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The Benefits of Epilepsy Surgery in Tuberous Sclerosis: A Case Report

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Introduction/Background: Epilepsy affects millions worldwide, with about one-third of patients remaining drug-resistant despite optimal medical therapy. In tuberous sclerosis complex (TSC), refractory epilepsy is common and severely impacts quality of life. Surgery targeting epileptogenic tubers offers a potential curative approach, contrasting with palliative options like callosotomy.

Case Presentation: A 6-year-old girl with TSC presented with daily drug-resistant focal and generalized seizures. MRI revealed multiple cerebral tubers, with EEG identifying a dominant epileptogenic focus in the left temporal lobe. After multidisciplinary evaluation, the patient underwent left temporal craniotomy and lesionectomy, guided by intraoperative electrocorticography. Postoperative monitoring showed no epileptiform activity. Seizure frequency reduced by 50% immediately postoperatively, reaching remission by one month. At one year, she remained seizure-free with reduced antiepileptic therapy and showed cognitive improvements.

Conclusions: Targeted tuber resection effectively controlled seizures and enhanced quality of life, avoiding more invasive palliative procedures. Careful preoperative evaluation to identify dominant epileptogenic foci is critical. Lesionectomy offers superior long-term outcomes over palliative options like callosotomy in selected TSC patients, supporting a tailored surgical approach based on detailed neuroimaging and electrophysiological data.

Keywords: Epilepsy Surgery, Tuberous Sclerosis, Tubers, Epilepsy, lesionectomy

INTRODUCTION

Epilepsy is a chronic neurological condition that impacts millions of individuals worldwide, characterized by recurrent seizures that can vary in severity, frequency, and intensity. Despite advancements in pharmacological treatments, approximately one-third of epilepsy patients do not respond adequately to antiepileptic drugs and continue to experience seizures despite optimal management. For these patients, epilepsy surgery serves as a potential curative therapeutic option.

In patients with tuberous sclerosis (TS)—a genetic condition that leads to the formation of benign lesions (tubers) in various organs, including the nervous system—refractory epilepsy is a prevalent and significant complication, affecting not only the patient's quality of life but also that of their caregivers. Surgical resection of cerebral tubers has been explored as a strategy to reduce seizure frequency and enhance the quality of life for these patients. This article reviews the background of palliative epilepsy surgery (callosotomy, VSN, etc…) that has been used to reduce the number of seizures and improve quality of life, against epilepsy surgery for tuber resection, examines recent relevant studies, and explores the clinical and therapeutic implications of this intervention.

Objective

To present a case of a patient with tuberous sclerosis complex and drug-resistant epilepsy associated with a temporal lobe tuber, where surgical intervention resulted in a 90% reduction in seizures, ultimately achieving sustained seizure control.

CASE REPORT

A 6-year-old female patient presented with developmental delay first noted at 6 months of age, as assessed using the Denver Developmental Screening Test. At one year of age, she began experiencing focal seizures characterized by automatisms, loss of consciousness, and leftward gaze deviation, subsequently progressing to generalized bilateral tonic-clonic seizures. The patient experienced up to 20 seizures daily and remained refractory to multiple antiepileptic medications, including vigabatrin, clobazam, levetiracetam, valproate, and cannabidiol oil,

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without achieving adequate seizure control, considered as multiple foci crises refractory to treatment according to the ILAE guidelines. (7)

The diagnosis of tuberous sclerosis was established based on clinical findings according to guidelines of tuberous sclerosis complex, including the presence of Shagreen patches in the lumbar region, bilateral renal cysts, and multiple cerebral tubers with subependymal nodules, confirmed through magnetic resonance imaging (MRI) (Figure 1). Following a multidisciplinary evaluation by the epilepsy surgery committee, further diagnostic workup included a 6-hour videoelectroencephalogram (VEEG) (Figure 2), which revealed prominent epileptiform activity in both cerebral hemispheres, predominantly originating in the left temporal lobe, corresponding to the location of one of the identified tubers. (8)

