Surgical Candidate (Skip)

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William O. Tatum and Sanjeet S. Grewal

Case Presentation

A 47-year-old right-handed Indian-American female was self-referred for uncontrolled seizures. She was healthy other than taking antiseizure medication (ASM) for epilepsy. When she was 2 years of age, she experienced a prolonged febrile convulsion lasting 15 min associated with a fever of 103°. At the time she was told "nothing was wrong" and that is was a benign occurrence. She developed normally throughout childhood with above average scholastic achievement. At 11 years of age, she developed her first afebrile seizure which recurred manifest as a staring spell that she referred to as a "petit mal" seizure. Her seizures involved a warning where she would experience an indescribable feeling just prior to a wide-eyed stare, manifest subtle lip smacking, and impaired responsiveness for 45 seconds in duration. Following this she would be sleepy with transient difficulty "getting the words out." She failed five ASM with ongoing seizures and was maintained on lamotrigine and levetiracetam. Several seizures per month occurred with rare injury mostly involving lacerations, abrasions, and contusions of the head. She never experienced a "grand mal" seizure. Her neurological examination was normal. A high-resolution brain MRI with an epilepsy protocol demonstrated left mesial temporal sclerosis (Fig. 41.1a). EEG revealed left anterior temporal interictal epileptiform discharges (Fig. 41.1b**).** A surgical evaluation was recommended to her by her neurologist after she fell down a flight of stairs. Subsequent evaluation included a FDG-PET scan of

W. O. Tatum (✉)
Mayo Clinic, Department of Neurology, Jacksonville, FL, USA
e-mail: tatum.william@mayo.edu

S. S. Grewal
Mayo Clinic, Department of Neurosurgery, Jacksonville, FL, USA
e-mail: Grewal.sanjeet@mayo.edu

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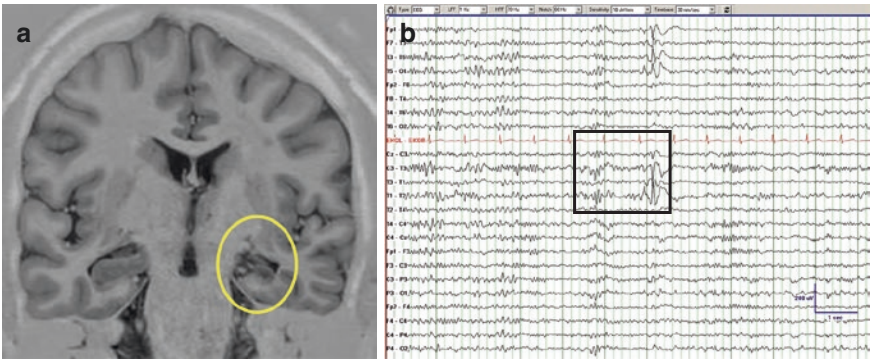

Fig. 41.1 (**a**) Brain MRI with left hippocampal formation atrophy (*yellow circle*) and (**b**) representative interictal EEG showing left temporal spikes (*box*)

