Chapter 17
Classification of Epilepsy

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Case Presentation

A 20-year-old, right-handed, white female had drug-resistant epilepsy. She had failed several ASDs as single agents due to tolerability issues and had been maintained on Phenytoin for years. She was born via an uncomplicated delivery and was without any known risk factors for epilepsy. Seizure onset began at 9 years of age, manifesting as "petit mal" seizures. These occurred weekly and were worse after menarche. She was initially given Ethosuximide after an EEG demonstrated "petit mal seizure discharges," though she had incomplete improvement in her episodic staring spells. Subsequently, "grand mal" seizures developed within the year following puberty, and she was changed to valproate. She continued with intermittent "petit mal" seizures on a weekly basis. Trials of ASDs included VPA, Dilantin, and Ethosuximide were ineffective. TPM and LEV lead to side-effects of "memory problems" and severe anxiety. When she was seen for another opinion regarding pregnancy and driving, she was taking PHT 400 mg PO qHS which had provided her the best control thus far. Her neurological examination was normal. A CT of the brain was normal. A high resolution brain MRI with an epilepsy protocol was performed (Fig. 17.1). A computer-assisted ambulatory EEG demonstrated a staring spells associated with 2 Hz generalized spike-and-waves with normal background electrocerebral activity.

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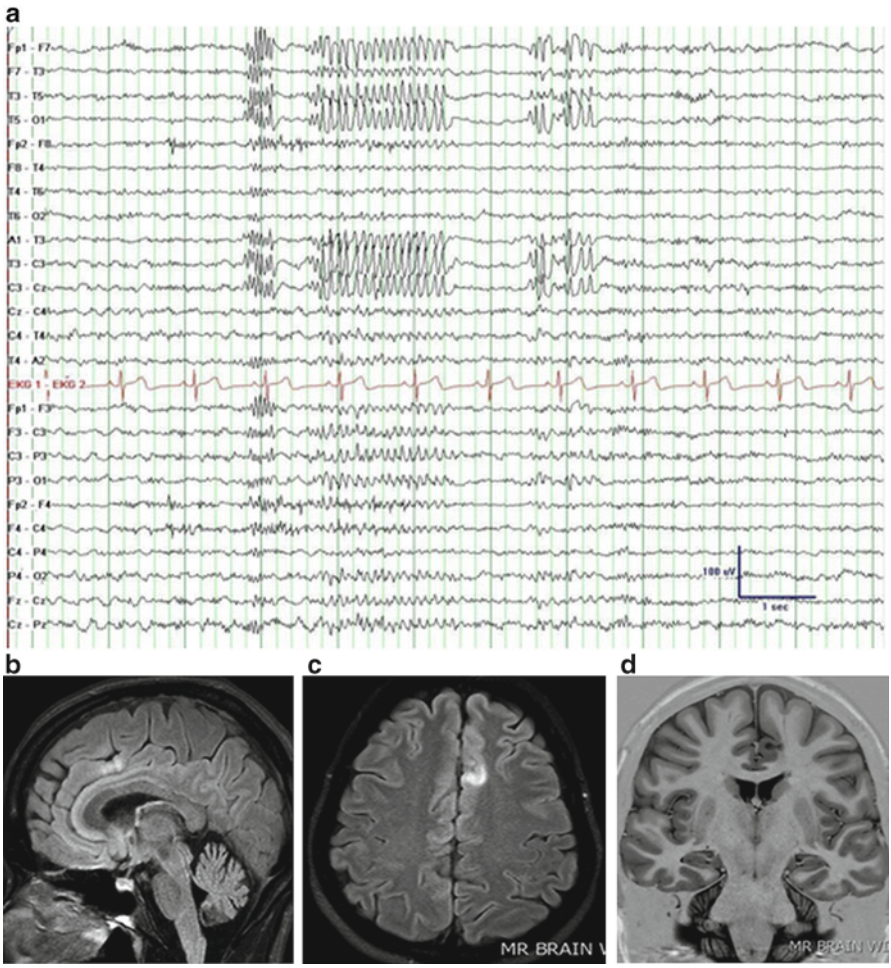

Fig. 17.1 (**a**) Interictal EEG demonstrating bilateral left hemispheric temporally predominant polyspikes. Note the temporal predominance despite the mesial frontal location of a lesion identified on brain MRI (**b–d**) with sagittal and transverse FLAIR, and coronal T1 images of a left mesial frontal lesion suggestive of cortical dysplasia. Note the cerebellar atrophy on brain MRI. EEG: longitudinal bipolar montage, sensitivity 7 μV, and filters 1–70 Hz

Clinical Questions

1. Does this patient have "petit mal" seizures?
2. How do the ancillary tests help classify the staring spells in this patient?
3. What type (classification) of epilepsy does this patient have?

4. What antiseizure drugs are appropriate for the corresponding classes of epilepsy?
5. What is the best course of action?

