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Surgical Management of Drug-Resistant Epilepsy through Corpus Callosotomy: Case Report and Literature Review

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Summary. Corpus callosotomy is a palliative surgical procedure used for a selected group of patients with *Drug-Resistant Epilepsy* (DRE) when antiepileptic drugs fail to achieve seizure control. While it significantly reduces seizure frequency, it does not cure epilepsy. In this article, we present the case of a 45-year-old man with DRE unresponsive to pharmacological treatment, who underwent a complete corpus callosotomy. Postoperatively, seizure frequency decreased by 80%, and functional independence improved, though some neurological deficits persisted. A systematic literature review was conducted on the role of corpus callosotomy in the treatment of epilepsy, patient selection criteria, clinical outcomes, and advances in surgical techniques. Future directions include minimally invasive approaches and neurostimulation therapy as complementary strategies for seizure management epilepsy.
Keywords: drug-resistant epilepsy, corpus callosotomy, seizure reduction, epilepsy surgery, neurostimulation.

Vaistams atsparios epilepsijos chirurginis gydymas atliekant kaliozotomiją: atvejo aprašymas ir literatūros apžvalga

Santrauka. Kaliozotomija yra paliatyvi neurochirurginė operacija, atliekama pacientams, sergantiems vaistams atsparia epilepsija, kai vaistai nuo šios ligos neužtikrina pakankamos priepuolių kontrolės. Nors ši intervencija reikšmingai sumažina priepuolių dažnį, visiškai pacientai nepasveiksta. Šiame straipsnyje aprašomas 45 metų vyro, kuriam medikamentinis gydymas buvo neveiksmingas ir dėl to buvo atlikta kaliozotomija, klinikinis atvejis. Pooperaciniu laikotarpiu priepuolių dažnis sumažėjo 80 %, pagerėjo paciento funkcinė nepriklausomybė, tačiau išliko tam tikri neurologiniai defektai. Kartu su klinikiniu atveju pristatoma literatūros apžvalga: kaliozotomijos vaidmuo gydant epilepsiją, pacientų atrankos kriterijai, klinikiniai rezultatai ir chirurginių metodų pažanga. Ateities kryptys apima minimaliai invazinių metodų taikymą ir neurostimuliacinę terapiją kaip papildomas priepuolių valdymo strategijas.
Raktažodžiai: vaistams atspari epilepsija, kaliozotomija, priepuolių sumažinimas, epilepsijos chirurgija, neurostimuliacija.

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Introduction

Epilepsy is one of the most common neurological diseases characterized by an enduring predisposition to generate epileptic seizures, which results in neurobiological, cognitive, psychological and social consequences. This disease affects around 50 million people of all ages worldwide [1]. Ensuring optimal care and accurate prognostication for individuals living with epilepsy necessitates a thorough understanding of the epilepsy classification systems and the application of a meticulous diagnostic approach. The most recent classification of seizures and epilepsies was the *International League Against Epilepsy* (ILAE; 2017), which was published in March 2017. In this current classification by ILAE, the clinical features of epilepsy are categorized into three levels: seizures, epilepsies, and epilepsy syndromes. Emphasis has been made to consider etiology and comorbidities at each level [2]. Antiseizure medications (ASMs) are the primary treatment strategy for epilepsy; currently, over 30 different medications are available on the market. Despite the broad spectrum of ASMs available, drug resistance is estimated to affect about a third of individuals with epilepsy. *Drug-Resistant Epilepsy* (DRE) prevalence differs in relation to the epilepsy syndrome, the cause of epilepsy, and other factors such as the age of seizure onset, and the presence of associated neurological deficits [3,4]. DRE is defined as failure of adequate trials of two tolerated, appropriately chosen and used ASM schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom. This definition is proposed as a testable hypothesis [5]. Surgical procedures are generally considered after the failure of two appropriate drug regimens. Major surgery including corpus colostomy may be considered as the final treatment option of significance in palliative care for intractable seizures [6]. Additionally, other non-drug therapies, such as *Vagus Nerve Stimulation* (VNS) and the ketogenic diet, have been explored as adjunctive treatments for drug-resistant epilepsy [7, 8].