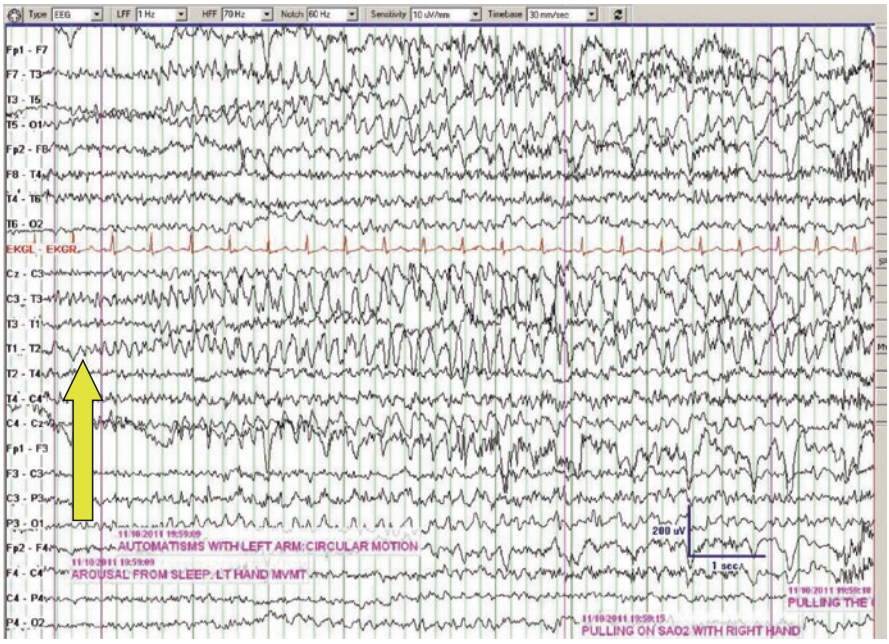

Fig. 41.2 Left temporal onset seizure manifest as evolving rhythmic temporal theta (*arrow*)

the brain that revealed hypometabolism of the left temporal lobe. She was admitted to the hospital's epilepsy monitoring unit and underwent video-EEG monitoring. During this time frequent state-independent left anterior temporal epileptiform discharges were apparent, and three focal seizures typical of her outpatient events were recorded (Fig. 41.2). Neuropsychological testing revealed mild verbal memory deficit. A Wada test was performed. Injection of sodium brevital revealed 8/8 object

recall and aphasia upon left hemispheric injection and 0/8 recall and dysarthria upon right injection. A left amygdalohippocampectomy was recommended; however, her son (an anesthesiologist) recommended against it. 10 years elapsed before surgery was performed. Following surgery, she became seizure-free for more than 2 years.

Clinical Questions

1. What parts of the clinical history suggest focal seizures?
2. What is the likelihood that further ASM will result in seizure freedom, and what are the reasons for drug resistance?
3. Why is seizure monitoring needed when the MRI is abnormal?
4. What further testing is required if surgery is to be pursued?
5. What is the prognosis after surgery for seizures, and what about surgical consequences?

Diagnostic Discussion

1. The diagnosis of epilepsy is suggested by the paroxysmal recurrent episodes of impaired consciousness, and a treatment algorithm is practical [1]. Many patients describe their seizures as "petit mal" seizures when they are nonconvulsive, though in 70% of adults, focal seizures rather than generalized seizures predominate. In two-thirds of these individuals, ASM will not result in sustained seizure control. Many adults with focal seizures experience a warning (aura), though it is the post-ictal state that is the characteristic feature of focal seizures to distinguish it from other events associated with transitory loss of consciousness including absence seizures or "petit mal." If uncontrolled seizures are permitted to continue, a greater risk for morbidity with higher accident and injury rates, psychiatric and cognitive deterioration (especially memory), social isolation, stigmatization, and impaired self-esteem, and even mortality from sudden unexplained death accrues.
2. Approximately one-third of patients with focal seizures and 15–20% with generalized epilepsy will remain refractory to ASM despite different treatment options [2]. After the failure of two appropriate ASMs given for an adequate duration, at an effective dose, there is less than a 5–10% likelihood that further ASM changes will result in seizure freedom. It is important to exclude pseudo-resistance as the reason for drug failure. An incorrect diagnosis may result in ongoing seizures because treatment of a nonepileptic seizure mimic is unlikely to respond to ASM. Similarly, treatment with an incorrect ASM choice targeting the wrong seizure or epilepsy type or too low a dose of ASM will result in apparent drug failure. Genetic generalized epilepsies for example may be aggravated by narrow spectrum ASM such as carbamazepine or phenytoin, and the use of ethosuximide to treat "petit mal" seizures will be ineffective in patients with focal

seizures. Patient-related issues are yet another reason for poor results. When noncompliance or an adverse lifestyle is encountered, the ASM may be the correct choice, though efficacy may be compromised due to reasons such as subtherapeutic use from non-compliance or drug and alcohol abuse. Epilepsy surgery is a standard of care [3] and remains a cornerstone of therapy due to efficacy proven in randomized controlled trials as a more effective treatment compared to continued medial therapy when seizures continue despite ASM [4, 5].

