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Case Report

Surgical Management of Super-Refractory Status Epilepticus with Successful Outcomes- A Presentation of 3 Case Series - @

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ABSTRACT

Refractory Status Epilepticus (SE) and Super-refractory status epilepticus have significant mortality and morbidity. Urgent neurosurgical intervention is rarely used, but in selected cases where medical therapy has failed, it can successfully help control refractory partial SE and also prevent associated morbidity and mortality. At our institution, urgent resective surgery was performed on three patients with medically refractory convulsive status epilepticus in the past 4 years. The etiology on histopathological analysis was focal cortical dysplasia on two patients and non-specific gliosis on the third patient. In all cases, surgery resulted in termination of status epilepticus, permitting de-escalation of therapy, and led to marked improvement in quality of life. There are recent advances in anatomical and functional neuroimaging techniques, which in combination with improved and relatively easier availability of continuous intracranial EEG recording, have markedly improved the diagnostic localization of epileptogenic cortex. Diagnostic work up and surgical intervention in a multistep algorithmic approach are crucial to achieving improved patient outcome. Our cases demonstrate the importance of timely surgical intervention in the management of selected patients with medically refractory status epilepticus.

Keywords: Super refractory status epilepticus; Surgical resection; Epilepsy surgical outcomes

INTRODUCTION

Refractory SE is defined as SE that has not responded to first-line therapy (benzodiazepine) or second-line therapy, and requires the application of general anesthesia. Super-refractory SE is a stage of refractory SE characterized by unresponsiveness to initial anesthetic therapy and is defined as SE that continues or recurs 24 hours or more after the onset of anesthesia, including those cases in which SE recurs on the reduction or withdrawal of anesthesia. Both Refractory and super-refractory SE are a life-threatening neurological emergency associated with high morbidity and mortality [1]. While the definitions of SE and immediate management of SE is well established, the management options for refractory and super-refractory SE as well as their outcomes are not as well established. However, there is evidence in published literature for pursuing surgical interventions in such cases [2,3]. By the time, second line medical therapy and anesthesia have failed, patients are often critically ill, with prolonged coma and respiratory problems accounting for more than 50% of deaths. We present 3 cases of focal onset seizures with secondary generalization who were in refractory status epilepticus despite use of barbiturates. Emergent/ Urgent surgical resection of seizure focus was undertaken in all these cases with good outcomes. We present these cases to highlight surgical resection as modalities that can be considered as treatment options in select population of patients with focal onset seizures in status epilepticus, with the intention of adding to the growing body of published literature in the matter.

Case 1

59 year right hand dominant male, with asymptomatic myasthenia gravis, coronary artery disease and hypertension, was diagnosed with bilateral occipito-parietal Arteriovenous Malformations (AVM). He developed seizures a year prior to presentation to our center. He had undergone obliteration of the left parieto-occipital AVM, had failed three antiepileptic medications, and was on a combination of three therapeutic medications at time of admission to the Epilepsy Monitoring Unit. He was in refractory SE by day 2, was intubated and subsequently placed on barbiturate induced coma. His seizures did not resolve despite escalation of medical therapies and he remained intubated and in medically induced coma. MRI showed abnormal increased T2/FLAIR signal without enhancement in the left hippocampus which was similar in appearance to his prior examinations. Subdural grids were placed with intention to resect the seizure foci 37 days after onset of SE. Based on invasive monitoring, he underwent left hippocampal resection as well as resection of ictal onset zones from the left parieto-occipital areas. Pathology report within both the left occipital seizure focus as well as left temporal

lobe tip were consistent with the diagnosis of focal cortical dysplasia, type IIA. Dysplastic features were likewise seen within the subiculum and there was evidence of mesial temporal sclerosis within the anterior hippocampus. At the fourth year follow up now, patient is independent in most activities of daily living, has some memory deficits and some higher order language dysfunctions. He continues to remain on one Antiepileptic medication at full therapeutic dose, with no reported convulsions in past two years.

Case 2

23 year right hand dominant male, presented with 20-30 seizures per day of eye fluttering, left side weakness and dizziness. Each episode lasted 20 seconds but he had no recollection of events for 3-5 minutes after. He also reported occasional generalized tonic clonic convulsions as well. He had failed five antiepileptic medications, and was at time of presentation on three with reported adverse effects from the medications. His scalp EEG showed multiple and near continuous right parietal onset seizures. MRI revealed a small focus of FLAIR hyper-intensity involving the high right parietal lobe just posterior to the post central sulcus. The signal abnormality involved the cortex and the subcortical white matter, with possible mild cortical thickening. No enhancement was seen. His seizures did not remit for 32 days, and surgical resection was performed due to significant disease burden impairing his learning and work, as well as due to the location and predicted ease of resection of the foci with minimal predicted deficits. Intraoperative mapping only was performed and the areas of ictal onset were adjacent to the scar tissue, which by itself was completely silent on EEG. Post-resection, there were no further spikes or other ictal discharges. Final surgical pathology was found to be focal cortical dysplasia with dysmorphic neurons and balloon cells type 2B. Post resection, he remains seizure free on monotherapy, has completed a masters and is employed full time now for past three years.

