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Review Article

Surgical Treatment for Refractory Epilepsy: Review of Patient Evaluation and Surgical Options

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Treatment of epilepsy often imposes an exposure to various antiepileptic drugs and requires long-term commitment and compliance from the patient. Although many new medications are now available for the treatment of epilepsy, approximately 30% of epilepsy patients still experience recurrent seizures and many experience undesirable side effects. Treatment of epilepsy requires a multidisciplinary approach. For those patients with medically refractory seizures, surgical treatment has increased in prevalence as techniques and devices improve. With increased utilization, proper patient selection has become crucial in evaluating appropriateness of surgical intervention. Epilepsy syndromes in which surgery has shown to be effective include mesial temporal sclerosis, cortical dysplasia, many pediatric epilepsy syndromes, and vascular malformations. Monitoring in an epilepsy monitoring unit with continuous scalp or intracranial EEG is an important step in localization of seizure focus. MRI is the standard imaging technique for evaluation of anatomy. However, other imaging studies including SPECT and PET have become more widespread, often offering increased diagnostic value in select situations. In addition, as an alternative or adjunct to surgical resection, implantable devices such as vagus nerve stimulators, deep brain stimulators, and direct brain stimulators could be useful in seizure treatment.

1. Introduction

Epilepsy is one of the most common neurological disorders affecting up to two percent of the population worldwide, and almost two million people in the United States alone [1]. Treatment of epilepsy often imposes an exposure to various antiepileptic drugs (AEDs) and requires long-term commitment and compliance from the patient. Despite the advent of new AEDs over the past 15 years, approximately 30% of epilepsy patients experience recurrent seizures [2, 3] and many experience undesirable side effects. Therefore, there are still unmet needs for the treatment of epilepsy by AEDs alone, and epilepsy surgery can provide significant reduction or complete control of seizures for those patients with medically refractory epilepsy. Prior to providing epilepsy surgery for patients, clinicians should be able to answer the following two questions. (1) Is seizure focus identified with an acceptable confidence? (2) Is it safe to remove the known seizure focus in terms of neurological outcome? Therefore, it is important to comprehensively evaluate the patient whether they meet specific selection criteria which are discussed in more detail in the following chapters.

Epilepsy surgery dates back to ancient times, when trephination, or the creation of burr holes in one's skull, was considered a potential treatment for seizures [4]. The advent of modern surgical treatment of epilepsy can be traced to 1886 with Sir Victor Horsley in London, England. Sir Horsley treated a patient with epilepsy who had multiple seizures a day. The man had suffered a head injury, resulting in a frontal depression fracture of the skull prior to seizure onset. Horsley postulated that resection of the cortical scar from the injury site would control the seizures. Horsley performed a surgical resection of the tissue, and the patient's seizures resolved. Since then, surgical techniques for treatment of seizures have evolved dramatically, and screening techniques for evaluating appropriate patients for surgical intervention

have become increasingly discriminating. This paper will review current indications for surgical treatment of epilepsy, patient selection, epilepsy syndromes that are amendable to surgery, and the direction of potential treatments in the future including implantable electronic devices.

2. Patient Evaluation

2.1. Electroencephalogram (EEG) Monitoring. Continuous EEG and video monitoring in an epilepsy monitoring unit (EMU) is a necessary step for almost all epilepsy patients considering surgical intervention. Ideally, a significant number of seizures are captured in the safest manner possible. If the patient has very medically refractory epilepsy and is having multiple seizures a day, AEDs generally should be continued at home doses. However, if the patient has fewer seizures, the EMU physician often will decrease or stop the AEDs during the hospitalization in order to allow seizure to occur in a controlled fashion. Gathering adequate ictal and interictal EEG data is paramount in facilitating localization of seizures in localization-related epilepsy. The epileptologists are able to evaluate if there appears to be one focus, many foci, or a general onset. If the focus appears to be in an eloquent area of the brain, if there is any ambiguity of the presence of a single focus or multiple foci, or if the lesion is not seen on imaging, one should consider invasive monitoring by temporarily placing subdural and/or intraparenchymal depth electrodes. These procedures, while more invasive, oftentimes increase sensitivity to definitively localize seizure onset. However, invasive monitoring may pose significant risks to patients such as infection, epidural hematoma, infarction, headaches, and increased intracranial pressure. These risks can be higher when subdural grid electrodes are utilized. A recent paper reviewed 198 cases [5] and found significant complications in cases with subdural grid electrodes as follows: infection (12.1%), transient neurologic deficit (11.1%), epidural hematoma (2.5%), increased intracranial pressure (2.5%), and infarction (1.5%). Increased complication rates were observed with left-sided grid insertion, longer monitoring period, and a greater number of electrodes (larger grid). However, they also found that complication rates had significantly decreased over years due to improvements in grid technology, surgical technique, and postoperative care [5].