3. When the MRI and interictal EEG are concordant, the likelihood of a correct localization is approximately 80%. The demonstration of a "lesion" (mesial temporal sclerosis on MRI in our patient) has the best predictive value as a localizing feature and as a favorable prognosticator for a successful outcome following epilepsy surgery [6–8]. Ictal EEG recordings are recommended to confirm the diagnosis of epilepsy. Approximately 20–30% of patients admitted for epilepsy monitoring will not have epilepsy. The majority of them have psychogenic nonepileptic attacks (PNEA). Even in patients with epileptic seizures (ES), about 10–15% may exhibit both ES and PNES. Excluding incorrect ASM choices will be made possible by accurately classifying the seizures correctly when they are captured during video-EEG monitoring. Recording EEG during seizures will also identify a single semiology and ictal EEG pattern that morphologically is able to support a diagnosis of unifocal epilepsy. Excluding more than one source for generating recurrent seizures may be difficult based solely upon semiology. An example of the latter situation may be seen in patients with bitemporal epilepsy where staring episodes may be caused by focal seizures arising from each hemisphere independently.
4. When all aspects of a "phase 1" evaluation (non-invaive) are concordant (i.e., history and semiology, MRI, PET, video-EEG monitoring, neuropsychological testing), these candidates may "skip" and proceed directly to surgery without the need to undergo further invasive EEG monitoring with intracranial electrodes for further seizure localization. In our patient, Wada testing was used to firmly localize language function and predict memory function after surgery which was robust, demonstrating a significant difference in participation between the hemispheres to predict a favorable outcome with respect to working memory in addition to anticipating seizure freedom. Functional MRI has been used to identify atypical areas subserving language and is increasingly being used in place of Wada testing as a noninvasive alternative. All of the results of the presurgical evaluation are favorable in our patient and provide localizing information to identify impaired hippocampal function within a limbic neural network. Each of the classic aspects of the presurgical evaluation strongly suggest a favorable outcome with respect to eliminating seizures through surgery.
5. This patient illustrates the most common surgically remediable syndrome of drug-resistant temporal lobe epilepsy (TLE). The presurgical evaluation above involving MRI, PET, and interictal and ictal EEG demonstrate concordance to support unifocal localization. Unfortunately, only a small percentage of potential surgical candidates are being referred to surgical epilepsy centers. Lengthy delays of 15–20 years are unfortunately common. However, 50–90% of patients

become seizure-free with limited morbidity postoperatively. Laser interstitial thermal therapy is another option that potentially has less cognitive consequences albeit with a slightly reduced likelihood of resultant seizure-free outcome [9, 10]. Overall, the most favorable predictor to obtain a seizure-free outcome following surgery or ablation exists when a lesion is present on neuroimaging. It has a high rate of success especially if it is due to hippocampal sclerosis as in our patient. Complications are related to the craniotomy and to the site and the extent of resected tissue. Nobody "wants" surgery, but it is important to present surgery as an option in a realistic and objective fashion. After declining epilepsy surgery for years despite experiencing uncontrolled seizures, our patient underwent successful surgery despite the urging of her family to the contrary. Early surgery has proven to be 15–21% more effective than delayed surgery [11]. She had no complications and became seizure-free as expected. She later wished she would have undergone surgery 10 years earlier and not listened to her son who advised against it.

Pearls of Wisdom

1. Epilepsy surgery is a standard of care and should be considered early when a patient with focal seizures has proven to be drug-resistant to ASM.
2. A lesion on neuroimaging is the best predictor for localizing seizure onset and for prognosticating a seizure-free outcome following epilepsy surgery or stereotactic laser interstitial thermal ablation.
3. Video-EEG monitoring is essential to perform before epilepsy surgery. It will verify the diagnosis of epilepsy and exclude the possibility of other seizure mimics as the reason for drug resistance. In addition, it can provide localizing information about the site of seizure onset by demonstrating electrophysiological information that is concordant with the other "phase 1" evaluations to allow the patient to "skip" invasive monitoring and proceed directly to surgical therapy when concordance is identified.
4. Temporal lobe epilepsy is the most common epilepsy surgery performed. TLE is often due to hippocampal sclerosis and the most common adult epilepsy syndrome that is amenable to surgery.
5. Overall, about 70% of patients are seizure-free after surgery, and an additional 20% have a significant reduction in their seizures. Though the ideal surgical candidate has the best predictability for a seizure-free outcome, epilepsy surgery is more likely to result in seizure freedom when patients have failed >2 appropriate trials of ASM.

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