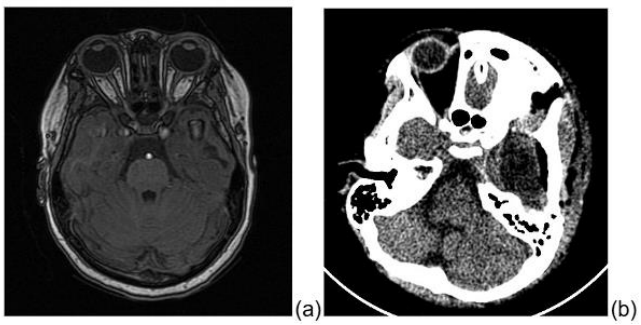

Figure 1- (a) Preoperative T1weighted MRI demonstrating a tuber in the left temporal region. (b) Postoperative plain CT scan showing postoperative changes consistent with resection of the left temporal tuber

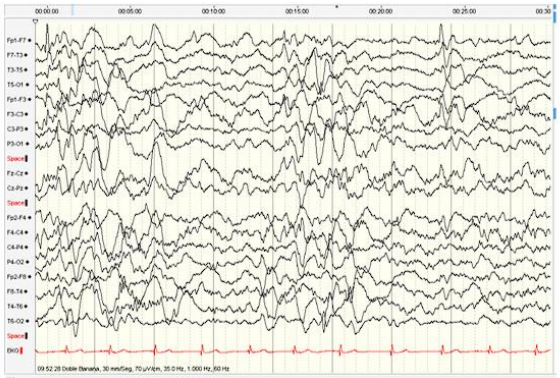

Figure 2 – six-hour VEEG recording exhibiting abnormal tracing, with poorly integrated baseline activity and multifocal epileptiform activity predominantly in the left temporal region across both hemispheres

The committee decided to proceed with a left temporal craniotomy, accompanied by intraoperative electrocorticography (ECoG) using a 20-channel grid and a 4-channel linear array. A resection of the left temporal tuber was performed, targeting areas of heightened activity identified through the 20-channel grid. Notable interictal spike activity was detected in channels 12, 17, 13, 18, 14, and 19, with contralateral propagation, as shown in Figure 3.

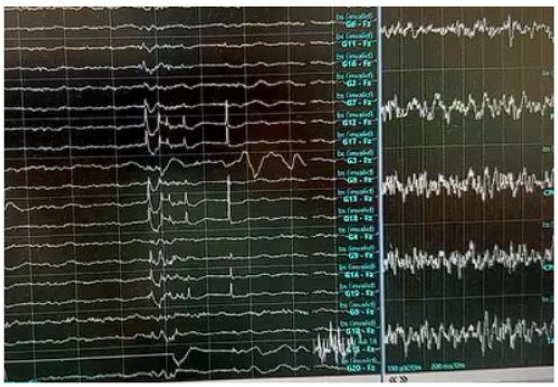

Figure 3 – Simultaneous tracing from corticography and surface elecrtoencephalography. The left screen displays corticography showing abundant interictal spike activity in channels 12, 17,13, 18, 14, and 19, with apparent contralateral propagation

Following the surgical resection, the electrode grid was reapplied, and both intraoperative ECoG and surface electroencephalography indicated the absence of ictal activity, irritative waves, or previously identified epileptogenic foci, as illustrated in images 4a and 4c.