Bilateral depth electrode placement in the amygdalohippocampal region is a common target for depth electrode placement. This can distinguish mesial temporal lobe epilepsy from lateral temporal lobe epilepsy, as well as determine lateralization in otherwise ambiguous cases [6] (Figure 1). Subdural grid electrodes more precisely localized cortical lesions, such as in cortical dysplasia, especially in cases of a normal MRI [7]. Risks of these procedures are minor, as most can be done with small burr holes through the skull. The risks include general risks of intracranial surgery as well as potential breakage and retention of electrodes.

2.2. Neuroimaging Techniques. When considering surgical treatment for a medically refractory epilepsy patient, there

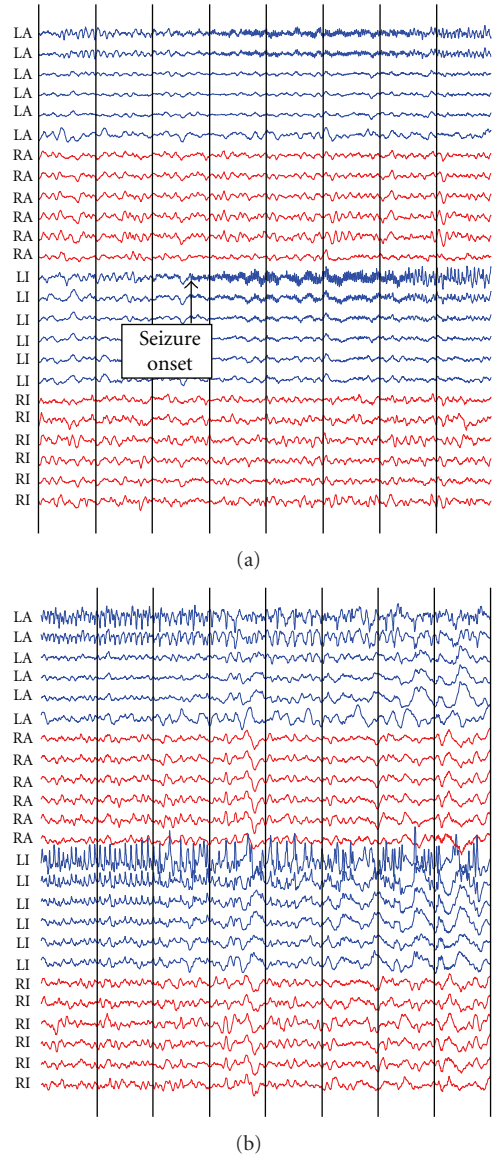

Figure 1: (a) Invasive monitoring with depth electrodes reveals initial low-voltage fast discharges over the LA1-2 and LH1-2 electrodes (left amygdalohippocampal regions). (b) Further ictal progression is seen over the same area as well as diffuse slowing (left > right) within 10 seconds of the seizure onset.

are a number of potential imaging modalities to choose from. It is currently standard to obtain an MRI of the brain to evaluate for a structural lesion. However, conventional MRI scans may be inadequate epilepsy evaluation since many of the findings are subtle and easily missed. Routine MRI consists of a short scan time, 3- to 5-mm thick slices with an interslice gap of 2-3 mm. The recommended epilepsy protocol MRI at 1.5T or 3.0T includes the entire brain from nasion to inion, T1-weighted magnetization prepared rapid gradient echo (MPRAGE), or spoiled gradient recalled (SPGR) images 1.5-mm slice thickness with no intervening gap obtained in the coronal oblique plane, coronal, and axial FLAIR sequences with 2- to 3-mm slice thickness and

0- to 1-mm interslice gap. Gadolinium is not often required unless a patient has new-onset epilepsy which could be due to tumor, vascular lesions, or neurocutaneous syndromes. If standard MRI shows a lesion and the EEG localizes the lesion to the same area, patients generally do not need further imaging. If there appears to be multiple foci, bilateral foci such as in bilateral MTS, a lesion on MRI with a nonlocalizing EEG, or no lesion on MRI with localization on EEG, other imaging studies can potentially provide further localization [8].

Single photon emission computed tomography (SPECT) imaging, especially during the ictal or immediately postictal phases, demonstrates areas of acute ictal hyperperfusion. Research has shown this imaging modality to be most useful in temporal lobe seizures [9, 10]. It is important to note that the hyperperfusion seen on SPECT after a seizure involves all areas that are ultimately involved in the seizure, not just the seizure focus. As it is often difficult to time the imaging correctly, the study can fail to localize the focus of a seizure with a large cortical spread. It is also not useful in patients with suspected multiple or bilateral seizure foci as it will only highlight the seizure focus that is active at the time of the particular seizure studied.

