Aerospace Medicine Clinic

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You are seeing patients in the Flight and Operational Medicine Clinic of a U.S. Air Force base when your next patient presents with a recent history of a seizure. He is a 33-yr-old male C-17 pilot who first sought care about 7 wk ago after having a "syncopal episode" where he fell and hit his face, suffering a nasal fracture that required surgical repair. About 6 wk later, he had a witnessed loss of consciousness, with generalized tonic-clonic movements of his body. Clinical suspicion in the emergency room after this visit was high for diagnosis of seizure. He has no past medical history and does not take any medications regularly (including over the counter or supplements). He denies a family history of seizures or any other significant condition. He also denies tobacco or illicit drug use and infrequently drinks alcohol.

On examination, he is 71 in tall, 173 lb, and has normal speech and comprehension. Heart and lung exam is normal. His nasal fracture (from 1 mo ago) is healing normally. Basic neurological exam (including cranial nerves, mental status exam, motor and sensory exam, reflexes, cerebellar testing) is normal. Vital signs are normal.

1. A differential diagnosis for a seizure includes all of the following except:
   A. Early stage dementia.
   B. Syncope.
   C. Migraine headache.
   D. Paroxysmal movement disorders.
   E. Psychogenic nonepileptic seizures (PNES).

ANSWER/DISCUSSION

1. **A.** Seizures are common throughout the world, with an estimated 50 million people affected with epilepsy (seizure disorder).[22] It is also estimated that the incidence of all seizures, whether a part of epilepsy or not, is 29–39 per 100,000 per year, or affecting up to 10% of the population over their lifespan.[8] There are several presentations for seizures, with most being divided into the classifications of either focal or generalized. Focal seizures have electrical activity start in only a specific part of the brain and then may spread (secondarily generalized). A larger area (both sides) of the brain is affected in generalized seizures, which can present as just staring spells, myoclonic jerks, or generalized tonic-clonic movements. In addition to the location of brain involvement, seizure types are divided into categories based on the type of or absence of motor activity.[8,16] Main categories of seizure type include focal onset, generalized onset, and unknown onset. Within these categories, seizures are further subdivided based on motor or nonmotor onset.[7]

Since the presentations of seizures can vary, there are multiple different conditions that can also mimic seizure activities. Depending on the presentation of the seizure and the presence of any potential comorbidities, syncope, migraine headaches, or paroxysmal movement disorders can all present similarly to different types of seizures. Syncopes specifically can have tonic-clonic type motor movements and can very much mimic generalized motor seizures. Additionally, PNES, also known as nonepileptic seizures, psychogenic seizures, or pseudo-seizures, can be the actual cause of up to 30% of patients admitted to epilepsy centers for evaluation and up to 60% of military members with a new diagnosis of seizure.[2,14] These patients have seizure-like motor movements, but do not have the epileptic brain activity causing the movements. Psychiatric/psychological underlying stressors are found in these members, and it is thought the PNES is a dissociation defense mechanism. Because of the multitude of seizure mimicking conditions, a good history of the event (from an observer) and past medical history are very important for determining where to focus the evaluation and subsequent treatment.

Upon review of the initial diagnostic studies for the patient, both from the emergency room (after the witnessed tonic-clonic event) and subsequent neurology evaluation, the diagnosis of epilepsy (seizure disorder) was given.

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2. Which of the following is not an appropriate study to obtain in the workup of a patient with a suspected seizure?
   A. Magnetic resonance imaging (MRI).
   B. Computed tomography (CT).
   C. Electroencephalogram (EEG).
   D. Electromyography.
   E. Complete blood count (CBC).

