Right frontal	3	Head injury in all 3
Bilateral frontal rights>left	3	Head injury in both
Right parietal	3	Head injury
Right posterior temporal	2	Idiopathic
Left posterior temporal	1	Idiopathic
Left temporal porencephalic cyst	1	Idiopathic
Left fronto-parietal porencephalic	1	Neonatal encephalitis
Left parieto-occipital porencephalic cyst	1	Neonatal encephalitis
Left hemiatrophy	1	Perinatal stroke
Right hemiatrophy	1	Perinatal stroke
Bilateral parieto-occipital	1	Perinatal ischemia

this was the side of seizure generation was confirmed only when VEEG/SPECT also revealed a right frontal focus. Both these patients underwent a right frontal focus resection with good outcome.

The two patients with hemiatrophy on MRI due to perinatal stroke included a 27-year-old male with seizure duration of 25 years and a 12-year-old male with seizure duration of 9 years. Both these patients were intellectually retarded and had hemiparesis with significantly impaired hand functions opposite to the diseased hemisphere. At the first glance, they were candidates for hemispherotomy and their pre-operative work-up included speech evaluation (in preparation for hemispherotomy) using a transcutaneous magnetic stimulator which caused speech arrest when applied to the hemisphere carrying speech function. Functional MRI was also done to identify the areas with speech function and the motor areas. SSEP was also done to evaluate the cortical functions of the diseased hemisphere. However, SPECT, VEEG, and EEG revealed one of these patients to have only a temporal focus and this patient opted to undergo only an anteromedial temporal lobectomy initially and a hemispherotomy only if it failed. The other patient had a hemispheric focus even on SPECT, but EEG/VEEG revealed only a frontal focus. This patient also opted to undergo only a frontal focus resection initially and a hemispherotomy only if it failed.

Functional MRI had been done in the two patients described above and in three more patients, one with bilateral posterior frontal foci, one with a parietal focus, and the other with a fronto-parietal porencephalic cyst. Functional MRI gave a fair pre-operative idea of the approximate location of the motor area in relation to the focus of encephalomalacia.

The last patient shown in Table 1 showed evidence of [Figure 1a] bilateral symmetrical parieto-occipital signal changes on MRI. SPECT (SISCOS: ictal SPECT subtracted from inter-ictal SPECT) localized to posterior right temporal lobe with evidence of crossed cerebellar activity [Figure 1b]. PET [Figure 1f] showed evidence of anterior temporal hypometabolism. The clinical semiology and VEEG corresponded to posterior temporal area (temporal plus syndrome). Since there was discordance between the data, invasive EEG [Figure 1d] was performed (three strips and a depth electrode was placed). Four ictal events were recorded, all of them from the posterior temporal area. The patient underwent only a posterior temporal resection without excision of the anterior part and the mesial structures. The patient had a good outcome (Engel I score) at follow-up at 1 year after surgery.

Two patients underwent awake craniotomies in view of close proximity of eloquent cortex to the focus of surgical interest, one with a left posterior temporal focus and the other with bilateral posterior frontal foci who had also undergone a functional MRI (which revealed very close proximity of the motor area to the focus of surgical interest). All patients underwent focus resections under intraoperative electrocorticographic (ECoG) guidance. Two patients, one with a temporal porencephalic cyst and the other with hemiatrophy on MR (but with a temporal focus on EEG/VEEG/SPECT), underwent formal anteromedial temporal lobectomies because of persistent spikes on intraoperative ECoG. The spikes disappeared after the temporal lobectomy in the patient with the temporal porencephalic cyst. However, they persisted in the frontal area even after temporal lobectomy in the patient with hemiatrophy.

Complications

One patient had postoperative meningitis which responded to antibiotics.

Transient hemiparesis (which improved to normal) was

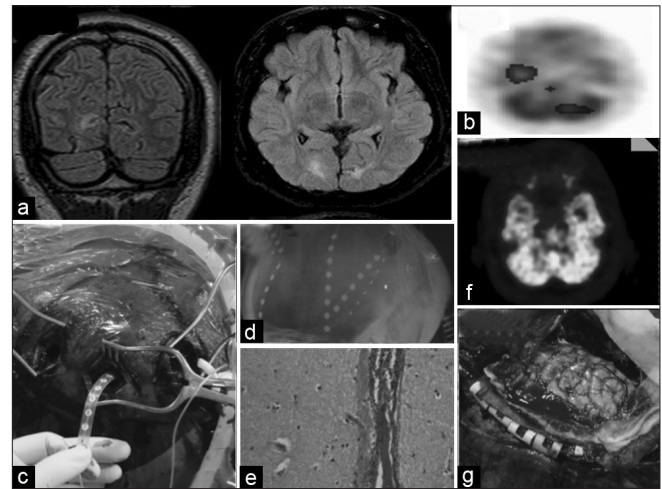


Figure 1: A 32-year-old male with moderate mental retardation (history of perinatal hypoxia) presented with complex partial seizures becoming generalized since 15 years of age, about 3–4 per day. Seizures were characterized by formed visual aura suggestive of parieto-occipital localization. MRI revealed (a) bilateral parieto-occipital signal changes. Ictal SPECT (SISCOS) (b) showed evidence of intense activity in the right posterior temporal area. (c) placement of grid during surgery (d) invasive EEG (three strips and a depth electrode was placed) (e) histopathology shows gliosis PET (f) showed hypometabolic area in the right anterior temporal area. VEEG correlated with clinical semiology and localized to posterior temporal area. In view of discordance between PET and other findings, the patient falling under the category of “substrate negative” epilepsy, he underwent invasive EEG. Three strip electrodes were placed over the right parieto-occipital-temporal area with a temporal depth electrode. From four ictal events recorded from the invasive EEG, the localization was primarily to the posterior temporal area not involving the mesial structures. In view of these findings, he underwent a posterior temporal resection leaving behind the anterior and mesial temporal structures. At 1 year of follow-up, the patient was free from seizures (Engel Ib outcome) (g) posterior temporal resection without excision of the anterior part and the mesial structures