Fluorodeoxyglucose positron emission tomography (FDG-PET) imaging is also a useful tool in evaluating for seizure foci, especially in cases of negative or ambiguous MRI results. This technique shows areas of hypometabolism and hypermetabolism of glucose within the brain. Seizure foci typically show interictal glucose hypometabolism on FDG-PET (Figure 2). It is a more sensitive test in temporal onset epilepsy than in frontal lobe epilepsy. Studies have shown good outcomes in resection procedures based on concordant FDG-PET and EEG studies. 11C-flumazenil-PET (FMZ-PET) is being studied as another marker to localize seizure foci. The labeled flumazenil binds GABA receptors within the brain. There is a distinct lack of 11C-flumazenil signal in areas of known seizure onset in these studies. The difficulty associated with this study is the short half-life of FMZ, which limits its use to certain facilities that can create and administer it in quick succession [8].

3. Common Epilepsy Syndromes for Surgical Intervention

3.1. Mesial Temporal Lobe Epilepsy. Mesial temporal sclerosis (MTS) is a common cause of localization-related epilepsy that has been shown to be very amenable to surgery in well-selected cases. The exact cause of MTS is unknown. The onset in the majority of these patients is in childhood or during adolescence, and approximately one third of patients have a history of febrile seizures as children. In many cases, there is good control of the seizures with a single AED for years, which overtime becomes medically intractable.

MRI is now very sensitive in showing mesial temporal sclerosis (MTS). Evaluation of MTS or other hippocampal abnormalities is dependent on the radiologist's experience. Having an MRI reviewed by a neuroradiologist in these cases can be very helpful. In patients with MTS, general review of the MRI will show one or both hippocampi are small in size with a hyperintensity on T2-weighted and FLAIR series. In addition, spoiled-gradient recall sequences (SPGR) show hippocampal atrophy as well [8, 11, 12] (Figure 3). Other features may be seen, including ipsilateral temporal horn dilation, loss of normal internal architecture of the hippocampus, and nearby structural atrophy, such as in the ipsilateral temporal lobe or fornix [13, 14]. Hippocampal volumetry can be performed by a skilled radiologist and gives objective, reproducible measurements for evaluation of hippocampal atrophy. This is particularly useful in evaluation of bilateral hippocampal sclerosis as these cases have no "normal" hippocampus for comparison. Automated hippocampal volumetry is being explored, which will make this imaging modality more widely available and standardized [12]. Pathological analysis of the resected area in MTS patients shows abnormalities that correlate to the imaging studies, including neuronal loss, atrophy, and gliosis [15].

Recent data suggest that temporal lobe epilepsy (TLE), especially in patients with medically refractory seizures, may be a progressive, degenerative process. Berhnardt et al. showed more marked cortical thinning in patients with TLE who had a prolonged history of seizures. The thinning occurred mainly in the ipsilateral mesial, frontocentral, and parietal lobes [14]. This suggests not only that intractable epilepsy may damage cortex, but that the damage may extend significantly beyond the lesion area. This finding underscores the importance of early surgical intervention.

Initially, anteriotemporal lobectomies were performed for MTS. Since the early 1990s, selective amygdalohippocampectomies (AH) technique was introduced and applied to patients with MTS. Three approaches are for AH have been well described: transsylvian, transtemporal, and subtemporal. A recent study by Little et al. demonstrated that the subtemporal approach can be performed through a small "keyhole" technique and avoid damaging surrounding areas of the temporal lobe [16]. This avoids disruption of the frontotemporal white matter pathways in the temporal stem and the visual fibers near the roof of the temporal horn that may be sacrificed in other techniques (Figure 4).

Prior to temporal lobe surgery, lateralization of language and memory function dominance should be evaluated preoperatively by Wada test and comprehensive neuropsychological testing. Although language impairment is extremely rare as postoperative complications, memory decline and visual field defect involving the contralateral upper quadrant may occur in patients after anteriotemporal lobectomy or AH.

Radiosurgery is also being explored as a treatment for epilepsy from mesial temporal lobe sclerosis. Barbaro et al. performed a prospective trial using Gamma Knife radiation with thirty subjects [17]. They had two treatment groups: low-dose and high-dose radiation. Both groups showed overall decrease in seizures, with the high-dose group having significant seizure freedom at 3 months. Combining both groups, seizure freedom was obtained in 67% of treated patients between 24 and 36 months postradiosurgery. Side effects were significant, with 53% of the low-dose group, and