ANSWER/DISCUSSION

2. **D.** The evaluation for suspected seizures consists of many different modalities. An MRI is recommended for the evaluation of all initial seizures, as it is effective at identifying structural findings associated with seizures. The timing of when the MRI should be performed is often debated, but most agree it can be done in an outpatient setting if the patient is clinically stable.[3,13] A CT of the head should be strongly considered in all patients with acute seizure if there is a clinical history of trauma, risk of bleeding, or other urgent matters that require evaluation.[10] An EEG, if it can be obtained during an actual seizure, is the gold standard for diagnosis to identify specific brain wave activity during a seizure. EEGs can generally be performed in an outpatient setting, but should be considered more urgently if a patient has not returned to baseline status after noticeable seizure activity has stopped.[13,18] Currently, electromyography has no role in the routine evaluation for seizures. Routine blood work, including comprehensive metabolic panel, CBC, glucose, pregnancy testing, and potentially cerebrospinal fluid evaluation, should be performed on all initial seizures to evaluate for any underlying abnormalities.[1]

The blood work from the emergency room showed a normal CBC and comprehensive metabolic panel (including glucose level). The CT of the head confirmed the nasal fracture, but was otherwise normal. Cerebrospinal fluid evaluation from lumbar puncture was normal except notable only for a protein level at the upper limits of normal at 56 mg · dL^{-1}. MRI of the brain was normal, and the EEG showed bifrontal intermittent rhythmic delta waves, consistent with significant brain dysfunction, probably postictal in this case.

3. Which of the following is incorrect regarding the initial stages of evaluating/managing a patient with a new onset suspected seizure?
   A. EEGs are very useful for the diagnosis of seizures, but their utility decreases the farther out from the reported activity the EEG is performed.
   B. History and risk factor evaluation are very important for making the correct diagnosis.
   C. A normal EEG and MRI rule out an epileptic seizure.
   D. For someone with an obvious acute/reversible cause of the seizure (such as hypoglycemia, eclampsia, or impact seizures from mild to moderate traumatic brain injury), antiepileptic drug therapy is generally not indicated for treatment.

ANSWER/DISCUSSION

3. **C.** Individuals with seizure disorders will not always have abnormal findings on EEG. The timing of conducting the diagnostic EEG after an initial seizure is important, with the best time to conduct the EEG being at the time of the actual seizure. Within 24 h is generally considered acceptable to do the EEG, but studies have shown that 50% of people will show no abnormal wave forms on EEG 24 h after a seizure, and 75–80% will have no abnormalities 48 h later.[4] A proper history is always an important part of making any diagnosis, including seizure disorder. Information from a witness can provide diagnostic clues to help make the diagnosis, particularly in the setting of someone who has risk factors for seizures (increased age, head trauma, family history, alcohol withdrawal, etc.). As described, EEGs and MRIs are very important for confirming the diagnosis of a seizure, but frequently they will not show any abnormalities, depending on the timing of the study or type of seizure. Since most people with a seizure have no identifiable underlying cause, and the risk of developing a second seizure is high (21–45% in the first 2 yr), some patients with an initial seizure get started on antiepileptic medication immediately following diagnosis, particularly those with a nocturnal seizure or EEG or MRI that portends a higher risk.[12] However, for those with an underlying treatable cause, most are not started on medication and instead obtain treatment of the underlying issue.[11]

Upon further questioning, the patient states that for 1-2 yr he has been having episodes lasting 15-20 s described as trouble perceiving speech. He knew that something was not quite right, but didn't think it was anything serious, as he was still able to function at home and work quite well.

4. Neurologically normal adults (particularly in a screened population) who experience an initial seizure most commonly have which of the following risk factors?
   A. Head injury.
   B. Infection.
   C. Cerebral tumor.
   D. Family history of seizure disorder.
   E. None of the above.

ANSWER/DISCUSSION

4. **E.** There are multiple risk factors for seizure, a common one being a history of a prior seizure. Head injury/trauma often can lead to a cerebral hemorrhage, which can lead to a seizure acutely or over time. Infection can cause inflammation of the brain tissue, which can lead to seizure activity. Tumors, with focal dysfunction from a variety of mechanisms, are a common cause of seizure. Individuals with epileptic seizures may be up to three times more likely to have a family member with epilepsy.[1] In the 35-64 age range, 15% of seizures are thought to be from cerebrovascular causes, 7% are posttraumatic, and 7% are

from tumors.[11] However, up to 60% of all patients with seizures have no known risk factors.[11,17,19]

Now that a seizure has been confirmed in your patient, he has many questions about seizure types. He is confused because he thought that all seizures involved convulsing of the body. You explain to him that the periods of amnesia he was having earlier likely were actually seizures as well. He wants to know more about the different types of seizures.