seen in two patients, one with a parietal focus and the other with a fronto-parietal porencephalic cyst, both of whom had undergone functional MRI before surgery. We feel that this low incidence of postoperative neurological deficits can be credited to our careful approach to focus resections for encephalomalacia using functional MRI and an awake craniotomy, if required.

Of the seven patients who had immediate postoperative fits, five patients had Engel's Class I seizure outcome at follow-up while two had Class III outcome. Therefore, we feel that immediate postoperative fits do not necessarily portend a poor prognosis.

Seizure Outcome

We have the postoperative follow-up for all 21 patients with a mean follow-up period of 21 months (ranging from 12 to 63 months).

Of the 21 patients, 17 had Engel's Class I seizure outcome.

Four patients had poor seizure outcome (two Class IV and two Class III).

Among the two patients with hemiatrophy on MRI, one patient who had a temporal focus on SPECT, VEEG, and EEG and opted for a temporal focus resection only as a first procedure underwent a formal anteromedial temporal lobectomy but had persistent supra-sylvian spikes even after temporal lobectomy. This patient not very unexpectedly had a Class IV outcome and is awaiting hemispherotomy.

However, the other patient with hemiatrophy is also an interesting case study. As detailed before, this patient underwent only a frontal focus resection initially because EEG/VEEG revealed only a frontal focus. Interestingly, even SPECT revealed a hemispheric focus in this patient. Intraoperative ECoG revealed no spikes at the end of surgery, and miraculously this patient who would have cursorily been a candidate for hemispherotomy had a Class I seizure outcome on follow-up.

Interestingly, all patients with post-traumatic encephalomalacia had excellent seizure outcome (100% Engel I outcome).

Discordance of EEG/VEEG/SPECT with a conclusively identified single focus on MRI did not lead to a worse outcome as two patients who had discordance of VEEG and six patients who had discordance of EEG with a conclusively identified single focus on MRI had Class I outcome following resection of the MR-localized foci irrespective of EEG/VEEG discordance.

Again, bilateral abnormalities on MRI do not portend a worse prognosis as long as adjunctive investigations such as EEG/VEEG/SPECT clearly demonstrate one focus for resection as is evident from our last mentioned patient who underwent invasive EEG followed by resection.

DISCUSSION

Surgery for encephalomalacias presenting with intractable epilepsy is surprisingly scanty, even though the reported literature has demonstrated good outcome.^[2,3]

Kazemi^[2] *et al.* reported 59% Class I and 11% Class II outcome among 17 patients who had undergone frontal focus resections for encephalomalacias. Our overall result showed 75% (12/16) Class I outcome among all 16 patients. However, if we include only the patients undergoing frontal focus resections, our Class I outcome improves to 91.67% (11/12).

We have demonstrated 100% Class I outcome among eight patients undergoing frontal resections for post-traumatic frontal encephalomalacia-related intractable epilepsy. A good outcome for this entity has also been reported by Andermann^[3] *et al.* who demonstrated 100% seizure free outcome among six such patients. Though Kazemi^[2] *et al.* did not mention it separately, a close reading of their article reveals that seven of their eight patients with post-traumatic frontal encephalomalacias had Class I outcome while the other had Class II outcome.

Both Kazemi^[2] *et al.* and Andermann^[3] *et al.* have stressed that the completeness of resection of encephalomalacia as determined on MRI is a key factor in determining a good seizure outcome.

Coming to the role of MRI, it is quite definite that a high-quality MRI employing FLAIR^[14] sequences is particularly good at picking up foci of encephalomalacia. We also use FLAIR sequences in our Epilepsy Surgery MRI protocol [Figure 1]. We feel that in patients with a conclusively identified single focus on MRI, EEG/VEEG/SPECT has a mainly adjunctive value and discordance of these with MRI may not mean a worse prognosis, as has been described before.

However, it must be stressed that MRI at best remains only a modality capable of picking up structural abnormalities without revealing the electrophysiological activity of these structural abnormalities. The limitation of MRI becomes evident in our two patients with bilateral frontal MR foci in whom the active foci were localized only with the help of EEG/VEEG/SPECT. Similar is the

case where invasive EEG recordings were performed. However, it must be noted that bilateral abnormalities on MRI do not portend a worse prognosis as long as adjunctive investigations such as EEG/VEEG/SPECT can clearly demonstrate one focus for resection as in both of our patients with bilateral frontal MR foci. The same has also been noted by both Kazemi^[2] *et al.* and Andermann^[3] *et al.*

CONCLUSIONS

The advent of high-quality MRI has made possible the detection of encephalomalacia as a surgically resectable cause of intractable epilepsy. The results of surgery using intraoperative ECoG to decide the extent of resection are good in terms of seizure outcome. Post-traumatic frontal encephalomalacias especially have a very good outcome following surgery.

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