Case 3

60 year right hand dominant female, with multiple medical comorbidities, most recent hospital admission significant for necrotizing pneumonia and septic emboli to left parietal-occipital and right frontal areas. She developed seizures secondary to these embolic areas and was admitted in SE due to same. She quickly became medically refractory even to barbiturate coma. Per patient's advance directives, she had indicated that she would not have wished to be on life-sustaining measures for prolonged periods of time. Surgical resection of the left parietal-occipital lesion was considered as a palliative approach alternative to terminal extubation at day 42 after onset of established SE. MRI repeated prior to surgical resection



showed an area of gyriform diffusion restriction in the left lateral occipital/posterior temporal lobe, possibly representing an area of acute ischemia versus diffusion restriction secondary to epileptic activity. This area was targeted based on scalp EEG recordings, subdural grids were placed to help guide resection and final pathology showed reactive gliosis with focal loss of myelin. Postoperatively, seizures were under control enough to allow extubation, patient was able to follow simple commands and was discharged to a skilled nursing facility.

DISCUSSION

Our case series highlights the efficacy of timely surgical intervention in refractory and super-refractory focal SE, even when a definitive underlying etiology is not established. The patient outcome in these cases demonstrates that good recovery can occur even after prolonged and severe SE. We guided the extent of surgical resection based on preoperative EEG data, anatomical neuroimaging findings, and demonstration of seizure onset zone on intraoperative Electrocorticography (ECog).

The most common etiologies of refractory status epilepticus of focal origin, for which resective surgeries have been performed include cortical dysplasia, low grade tumors and Rasmussen's syndrome. Since there are no established guidelines for optimal management of super-refractory SE, frequently by the time surgical intervention is considered, the cumulative effect of morbidity from prolonged status epilepticus and intensive medical management has minimized the chances of good post-surgical outcome [4]. Therefore neurologists should exercise vigilance in early identification and aggressive management of refractory and super-refractory cases of SE to identify those who can benefit from surgical intervention.

Focal electrographic and neuroimaging findings can guide identification of epileptogenic cortex. However, even in the absence of identifiable lesions on brain MRI, successful surgical treatment of patients in refractory SE is possible, which emphasizes the fact that lesions like MRI-occult cortical dysplasia can respond well to surgery. Advances in anatomical and functional neuroimaging techniques (ictal SPECT and FDG-PET), in combination with utilization of ECoG recording can now allow a greater degree of certainty in localization of epileptogenic cortex, even in non-lesional cases [5]. Limitations to this approach include the fact that mapping the eloquent cortex and the precise extent of adjacent epileptogenic zone can be a challenging task in patients with refractory SE. Infusions of anesthetics used to control the SE can often complicate precise seizure localization and lower the efficacy of resection. It is also prudent to have honest discussion with the family regarding realistic and acceptable outcomes, while performing resective surgery in the setting of relatively suboptimal pre-surgical evaluation in a critically ill patient.

The accurate delineation of the epileptogenic network or the Epileptogenic Zone (EZ) which includes determination of regions that generate inter-ictal spikes (irritative zone, IZ) and those involved in the initiation of seizures (seizure onset zone, SOZ) is a fundamental step to determine extent of surgical resection and ensure good surgical outcome in patients with refractory SE. ECoG provides the greatest precision in estimating the location and boundary of the EZ. More recently, High Frequency Oscillations (HFO) have been proposed to be better markers than the inter-ictal spikes to identify the SOZ. Literature review showed that resection of the area with HFO may lead to a favourable surgical outcome. Recent studies have shown that examining higher (80–1000 Hz) and lower band (0.016–0.5 Hz) EEG frequencies can provide additional diagnostic information and help to improve the surgical outcome [5].

CONCLUSIONS

There are no guidelines regarding how early surgical therapy should be carried out. Surgery has been carried out as early as 8 days after the onset but generally considered only after weeks of status epilepticus. Some authors recommend strong consideration after a 2 week period of failed medical therapy. A timely algorithmic approach, involving meticulous understanding of diagnostic tools and intervention is the key to achieving favorable outcomes. The surgical procedures documented in literature for refractory and super-refractory cases include focal cortical resection, lobar and multi-lobar resection, anatomic and functional hemispherectomy, corpus callosotomy, multiple sub-pial transaction and vagus nerve stimulation. There are no valid data regarding Deep Brain Stimulation (DBS).

In summary, our case series, in combination with published literature suggests that surgical treatment relatively early in the course of refractory and super-refractory focal SE may lead to improved outcome in well-selected patients.

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