Diagnostic Discussion

1. This patient does not have true "petit mal" (aka absence seizures). Episodes of staring may be differentiated by a sudden stare for 10–15 s in absence while focal seizures with impaired consciousness typically last 30–40 s and manifest a warning (aura). Absence seizures begin and end abruptly while focal seizures often exhibit post-ictal disorientation and lethargy. Automatisms may occur in absence seizures that are longer in duration. Our patient is manifesting focal seizures, as supported by a focal lesion on brain MRI. Many patients refer to staring episodes as "petit mal" because they are mean to indicate to the non-convulsive nature of the events.
2. The EEG has left hemispheric predominant polyspikes. Generalized epileptiform discharges may occur in patients such as ours due to secondary bilateral synchrony. This bilateral diffuse epileptiform discharge occurs as a consequence of a localized process such as the left mesial frontal lesion. A generalized EEG pattern is probably due to the proximity of the lesion to the corpus callosum. Mesial frontal lesions have a rapid transit time via the callosum to manifest as bilateral synchronous epileptiform discharges on the EEG. There may be a "lead in" to generalized discharges that can appear, and the generalized spikes (or polyspikes) usually have a repetition rate of <3 Hz when it occurs. In this case, the burst of polyspikes is lateralized to the left and the brain MRI clearly shows an area of FLAIR abnormality that probably reflects focal cortical dysplasia to strengthen the classification of the seizures in this case.
3. This patient has localization-related epilepsy manifest as brief focal seizures with impaired consciousness and focal seizures that evolve to convulsions. Focal seizures that evolve to convulsions are a commonly recognized entity in patients with localization-related epilepsy. In addition, lateralized semiologies and EEG features may occur in patients with generalized seizures associated with genetic epilepsy (i.e., JME) are common. Terminology and concepts for reorganization of the epilepsies have been recently performed dichotomizing common focal and generalized seizures. Overlap between generalized and focal seizures may rarely occur. The clinical onset of absence ("petit mal") with subsequent convulsions "grand mal" suggests one of the genetic generalized epilepsies. However secondary bilateral synchrony on the EEG (and generalized discharges from a focal lesion) or focal abnormality on brain MRI suggests focal seizures as the correct classification.
4. Treatment is predicated upon proper seizure and epilepsy classification. Narrow-spectrum ASDs such as carbamazepine and phenytoin may aggravate seizure control or worsen some generalized seizure types (absence and myoclonic

seizures). Similarly, some ASDs for generalized seizures (ethosuximide) as in this case may be ineffective for the treatment of focal seizures. EEG is fundamental to seizure classification when semiology is unclear, such as when dealing with staring episodes and convulsions. Even EEG may be challenging when a lack of defining interictal discharges or secondary bilateral synchronous epileptiform discharges are present. Brain MRI may reveal a focal lesion (as in this case) that supports localization-related epilepsy and guide AED choices for focal seizures. Most ASDs have been approved by the US Food and Drug Administration for clinical use in the treatment of focal seizures. Valproate, lamotrigine, topiramate, levetiracetam, and zonisamide have demonstrated efficacy in some patients with both focal and generalized seizures. The barbiturates and benzodiazepines may also demonstrate benefit in both seizure types.

5. The best course of action for this patient is to treat her for drug-resistant seizures. Following the failure of two appropriate AsDs for an adequate time period, the substitution or addition of alternative agents carries a low yield of success. Because our patient has a definable lesion on brain MRI, surgical therapy was recommended, which she refused, noting that her seizures were not a "disability" for her. A change to Lamotrigine as a non-enzyme inducing AED was also recommended given the long-term consequences that were possible on PHT with uncontrolled seizures; however, she felt too comfortable with her treatment to accept a change. Her wishes were respected, and she continues to have infrequent seizures. She has since delivered two healthy children on PHT monotherapy.

Clinical Pearls

1. Petit mal is a common colloquialism used by patients to reflect non-convulsive staring spells. Adults reporting "petit mal" and "grand mal" seizures beginning after adolescence likely reflect focal epilepsy with focal seizures with/without impaired consciousness and focal seizures that evolve to convulsions.
2. Brain MRI may be a useful ancillary test in the classification of epilepsy in patients with poorly defined stereotyped events. Furthermore, it may support localization (in this case, the frontal lobe). EEG is the most useful test when the brain MRI is normal or nonspecific. When clear focal or generalized interictal epileptiform discharges are present, this supports the diagnosis of epilepsy and the mechanisms for the recurrent seizures. However, secondary bilateral synchrony may occur in patients with extratemporal epilepsy, as in this case, which may make it more difficult to distinguish from a primary generalized discharge.
3. Broad-spectrum, antiseizure drugs are useful treatments when the classification of the seizures and epilepsy type is unknown. These agents are effective for both focal and generalized seizures and do not aggravate a specific seizure type.
4. Drug-resistance is a definable entity and a prerequisite to epilepsy surgery independent of a need for surgery based upon a lesion. However the acceptance of

epilepsy surgery by patients is an individual decision and one that is relative to their seizure type and self-perceived disability.

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