Patients with drug-resistant epilepsy (DRE) have increased risks of premature death, injuries, psychosocial dysfunction, and a reduced quality of life [9]. In general, SUDEP is the most common epilepsy-related cause of death, with around 1 to 2 deaths per 1000 patients per year [10]. *Status Epilepticus* (SE) is a neurological and medical emergency, defined as a condition resulting either from the failure of the mechanisms responsible of seizure self-limitation, or from the initiation of mechanisms which lead to atypically prolonged seizures. Apart from death, SE can have long-term consequences, including neuronal injury, depending on the type, cause and duration of seizures with severe associated disabilities. In Europe, SE shows an incidence rate ranging from about 9 to 40/100,000/y. In adults, mortality of patients with SE is ~30%. To date, etiology, duration, the presence of comorbidity, the level of consciousness, semiology and age are the main clinical predictors of the SE outcome. In patients with SE, mortality reaches up to 30% in adults. Outcomes in refractory SE is worse, with mortality reaching up to 39%. Multiple factors have been reported as important determinants of poor outcome and mortality including: etiology, comorbidities, older age, ethnicity, semeiology, duration, EEG pattern and time to treatment [11].

This study examines the case of a 45-year-old patient with drug-resistant epilepsy, managed through callosotomy due to treatment resistance. After various unsuccessful conservative treatments, including multiple antiepileptic drug trials and intensive care interventions, he underwent corpus callosotomy. The procedure resulted in a significant reduction in seizure frequency and an improvement in the quality of life. This case highlights the importance of considering surgical options, such as corpus callosotomy, for patients with refractory status epilepticus when standard medical therapies have failed.

Clinical Case

A 45-year-old male was admitted to the *Epilepsy Monitoring Unit* (EMU) due to recurrent tonic and tonic-clonic seizures. Epilepsy was diagnosed in his early childhood, and, despite treatment with various antiepileptic drugs and their combinations, seizures persisted multiple times per day, significantly impairing his quality of life. Over the years, multiple ASMs – including *Levetiracetam* (3000 mg/day), *Valproate* (2000 mg/day), *Lamotrigine* (400 mg/day), *Topiramate* (400 mg/day), *Sultiam* (400 mg/day), and *Clonazepam* (4 mg/day), but none provided adequate seizure control. MRI scan showed no obvious focal abnormalities that could be surgically removed, but genetic analysis detected a deletion of chromosome 16p12.2, suggesting that the patient had inherited drug-resistant epilepsy.

On admission, the patient presented with uncontrolled seizures, requiring intensive care management. Despite aggressive treatment – including *Midazolam* and ketogenic diet – seizures persisted, and continuous EEG monitoring showed repeated generalized epileptic activity. Following 39 days of unsuccessful medical management, a multidisciplinary team of epileptologists recommended corpus callosotomy as a last-resort intervention.

The surgery proceeded without complications, and seizure frequency was significantly reduced in the first few weeks after the surgery, but focal motor seizures still persisted. Initially, confusion and speech difficulties were present, but improved over time. He needed a comprehensive postoperative rehabilitation plan. Upon arrival at the rehabilitation center, he presented with severe quadriplegia affecting the lower extremities more profoundly (MRC score: 3/5 upper limbs, 2/5 lower limbs, with distal hemiplegia). He was completely dependent on caregivers and needed assistance with all daily activities. Postoperative medication included *Levetiracetam* (2000 mg twice daily), *Valproate* (500 mg twice daily), *Lamotrigine* (75 mg twice daily, later increased to 150 mg/day), *Topiramate* (150 mg in the morning and 175 mg at night, later adjusted to 150 mg twice daily), *Clonazepam* (2 mg twice daily), *Metoprolol* (50 mg twice daily, then adjusted to *Metoprolol* 25 mg and *Ibabradine* 5 mg twice daily), *Tiogamma* (600 mg/day), *Flaxiparin* (0.3 mL subcutaneously twice daily). Due to persistent dysphagia, the patient initially required enteral nutrition with *Nutrisone* (1000 mL/day), *Nutri-Drink* and *Protiphar* three times daily.

The patient's rehabilitation focused on restoring mobility and communication. Initially, the patient was unable to stand or move on his own, but gradually became able to sit upright and turn over with minimal support. As treatment progressed, he became capable of standing with assistance and walk short distances with a walker. Contractures in both knee joints were managed with intensive physiotherapy and vitamin B supplementation to aid neuromuscular recovery. Speech therapy played an important role in improving his communication skills. Initially, he could only utter one word, but, by the end of his rehabilitation, he was already able to form short sentences, and successfully transitioned from enteral nutrition to a pureed diet.