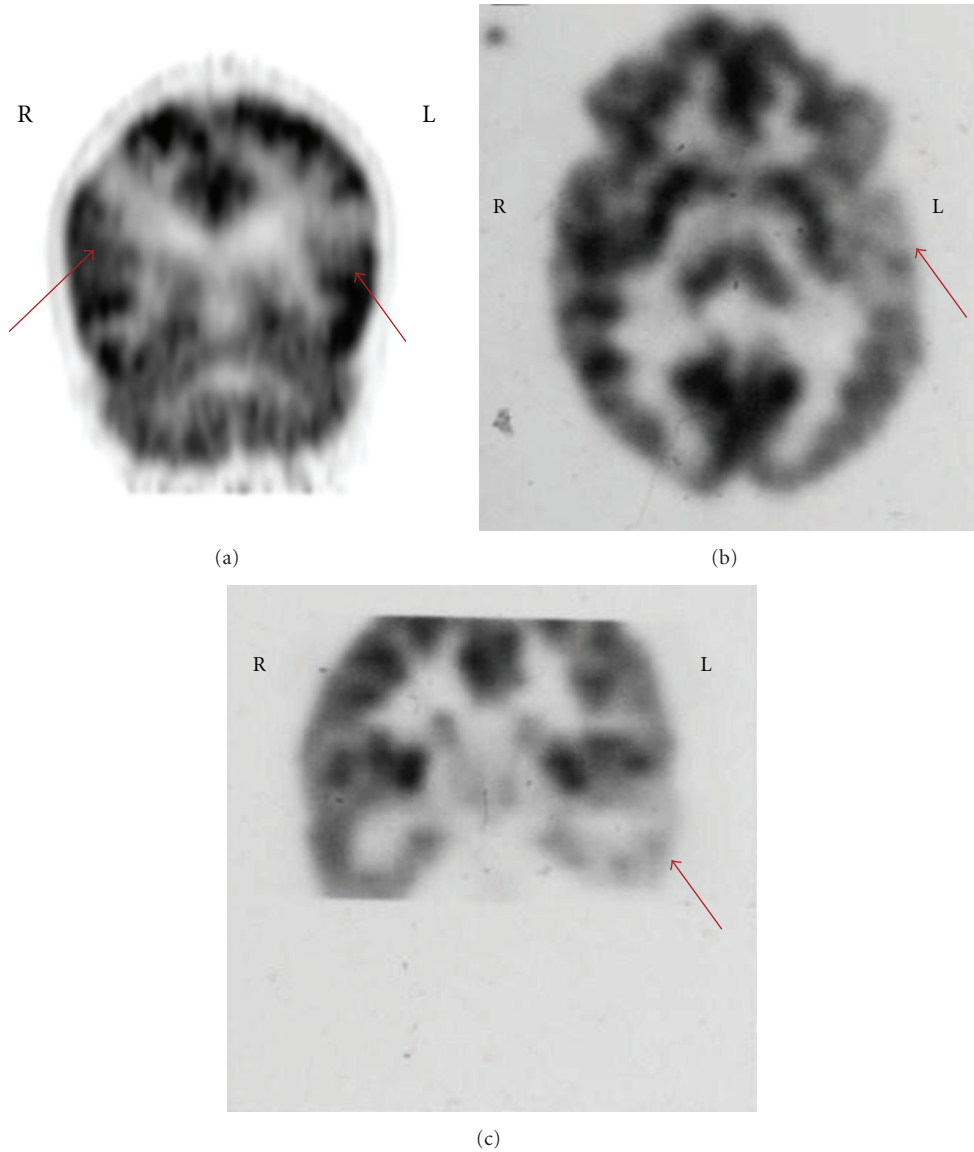

Figure 2: (a) Coronal FDG-PET scan showing bilateral parietal areas of hypometabolism in a patient with tuberous sclerosis. (b) Axial FDG-PET scan showing left temporal hypometabolism in a different pateint. (c) Coronal FDG-PET scan showing the same patient in b.

61% of the high-dose group receiving steroids for temporary symptoms of headache and edema. One patient required a temporal lobectomy for postradiation edema. Further investigation is needed to fully elucidate the potential role of radiotherapy in the treatment and management of epilepsy.

3.2. CNS Neoplasms. Intracranial tumors have long been recognized as a cause of epilepsy. Tumor type and location both play a role in determining the probability of seizure development. Tumors that cause epilepsy without other significant associated symptoms tend to be slow growing. Typically, neoplasms cause seizures by gradually infiltrating and irritating surrounding cortex. Breakdown of the blood brain barrier by the tumor may cause a change in the chemical composition of fluid surround cells, causing a disruption in homeostasis and increased likelihood of seizures [18]. Lesions most likely to cause epilepsy include low-grade astrocytomas, oligodendrogliomas, gangliogliomas and meningiomas in adults, and dysembroblastic neuroepithelial tumors (DNETs) in children. Gangliogliomas and DNETs are unique in that they are glioneuronal tumors and likely have intrinsic epileptogenic foci. While high-grade gliomas can present with seizures, those that do cause seizures tend to be smaller than typical high-grade gliomas that present with other symptoms such as headaches and hydrocephalus. In addition, brain metastases from primary cancers including melanoma can lead to seizure development. As for location, cortical tumors are much more likely to cause seizures than tumors located deeper within the brain [19].

