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Letter to the Editor: New Observation

Functional Seizures in the Elderly: Accurate Diagnosis Can Reduce Iatrogenic Harm

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An 87-year-old man with multiple vascular risk factors presented to the emergency department four times in eighteen months with new, recurrent paroxysmal events, without loss of awareness and able to recall the events. At the onset of the events, he felt that "the world changed around [him]," and everything seemed far away. He then felt a pulling sensation in his right face, and right arm and leg heaviness. He was unable to get words out, despite knowing what he wanted to say, with involuntary vocalization instead. These episodes typically lasted 20 to 60 minutes, although some were much shorter lasting only minutes, after which he felt tired, but not confused. This description was corroborated by witnesses.

Since onset, these events were occurring in clusters every 3–4 months. During the first event, an urgent computed tomography (CT)/CT angiogram of the head and neck revealed occlusion of the right internal carotid artery (ICA) and 50% stenosis of the left ICA, without acute abnormality. He was treated with tissue plasminogen activator, and his symptoms resolved over the following hour, but with recurrent episodes during admission. Magnetic resonance imaging (MRI) of the brain showed a remote right caudate nucleus infarct, without acute infarction. CT perfusion performed during one of the events did not demonstrate any abnormalities. Electroencephalogram (EEG) was normal, but an event was not captured. Given the repeated events in hospital without imaging features of acute stroke, a provisional diagnosis was made of non-lesional focal onset epilepsy with focal aware cognitive seizures, and he was started on levetiracetam 750 mg twice daily.

He presented to the emergency department 15 months later with a recurrent, prolonged event and was admitted to inpatient neurology. All investigations were unremarkable including MRI, EEG, blood work with paraneoplastic and autoimmune encephalitis antibodies, echocardiogram, and Holter monitor. He continued to have events in hospital, despite escalation of antiseizure medications. At discharge, he was taking levetiracetam 3000 mg daily, valproic acid 1000 mg daily, and clobazam 30 mg daily. He was re-admitted shortly after with delirium and falls, presumed secondary to antiseizure medications. He was weaned off clobazam, and valproic acid was reduced, with improvement in his gait and cognition.

At the time of his final admission for recurrent events, the working diagnosis remained drug-resistant focal onset epilepsy. However, given the unusual and prolonged semiology, and treatment resistance, an alternate diagnosis of functional seizures (FS; also known as psychogenic non-epileptic seizures/events/attacks, dissociative seizures, or pseudoseizures) was considered. Continuous video EEG monitoring (VEM) captured two habitual events. These two events were not completely stereotyped, with different patterns of symptom occurrence and vocalizations. In the second event (Supplemental Video), the patient appeared to feel something at the onset and started moaning. In response to his nurse, he nodded appropriately, but was unable to respond verbally. There was no objective unilateral weakness. EEG and electrocardiogram demonstrated no change to his background rhythm and no epileptiform activity (Figure 1), agreed upon by three epileptologists with mean 19 years of practice experience (SD 13).

Given the inconsistent and incongruent semiology (with both positive and negative symptoms), treatment resistance, and normal VEM, his diagnosis was revised to functional neurological disorder (FND), with episodic symptoms, difficult to classify, but most consistent with FS. This diagnosis was explained, and he was taught basic sensory grounding techniques. He identified a precipitating factor as stress related to his wife's stroke. Perpetuating factors included fear of injury and medication side effects. His antiseizure medications were tapered to discontinuation. He was offered referral to psychology, but favoured to first practice sensory grounding techniques.

It has now been 3 years since his diagnosis of FS, and he remains off antiseizure medications. He has only had two further events (versus clusters of events occurring every 3–4 months), the first one two months after discharge and the second occurred two years after discharge in the context of diverticulitis.

Functional seizures are a subtype of FND, characterized by events that resemble epileptic seizures or syncope, but do not arise