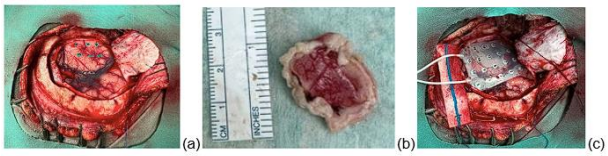

Figure 4 – (a) Left vraniotomy, exposing the temporal lobr. (b) Left temporal tuber following resection. (c) Placement of the grid in the left temporal region

The surgical procedure was executed without complications, both intraoperatively and in the postoperative period. In the immediate postoperative phase, there was a 50% reduction in seizure frequency, resulting in an ILAE Outcome Scale classification of class 4 and an Engel classification of 2D. The patient was discharged with a regimen of magnesium valproate 8 ml every 8 hours, in conjunction with clobazam and levetiracetam at a dosage of 8 ml every 12 hours.

At the one-month follow-up, the patient experienced a total of only 20 seizures per month, ultimately achieving remission. During the six-month follow-up, the patient continued on the same medication regimen without experiencing any seizures. At the one-year follow-up, clobazam was discontinued, and the dosages of levetiracetam and valproate were decreased, with the patient remaining seizure-free and continuing regular follow-up care, with qualitative improvements such as attention to speech, eye tracking, more reactive to external stimuli.

DISCUSSION

There are multiple surgical interventions available for epilepsy treatment; however, the selection of a specific procedure should be tailored to the patient's clinical profile. In this case, anterior callosotomy was considered against lesionectomy. Anterior callosotomy is widely regarded as a palliative intervention, as it entails partial or complete sectioning of the corpus callosum, which typically reduces the interhemispheric propagation of epileptic discharges. For patients experiencing multifocal seizures that are challenging to localize—such as the patient in this case—this intervention can be particularly effective in decreasing the frequency and severity of drop attacks or generalized tonic-clonic spasms, secundariy it can serve as a focal locator, by isolating the hemispheres and asking to identify foci that have a greater predominance of epileptic discharges .Nonetheless, it does not reliably reduce focal seizures, nor does it address the underlying epileptogenic source. (1-3)

In this case, lesionectomy was selected. This procedure involves resecting specific tubers identified as epileptogenic foci, a characteristic feature of tuberous sclerosis. Prolonged electroencephalogram monitoring allowed for the identification of a lesion responsible for seizure propagation throughout the cerebral parenchyma. Evidence suggests that lesionectomy offers superior long-term seizure control and may even achieve complete remission in some patients. Studies have demonstrated that directly removing epileptogenic tissue results in improved outcomes in terms of seizure control, cognitive development, and quality of life compared to callosotomy, particularly in patients with a dominant focus, as seen in this instance.(3-6)

A review of the literature supports the decision to prioritize lesionectomy over callosotomy based on several key considerations. Lesionectomy is generally more effective in reducing or eliminating seizures in patients with clearly identifiable epileptogenic foci and is associated with better quality of life and neuropsychological outcomes due to the removal of the underlying cause. In contrast, callosotomy, which primarily aims to reduce seizure propagation rather than addressing the root cause, is a palliative option that often achieves only partial seizure control. While callosotomy may lead to complications such as interhemispheric desynchronization, bimanual coordination difficulties, and behavioral changes, lesionectomy's risks, such as potential damage to eloquent brain areas, have been mitigated by advances in intraoperative cortical mapping. Ultimately, the choice of procedure depends on factors such as the presence of a distinct epileptogenic focus, seizure type, and neuroimaging findings, with lesionectomy offering superior outcomes for patients with accessible lesions and a dominant focus, while callosotomy may be considered for multifocal cases without a clear target. (9,10)

There are multiple studies that evaluated the long-term outcomes of tuber resection in pediatric patients with TS and refractory epilepsy; all the authors concluded that surgical resection of tubers in selected individuals with TS and refractory epilepsy is both an effective and safe approach to enhancing long-term clinical outcomes. (10-12)

Moreover, a meta-analysis conducted by Smith et al. evaluated findings from multicenter studies on epilepsy surgery in patients with TS. This comprehensive analysis included data from over 1,000 patients and underscored that tuber resection demonstrated a substantial success rate in reducing epileptic seizures. Many patients and their caregivers reported an improvement in quality of life postoperatively. Nevertheless, the analysis also highlighted the critical importance of thorough preoperative assessment and personalized surgical planning to optimize clinical outcomes. (11-14)