Surgical treatment involves as complete a resection as possible. Often even with full resection, treatment with AEDs

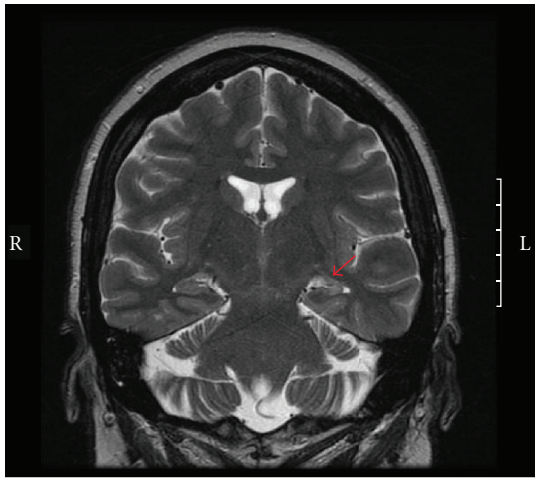

Figure 3: High-resolution (3T) coronal MRI T2 weighted sequence showing signal hyperintensity and volume atrophy in the left hippocampus (arrow) compared to the right, suggesting left hippocampal sclerosis.

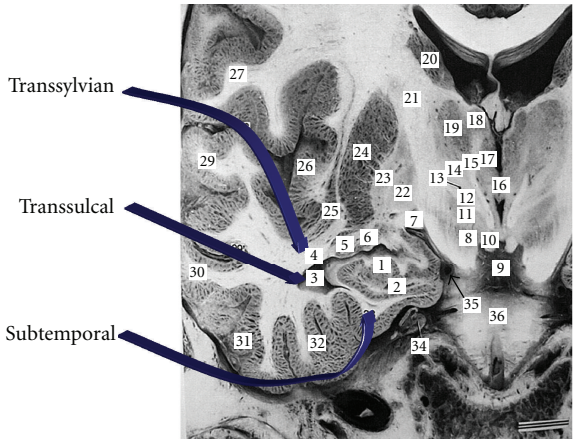

Figure 4: Pathological specimen demonstrating three different approaches for selective amygdalohippocampectomy.

will need to be continued for years afterwards and occasionally indefinitely. Prolonged AEDs treatment postresection is even more likely if the tumor is incompletely removed or involves a high-grade neoplasm, as these lesions are likely to recur. In addition, the surrounding cortex may still have a propensity to cause seizures as epileptogenic focus even after the tumor itself is resected.

3.3. Focal Cortical Dysplasia. Focal cortical dysplasias are the cause of approximately ten percent of intractable epilepsy [20]. These can be difficult to see on standard MRI, so performing an MRI with previously discussed epilepsy protocol is important in attempting to locate lesions (Figure 5). Recently, PET and image postprocessing techniques enabled the identification of subtle dysplastic lesions in patients with "cryptogenic" epilepsy [21]. Cortical dysplasias are classified to minor malformations of cortical developments (mMCDs) and more severe focal cortical dysplasias (FCDs) based on histopathology, clinical, and imaging findings [22, 23]. Depending on the derangements of underlying focal cortical architecture, mMCDs are further divided into type 1 (ectopic neurons involving or adjacent to cortical layer 1) and type 2 (microscopic neuronal heterotopias outside layer 1). FCDs are also further divided into Type I (without dysmorphic neurons or balloon cells) and Type II (with dysmorphic neurons). In addition, Type I FCDs are further classified into Type 1A for those with isolated architectural abnormalities only, such as laminar or columnar disorganization, and Type IB for those with architectural abnormalities and giant or immature neurons. Type II FCDs also further classified into is Type IIA for those with dysmorphic cells that are not balloon cells and Type IIB (with characteristic balloon cells). Type III FCDs are associated with other clinically relevant abnormalities. These are IIIa (with hippocampal sclerosis), IIIb (adjacent to glial or glioneuronal tumors), IIIc (adjacent to a vascular malformation), and IIId (associated with other early-in-life cerebral abnormalities). Although these classifications are mainly based on visual findings, they may provide useful insight in terms of surgical outcome as well. Complete resection of FCDs appears to be the key to have better postsurgical outcome: In a study by Krsek et al., 70% of patients with focal cortical dysplasia (FCD) were seizure-free with complete resection of the area compared with 22% of those who could only have incomplete resections [24]. Other predictors of surgical outcome continue to be debated, with conflicting evidence on the prognostic value of histological type of FCD, age of patient, and location of the lesion [25–27].

If the EEG is suggestive of a focal lesion, but the standard MRI does not show a lesion, further imaging with PET, SPECT, or fMRI, as described above, can be useful. A study by Lee et al. showed that 73% of the patients in their series with localization-related epilepsy that was nonlesional on MRI had histology consistent with FCD. Of those patients, almost half were seizure-free at 2-year followup [27]. The question remains regarding how extensive of cortical resection should be performed to ensure the best surgical outcome. At times, electrocorticography is performed during the operation to detect interictal epileptiform discharges in order to sufficiently remove potential epileptogenic tissues.