The treatment plan continued to be adjusted throughout his recovery. Tachycardia was thought to manifest due to poor condition and anemia and was managed with *Metoprolol* and *Iverbradine*. *Metoclopramide* (5 mg before meals) and *Pyridostigmine* (30 mg three times daily) were administered as digestive support. Infection at the tracheostomy site was treated with *Oxacillin* (2 g four times daily). Urinary incontinence remained a problem, but removal of the Foley catheter enabled spontaneous voiding.

At the end of rehabilitation, the seizure frequency was reduced by about 80%, and both the number of hospitalizations and the caregiver's workload were significantly reduced. He continued to need assistance with dressing and transfers, but regained partial independence in daily

tasks such as eating and personal care. His overall quality of life improved significantly, although language impairment and occasional seizures persist.

This case highlights the value of encephalotomy as an effective palliative option for patients with drug-resistant epilepsy. A multidisciplinary approach integrating intensive care, surgical expertise and long-term rehabilitation has proven beneficial in achieving meaningful functional improvement. Although it does not serve as a cure, the procedure significantly reduces the seizure burden and increases the patient's autonomy, emphasizing the need for a comprehensive and collaborative strategy in the management of complex epilepsy cases.

Discussion and Literature Review

The Role of Corpus Callosotomy in the Treatment of Drug-Resistant Epilepsy

Corpus callosotomy is a well-established palliative procedure in selected patients with *Drug-Resistant Epilepsy* (DRE). It has a beneficial role in ameliorating generalized seizures, mainly drop attacks. Once associated with a high risk for morbidity and mortality, microsurgical techniques and surgery limited to the anterior region of the callosum have greatly diminished complications of corpus callosotomy surgery [12, 13]. Corpus callosum is the largest commissure of the brain which connects the two hemispheres, and many studies have shown that seizures utilize it for their spread to the contralateral hemisphere. Oligodendroglioma lesions that are directly connected to the genu of corpus callosum have been shown to be significantly more likely to cause generalized tonic-clonic seizures than lesions in other brain regions, whereas no correlation was observed between the tumor size and the generalized seizure frequency. A corpus callosotomy study indicated that seizures were reduced by 50% in 79% of patients who underwent callosotomy, whereas, in another study, two-thirds of patients experienced total cessation of generalized tonic-clonic seizures and drop attacks [14].

When evaluating patients for possible callosotomy, a number of factors must be considered. Medical intractability must be confirmed with failure of multiple medications, and, typically, seizures should be of the type that can produce bodily injury from falls. The impact of seizures on a patient's life must be assessed; the effect of seizures on the family and caregivers may also be considered. Callosotomy is rarely curative, and seizures usually persist to some extent after the operation. How a potential reduction in the seizure frequency or intensity or the elimination of certain seizure types would affect the patient and the family must be addressed before the operation. The goals and expectations, as well as the uncertainties, must be discussed with the patient and the family. If there is a possibility that a resective epilepsy surgery might eliminate seizures without producing unacceptable neurological deficits, then this should be considered first. Finally, the presence of a progressive neurological or medical disease and the presence of severe psychiatric problems might be absolute or relative contraindications to any epilepsy surgery, depending on the specific circumstances of each patient [15].

Post-Surgery Outcomes

The overall seizure-free rate after corpus callosotomy (19%) is, as expected, much lower than focal resection for epilepsy, given that this is a palliative surgical procedure. For example, results from a systematic review and meta-analysis of epilepsy surgery demonstrated that 66% of patients undergoing temporal resection were seizure-free postoperatively, whereas approximately 50% of individuals achieve seizure freedom following extratemporal resection for epilepsy. However, the primary goal of corpus callosotomy is often to alleviate drop attacks or atonic seizures,

and thereby prevent falls, and this favorable outcome was observed in 55.3% of cases. Thus, corpus callosotomy should be considered for patients with substantial disability from attacks who are not favorable candidates for focal resection [16].