The current evidence substantiates the role of epilepsy surgery for tuber resection as a viable and effective therapeutic intervention for patients with TS and refractory epilepsy. The studies reviewed consistently demonstrate a significant reduction in the frequency of postoperative seizures and, in numerous instances, a complete cessation of convulsive episodes. These findings have not only positive implications for the quality of life of patients but may also mitigate the economic and emotional burdens associated with the ongoing management of refractory epilepsy. (10-12)

One of the most recent meta-analyses, conducted by Zhirong Wei et al., performed a systematic review and meta-analysis to determine whether tuberectomy and tuberectomy plus yield different postoperative seizure outcomes in patients with epilepsy associated with tuberous sclerosis complex (TSC). This study analyzed a total of 327 participants. Among them, 160 patients underwent tuberectomy alone, with 93 (58.1%) achieving postoperative seizure freedom. The remaining 167 patients underwent tuberectomy plus, with 128 (76.6%) becoming seizure-free after adequate follow-up. The findings indicated that tuberectomy plus is a more effective treatment than tuberectomy alone for patients with TSC-related intractable epilepsy. Increasing evidence supports the efficacy of lesionectomy and related procedures in improving outcomes for patients with tuberous sclerosis complex, as demonstrated in this analysis.(13-15)

However, various challenges remain in the practical implementation of tuber resection surgery. Accurate identification and characterization of cerebral tubers continue to be areas of active research, with advancements in imaging modalities and molecular biomarkers poised to enhance diagnostic accuracy and surgical planning. Furthermore, the judicious selection of candidates for surgical intervention is essential, taking into account factors

such as the location and number of tubers, the presence of additional epileptogenic foci, and preoperative neuropsychological assessments. (14-16)

Ethical considerations are also significant, particularly regarding shared decision-making among patients, families, and healthcare providers. The context of epilepsy surgery for tuber resection raises questions concerning the equilibrium between risks and benefits, the autonomy of patients, and the capacity for informed consent, especially in pediatric populations or individuals with cognitive impairments associated with TS. (15-17)

CONCLUSION

The case presented herein exemplifies the critical role of epilepsy surgery not only in controlling seizures but also in improving the quality of life for both the patient and the caregiver. This particular case illustrates that by identifying the tuber exhibiting the highest level of ictal activity, it is possible to enhance seizure control without resorting to more invasive procedures such as anterior callosotomy. Specifically, a 90% reduction in seizures was achieved, and at the one-year follow-up, the patient remained seizure-free on a regimen of two medications. According to the International League Against Epilepsy (ILAE) Outcome Scale, the patient was classified as Class 3 (1-3 seizures per year), while the Engel Outcome Scale indicated a classification of IIB (rare disabling seizures since surgery). (16,17)

Utilizing the full range of available epilepsy surgical techniques is essential for achieving optimal seizure control. Anterior callosotomy may serve as an initial step when precise localization of isolated foci proves challenging. When a dominant focus is identified on the electroencephalogram, lesionectomy or lesionectomy plus should be considered as viable options. In our case, the identification of a temporal epileptiform focus associated with a tuber guided the decision to perform lesionectomy, which was an effective initial approach. However, if seizure control remains inadequate, palliative treatments such as callosotomy, vagus nerve stimulation, deep brain stimulation, or lesionectomy plus should be explored if a focus is later identified.

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DISCLOSURES

Ethical approval

The following clinical case does not enter into a research protocol.

Consent to participate

The patients gave consent to use their information and images for research purposes. *Consent for publication*

The patient gave consent to use his information and images for publication.

Conflict of interest

The authors report no conflicts of interest with respect to the materials or methods used in this study or the findings specified herein

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CONTRIBUTIONS

-**Eduardo Trejo Olguín**: Writing – original draft
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