Multiple subpial transections (MSTs) with or without resection is also an option, especially in areas of eloquent brain function to minimize the adverse functional outcome. In adults, awake craniotomies and resections with electrocorticography can be performed to minimize damage to eloquent areas of the cortex. This requires extensive evaluation and preparation of the patient by the neuropsychology team prior to the surgery [26].

Schizencephaly is a rare congenital condition that can lead to intractable epilepsy caused by abnormal neuronal migration. A cleft is formed by the abnormal migration that is lined by a poorly structured polymicrogyric cortex, and it is this cortex itself that is epileptogenic. The lesion is often large and communicates with the lateral ventricle; however smaller schizencephalies do occur. Some small studies have shown good results with focal resection of a small schizencephaly for seizure control. In situations with

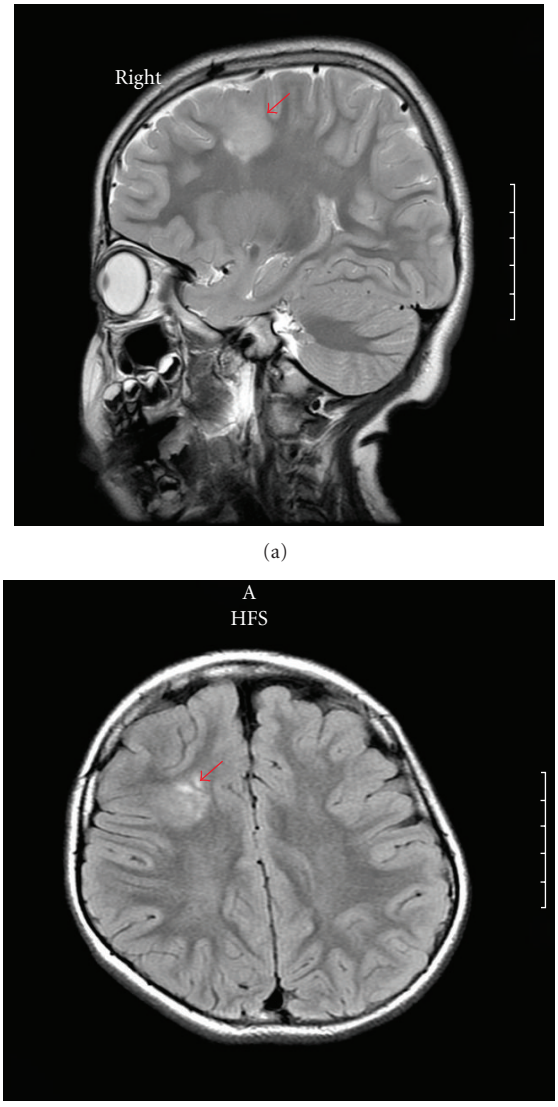

Figure 5: T2 weighted brain MRI showing an area of cortical dysplasia (arrow).

a larger schizencephaly, a partial or complete lobar resection has been performed with good seizure control as well [28]. As these areas are often located near eloquent areas of cortex, the potential benefit must be weighed against the risk.

3.4. Vascular Malformations. Arterial venous malformations (AVMs) and cavernous malformations (CMs) frequently present as seizures. Seizures, without evidence of hemorrhage, are the presenting symptom in up to half of all AVMs. If the AVM does hemorrhage, seizure is often one of the symptoms along with headache, focal neurological signs, and signs of increased intracranial pressure. The risk for bleeding in AVMs is high—approximately 3% per year, so identification and treatment of the lesion is of paramount importance [29]. Treatment options include open surgical resection, embolization, and gamma knife radiation.

In one study, 40% of patients who suffered seizures from a cavernous malformation had medically refractory epilepsy. Resection of the cavernous malformation can be curative. It appears that removing the hemosiderin-stained cortex surrounding the lesion does not improve outcome. Risk factors for poor outcome include subtotal resection of the CM, multiple lesions, or the presence of other possible epileptogenic foci, such as MTS. AEDs are typically continued one to two years postoperatively. If the patient has not experienced any further seizures, a slow taper off the AED has a good likelihood of being successful [30].

3.5. Other Specific Pediatric Epilepsy Syndromes. Symptomatic epilepsies of childhood, such as Lennox-Gastaut syndrome, West syndrome, and other epileptic encephalopathies, can be extremely difficult to treat medically and can result in devastatingly frequent and serious seizures. Atonic seizures, or drop attacks, can occur in these types of epilepsy and can lead to serious secondary injuries, including head injury. If the seizures are considerably hazardous, the risks and benefits of epilepsy surgery should be addressed. One choice is implantation of a vagus nerve stimulator (VNS), as described below. Another option for prevention of drop attacks is a corpus callosotomy. While this surgery has fallen out of favor recently, it is still a good option for uncontrolled atonic seizures as well as tonic seizures [31]. Techniques include the traditional open surgery with partial or full resection, as well as radiosurgery [32]. Currently, surgeons commonly perform a partial callosotomy as an initial surgery. If this does not adequately control the seizures, a full callosotomy can be performed in a second surgery. This stepwise approach is taken because a full callosotomy has a higher potential for functional morbidity.