Advances in Surgical Techniques

Magnetic Resonance Imaging guided Laser Interstitial Thermal Therapy (MRIgLITT) is a promising treatment for drug-resistant epilepsy (DRE) and an alternative to open surgery. However, the relationship between clinical and radiological factors and postoperative outcomes is unclear [17].

A retrospective single-center analysis was performed. Postoperative follow-up averaged 33 months. Among HS patients, 71.42% achieved Engel I, and 21.43% reached Engel II. In HH, 85.7% initially became gelastic seizure-free, with complete freedom after additional treatment. Engel I outcomes were 28.6%, while 57.2% showed a significant improvement (Engel I + II). FCD patients had a 66.6% Engel I success rate. One PVH patient became seizure-free, while the TSC patient was Engel III at the latest follow-up. RCI analysis showed that 71.44% of patients experienced cognitive stability (RCI > −1.64) or improvement (RCI > 1.64) at one-year post-procedure [17].

In conclusion, MRIgLITT is a safe, minimally invasive alternative for epilepsy surgery, offering a quicker recovery and showing better performance in terms of preserving the cognitive function. It is particularly effective for deep or complex epileptic foci, as well as for patients who might refuse open surgery [17].

Prognostic Factors in Callosotomy

Many researchers have investigated which clinical features predict success after callosotomy. However, differences in methodology, including the patient selection (e.g., different age groups, different spectrum of cerebral disorders) have sometimes resulted in conflicting and controversial results. Development of a reliable prognostic and outcome scoring system may allow physicians to more carefully select the patients for callosotomy. Some prognostic factors for success after callosotomy are summarized below:

- Seizure type. Drop attacks, atypical absences, and GTC seizures respond relatively well; myoclonic seizures respond poorly [15].
- Age. A younger age at the time of surgery is a predictive factor for improvement in the daily function, family satisfaction, psychosocial adjustment, and the overall quality of life. Adverse effects of callosotomy are less severe in children [15].
- Ictal EEG. Generalized slow spike-wave, electrodecrement, or nonevolving low-amplitude fast activity is associated with a better outcome [15].
- Interictal EEG. Slow spike-wave activity has been associated with a better outcome, and bilateral independent spikes have been associated with a poor outcome [15].
- Postoperative EEG. Diminishment of synchrony of the epileptic discharge is a good prognostic sign [15].

Future Directions in Epilepsy Surgery

Brain stimulation has recently become available as an alternative treatment option to reduce symptomatic seizures in short- and long-term follow-up studies. *Responsive Neurostimulation* (RNS) is a treatment for medically refractory focal epilepsy which involves delivering electrical stimulation to the seizure focus upon detection of abnormal electrocorticographic activity. RNS was designed to detect and terminate seizures shortly after they have occurred. In contrast to

DBS, RNS has a closed-loop design that uses real-time analysis of multi-channel electrocorticography recordings to trigger a stimulus pulse when seizure-like activity has been detected. However, the underlying mechanism that drives the therapeutic effect of responsive neural stimulation remains unclear. While the device was designed to acutely terminate detected seizures, the current methodology typically involves tuning the detection algorithm to have a high sensitivity, such that between 600 and 2000 stimulations are typically triggered per day, even though patients in the cohort typically had less than one clinical seizure per day. This means that the majority of stimulations may be triggered by false positive detections, including interictal spikes, non-epileptiform EEG, and artifacts. Therefore, RNS effectively may be using a combination of both open-loop (false detections) and closed-loop stimulations to produce a combination of seizure suppressive and seizure termination effects; how each of these effects contributes to the outcome remains unknown. Responsive neurostimulator implantation achieved 50% or more seizure reduction in approximately 80% of patients. Even in those patients who did not achieve seizure freedom, a significant improvement in the seizure duration, severity, or postictal state was reported in more than 68% of cases. Infection (7%) was the most common complication [18].

Conclusion

Corpus callosotomy remains a valuable palliative option for patients with drug-resistant generalized epilepsy. Although it does not cure epilepsy, it significantly reduces the burden of epileptic seizures, increases the functional independence, and improves the overall quality of life. Multidisciplinary management involving neurologists, neurosurgeons and rehabilitation specialists is essential to optimize postoperative outcomes. As surgical techniques continue to improve, further research into minimally invasive surgery and neuromodulatory therapies will lead to improved epilepsy treatment strategies.

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