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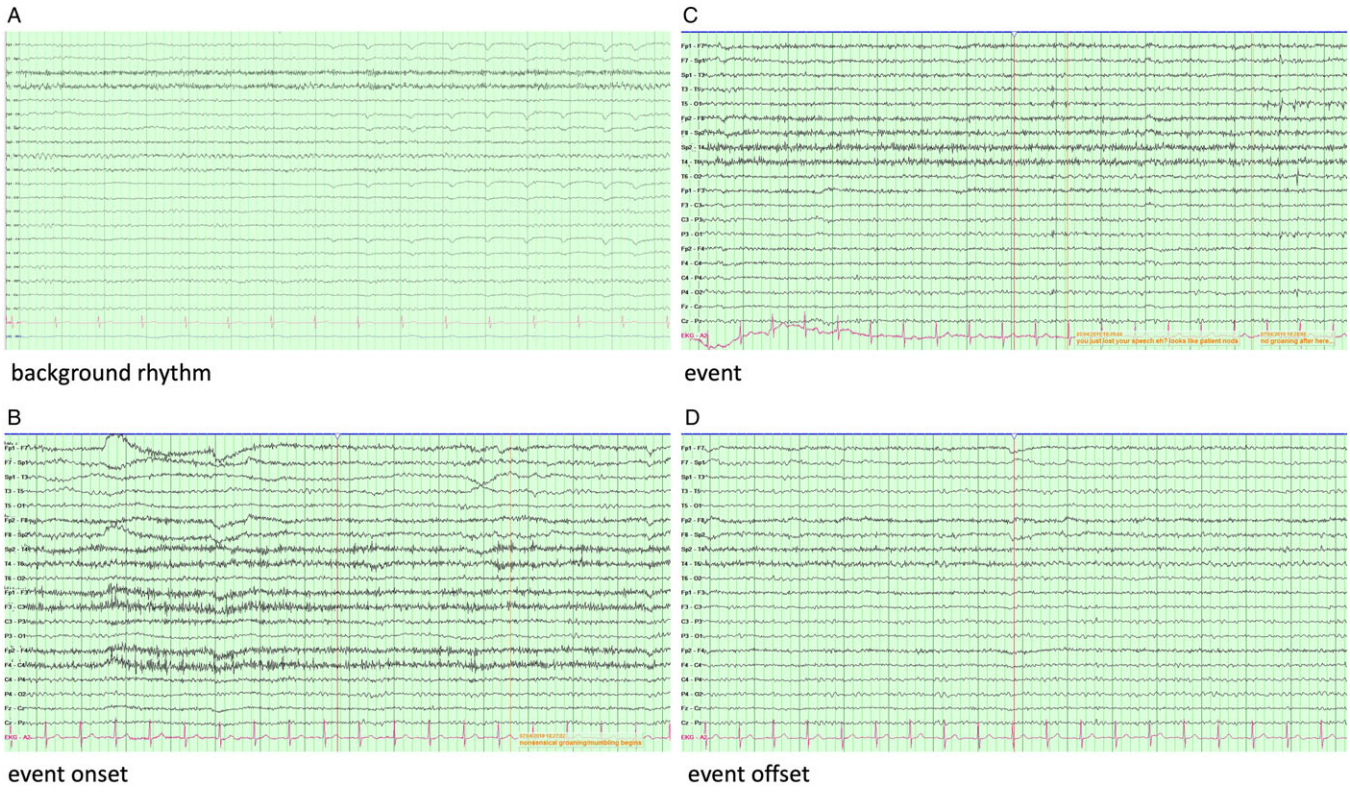

Figure 1: Surface EEG recordings from prolonged video electroencephalography monitoring capturing a habitual event. (a) Normal interictal background rhythm while awake. (b) At the event onset, no change is seen in the patient's background rhythm or electrocardiogram tracing. (c) Likewise, as the event is ongoing, there is no change in the patient's background rhythm. Notably, there are no epileptiform discharges or abnormal slowing. (d) At event offset, there is no change from the interictal background rhythm.

as a result of abnormal cortical electrical activity.[1] They may present as recurrent events of altered behaviour, including changes in the level of awareness, motor activity, or sensory symptoms. The gold standard for diagnosis of FS is VEM, although positive signs have been described that may facilitate diagnosis.[1] Ictal features present in our patient consistent with FS included dissociation, eye closure, prolonged duration, and non-stereotyped events. FS are common, with one report indicating 12% of patients referred to neurology for loss of consciousness received this diagnosis.[2]

Functional seizures are much more common in younger patients, with the median age of onset being 28 years.[3] However, FS are not uncommon in the elderly.[4–6] Among patients diagnosed with FS, 10% were older than 60 years.[4] Men have an approximately equal rate of developing FS across the age range.[3] A number of studies have been published characterizing features of the final diagnosis of patients over 60 years admitted for VEM, finding approximately half of patients experiencing non-epileptic events had FS.[5,6] In many cases, a diagnosis of epilepsy was revised to FS, highlighting the importance of pursuing VEM to establish this diagnosis.

Although FS are not uncommon in the elderly, there are unique challenges in the diagnosis. Higher numbers of medical comorbidities are associated with increased age.[5] Physiologic non-epileptic events, including syncope, movement disorders, sleep disorders, and behavioural events, are as common as FS in elderly patients undergoing VEM.[5,6] Evidently, maintaining a broad differential diagnosis is necessary. Furthermore, it is known that FS often coexist in patients with a diagnosis of epilepsy. Given that rates of epilepsy increase after age 60, it may be difficult to confidently exclude comorbid epilepsy in elderly patients.

Misdiagnosis of FND as other conditions places patients at significant risk of iatrogenic harm related to medications and interventions, invasive diagnostic tests, hospital admissions, inclusion in research trials, and lack of access to appropriate treatment.[7] These risks are even greater in elderly patients, who are more susceptible to adverse events. Our patient experienced severe side effects from antiseizure medications, resulting in admission for falls and delirium. His presentation with drug resistance would be unusual for late-onset epilepsy, since up to 80% of these patients are rendered seizure-free, with up to 95% achieving this on modest dose monotherapy.[8] Polypharmacy is common in patients with FS incorrectly diagnosed as having epilepsy.[1] Furthermore, prolonged events are common in patients with FS, occurring in 18-77% of patients.[9] Prolonged events may be mistaken for status epilepticus, resulting in increasing doses of benzodiazepines and other antiseizure medications, leading to sedation and apnoea, ultimately requiring intubation and intensive care unit admission.[9] In general, when treating prolonged epileptic seizures where awareness is retained, non-sedating antiseizure medications should be prioritized over sedating medications such a benzodiazepines, particularly in elderly patients susceptible to significant sedation and at high risk of requiring intensive care unit admission.

This case of an elderly patient with FS serves to illustrate the importance of including FS on the differential diagnosis for paroxysmal events resembling epileptic seizures, regardless of a patient's age, particularly in the event of normal investigations and unexpected drug resistance. Patients with FS, misdiagnosed as epilepsy, are at risk of iatrogenic harm, and this risk is amplified in the elderly.

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