Hemispherectomy is another option in certain refractory epilepsy syndromes, especially Rasmussen's encephalitis. Rasmussen's encephalitis is a rare syndrome of partial seizures that are typically medically resistant, decline in cognitive function, hemiparesis, and atrophy of one cortex on imaging and pathologic studies. Epilepsia partialis continua occurs frequently with this syndrome, and although medical treatment is often attempted, many cases are responsive only to a hemispherectomy. In one study with 111 subjects, 65% were seizure-free, 21% had occasional seizures, and 14% had intractable seizures after hemispherectomy. Eighty percent were taking one anticonvulsant or none at all. Eighty-nine percent of young children studied were able to walk without assistance on followup [33].

Hypothalamic hamartomas (HH) are uncommon midline lesions associated with gelastic epilepsy and precocious puberty (Figure 6). Gelastic seizures are brief, stereotyped episodes of sudden laughter at random, often inappropriate, times. These seizures can progress to become secondarily generalized tonic-clonic seizures and drop seizures. Epilepsy from HH is often very hard to control with antiepileptic medications. Behavioral issues and cognitive deterioration can develop if the seizures are not controlled quickly. Options for surgical treatment are full resection, partial resection, gamma knife radiosurgery, and endoscopic disconnection [34]. While resection is the traditional approach

to hypothalamic hamartomas and full resection is the goal for best seizure control, other techniques have showed promising results [35]. Shim et al. showed success with an endoscopic disconnection technique. In eleven patients with a diagnosis of HH based on clinical and MRI data treated with endoscopic disconnection, eight were seizure free on six-month followup [36]. For HH patients, gamma knife radiosurgery is also an option for poor surgical candidates. Indications for gamma knife include tumor located deep within the hypothalamus (type I), and type III tumors which are near the mamillary bodies and fornix. Régis et al., in a prospective study, showed an outcome of 60% good or excellent improvement in seizures 3 years after radiation [37]. No neurological deficits were noted from the radiosurgery. There is a delay in seizure improvement using this technique, which is problematic when patients are experiencing significant seizure frequency and behavioral difficulties from the lesion.

Tuberous Sclerosis Complex (TSC) is a syndrome that is associated with severe epilepsy that is often medically refractory. Molecular studies indicate that neuron groups within cortical tubers can be intrinsically epileptogenic. Detailed screening and evaluation are important in planning surgery as 90% of patients with TSC have at least one region showing interictal epileptic activity on routine EEG. Often, there are only one or two foci that produce clinical seizures despite numerous intracranial tubers [38, 39]. Comprehensive evaluation includes continuous EEG and video monitoring in an epilepsy monitoring unit and neuroimaging. MRI should be performed, and PET scan is seriously considered for further localization. Favorable outcomes have been associated with concordant MRI and EEG findings: a single epileptogenic focus, a focus in noneloquent cortex, and normal neurological development at the time of surgery. Seizure freedom is as high as 90% in candidates with those features. Surgery has also been performed on patients with resection of two seizure foci that have good MRI and EEG correlates [40]. Many of these surgeries have good outcomes by improving seizure control and improving overall quality of life. Jansen et al. performed a systemic review of surgery for tuberous sclerosis and found that out of 177 patients who had resection of tubers for treatment of epilepsy, seizure freedom was achieved in 101 patients (57%). In addition, thirty-two patients (18%) had a result of seizure frequency which was improved by >90% [41].

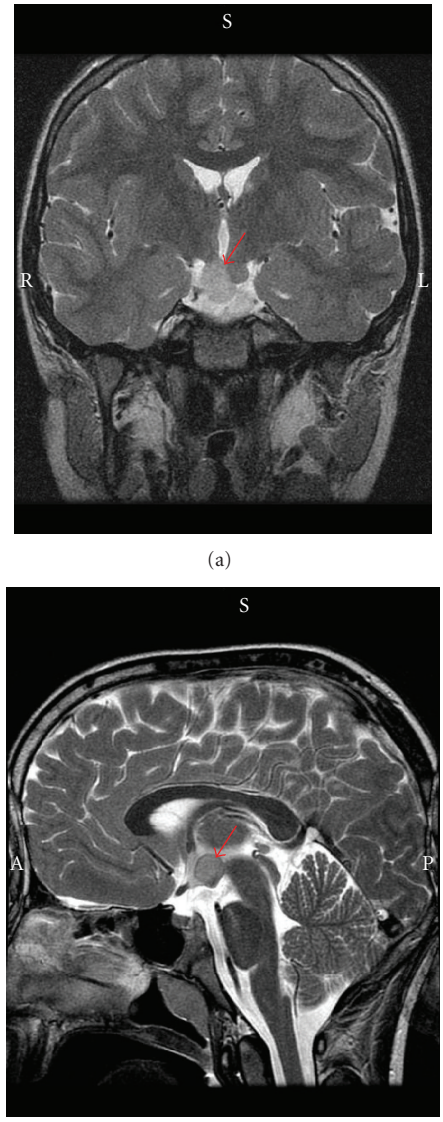

Figure 6: T2 weighted MRI showing a large round midline lesion that is isointense to the grey matter (arrow). Pathological analysis showed the lesion to be a hypothalamic hamartoma.