5. What is the most likely seizure type that neurologically normal adults will have as their first seizure (not necessarily the first seizure type for which they first seek medical care)?
   A. Generalized tonic-clonic.
   B. Focal impaired awareness (formerly known as complex partial seizure).
   C. Generalized nonmotor (absence).
   D. Generalized myoclonic.
   E. Focal atonic.

ANSWER/DISCUSSION

5. **B.** While the classic clinical presentation of a generalized tonic-clonic seizure tends to be more obvious, where the patient has usually less than a minute of full body jerking and shaking with loss of consciousness and/or confusion, many seizures have different presentations and may occur for an extended period of time before a diagnosis is made. In focal impaired awareness seizures (formally known as complex partial seizures), only part of the brain is affected, and oftentimes no dramatic tonic-clonic activity is seen. However, small, subtle, stereotyped automatisms are common. In these seizures, the patient may have brief periods of confusion and amnesia and present with or without muscle tension. Oftentimes these patients report needing to have conversations repeated back to them because they frequently don't remember what was happening to them in the prior few minutes (which is also common in generalized nonmotor seizures). Amnesia is common in complex partial seizure types, making the diagnosis challenging.[5] This may happen for a long time before it is recognized, by the patients or someone close to them, or a new seizure type occurs, and medical attention is sought.

As a U.S. Air Force pilot, the member is very concerned about his ability to resume his flying career in the future. He realizes he has a serious medical condition, but also knows that waivers are granted regularly to experienced pilots such as himself for many different medical conditions.

6. Based on this member's clinical presentation, workup, and treatment, the likelihood of this member returning to flying duties in the U.S. Air Force is:
   A. Zero chance. Seizures are not compatible with flying duties, and there is no chance for waiver potential, as there have never been any waivers granted for aviators who have had a seizure.
   B. Minimal chance. Seizures are not compatible with flying duties. Few waivers have been granted in situations where risk of recurrence and risk to mission and human life were thought to be low, but they were rare situations.
   C. Pretty good chance. While the Medical Standards Directory states that seizures are not compatible with flying duties, if a member can stay seizure free for multiple years on appropriate treatment, a waiver is likely to be granted.[20]
   D. Excellent chance. As long as a pilot can demonstrate stability on appropriate treatment, then he or she should be returned to flying duties.

ANSWER/DISCUSSION

6. **B.** According to the U.S. Air Force Medical Standards Directory, the accompanying medical standards document to Department of the Air Force Manual 48-123, Medical Examinations and Standards, seizures are not compatible with flying duties. (Waivers can be considered on a case-by-case basis when a single seizure was obviously provoked by trauma or an extrinsic factor.)[20] Because the risk of recurrence for unprovoked initial seizures is so high (greater than 40% over 5 yr), waivers for these types of seizures are rare. In 2019, a search of the Air Force waiver tracking system showed that of the seizure waivers approved for flying duties, the large majority were for initial applicants who had a history of childhood febrile seizure (which does not portray a higher risk for future seizures as an adult). A few waivers were granted for provoked seizures where the member had shown subsequent stability. The high risk for recurrent seizures in unprovoked initial seizures is the primary reason that waivers are usually not recommended for continued flying duties.[9,20] The U.S. Army and U.S. Navy have similar standards for waivers among aviators. Any seizure is disqualifying for aviation duties.[15,21] According to the Federal Aviation Administration, an aviator with epilepsy, or any seizure that cannot be explained by an underlying cause, may not be approved for flying by a local Aviation Medical Examiner. All cases must be deferred for Federal Aviation Administration disposition and are considered on a case-by-case basis.[6] However, for a Special Issuance to be considered, historically, the pilot must be at least 4 yr removed from the seizure and 2 yr off medications. Generally, for a pilot with multiple seizures (or a diagnosis of epilepsy), the pilot must be at least 10 yr seizure free and 3 yr off medications (Hesselbrock R. Personal communication; 2021. Murphy R. Personal communication; 2021).

After 2 yr of treatment, your pilot had yet to obtain clinical stability. He had tried and failed different treatment regimens and was still having breakthrough seizures. He was given a medical disqualification from flying with the U.S. Air Force.

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