4. Implantable Devices

4.1. Vagus Nerve Stimulation (VNS). VNS has the most data and has been available for the longest period of time, since the 1990s. It has been shown effective in children and is minimally invasive. A generator is placed subcutaneously, usually in the left chest area, and an electrode is placed with the end wrapping around the ipsilateral vagus nerve, connecting to the generator. The treating physician programs intermittent periods of stimulation into the generator. Voltage and timing of the stimulation can be altered using a wand device connected to a hand-held computer system to optimize individual devices. Large series have shown that approximately 30% to 50% of patients treated with VNS will have a good outcome of greater than 50% reduction in seizures [42, 43]. In one study in children, VNS therapy provided similar seizure reduction for many different types of seizures [44]. Side effects of the stimulation include voice changes (decreased volume or hoarseness), cough, and headache. These can be decreased by changing the parameters of stimulation intensity [42, 43]. Device and lead infections are rare but serious side effects.

4.2. Deep Brain Stimulation (DBS). DBS has proven to be effective for treatment of movement disorders overtime, in particular Parkinson's disease. Areas of stimulation in those disorders are commonly the ventralis intermedius nucleus of the thalamus, the subthalamic nucleus, and the

globus pallidus pars interna [45]. A study by Zumsteg et al. showed evidence that DBS stimulation of the anterior thalamus directly affects the ipsilateral hippocampus and mesial temporal lobe, but not the lateral temporal lobe or the contralateral hemisphere [46]. Previous studies have shown efficacy with this treatment in medically refractory epilepsy, with a rate of seizure reduction of 20–92% [47, 48]. More recently, a randomized, double-blind, multicenter SANTE (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy) trial had been completed [49]. The trial enrolled 110 people with partial-onset seizures. After 25 months, 56% of 110 patients showed a reduction in seizures. The parameters chosen in this study were a stimulation of one minute "on" with five minutes of nonstimulation, or "off," mode. Thalamus is not the only area that has been of interest and other investigators have targeted subthalamic nucleus or cerebellum [50, 51].

Risks in DBS surgery are small but significant and must be considered when being considered for treatment of epilepsy. The most worrisome risk is local hemorrhage in the site of probe placement. Incorrect probe placement is also an issue, especially when targeting very specific areas such as the centromedial thalamus, or more caudal areas such as the subthalamic nucleus. Infection can occur—either intracranial during the surgery or surrounding the device and leads extracranially. Some studies in Parkinson's patients have noted depression or other neuropsychiatric side effects after DBS [52]. There is an overall 1–3% risk of serious side effects from placement of DBS. DBS placement at an institution with a high volume of DBS surgeries minimizes surgical risk and is recommended [49].

4.3. Responsive Direct Brain Stimulation. Recent investigations have begun in a closed-loop circuit for epilepsy management. It is similar to DBS in that implanted electrodes apply electrical stimulation directly to the brain. The areas of stimulation studied at this point are the bilateral anterior thalamus and the hippocampus [53]. In responsive stimulation, an additional, receptive electrode is placed that measures for epileptogenic activity, ideally near the epileptic focus. If epileptogenic discharges are detected, a high-frequency stimulation is sent, theoretically aborting the seizure. Data can be downloaded into a computer via a handheld wand and settings can be adjusted for the receptive and stimulating electrodes. A randomized control trial of the responsive neurostimulator RNS system with 191 subjects is being conducted. Preliminary data suggest that it is effective in reducing the seizure frequency in medically refractory unilateral or bilateral MTS without significant side effects compared to the sham group in the subjects tested over a two-year period [54]. The study was not completed at time of publication of this paper.

5. Conclusion

Surgical treatment of epilepsy is an important consideration for patients with medically intractable epilepsy and epilepsy syndromes with underlying lesions. Localization-related epilepsies that are good candidates for surgery include MTS, FCD, and neoplasms. Surgery should also be considered for certain pediatric epilepsy syndromes, especially when atonic seizures are a safety issue. The implantable devices available currently include VNS, DBS, and yet to be approved responsive direct brain stimulation offer an alternative, palliative approach to treatment of medically refractory epilepsy. In conjunction with careful consideration of risks versus benefits, and comprehensive imaging with evaluation and localization through EMU monitoring, surgical treatment of epilepsy can greatly improve a patient's seizure control and quality of life.

Author Disclosures

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