The wilting widow's masquerading illness

Philip Saragoza, MD, and Daniel F. Maixner, MD

How would you handle this case?

Visit **CurrentPsychiatry**.com to input your answers and see how your colleagues responded

Mrs. D seems depressed since being treated for sepsis, and she has abrupt episodes of unresponsiveness and confusion. What's causing these events?

CASE Unexplained unresponsiveness

One month after being hospitalized with *E coli* sepsis—and just after completing a course of ciprofloxacin—Mrs. D, a 79-year-old widow, becomes withdrawn and has several days of worsening fatigue, weakness, and somnolence. Within 2 hours of being admitted to the hospital, she becomes flaccid and unresponsive, although she seems to be awake. She has decreased respirations and is intubated.

The neurology team finds her unresponsive to verbal and noxious stimuli, with some resistance to eye opening. Neurologic exam is nonfocal. Cranial nerve testing is intact, muscle strength and reflexes are normal and symmetrical, and sensory function is intact to light touch. MRI, ECG, chest radiography, and laboratory tests—including metabolic and infectious screenings—do not reveal acute pathology. Within hours, Mrs. D becomes much more responsive and is successfully extubated. Her rapid improvement rules out locked-in syndrome.

The next day, Mrs. D has another episode of reduced responsiveness that lasts several minutes and resolves quickly. The neurologist observes this episode—which occurred when Mrs. D's daughter entered the room—and recommends a psychiatric consultation.

For the past 3 weeks Mrs. D has experienced depressed mood, low energy, poor sleep, memory complaints, and feeling as if her mind was "scattered." She has stopped attending church, is isolating to her home, and has been hiding valuables because of an irrational fear that she would lose possessions from her estate. Her primary care physician noted markedly reduced speech during recent office visits and agrees with the family that Mrs. D seems depressed.

On psychiatric exam, Mrs. D's speech is quiet and slow but coherent. Her mood is depressed with a flat affect. Her thought process is goal-directed, and her Mini-Mental State Examination (MMSE) score is 27/30, indicating her cognition is grossly intact.

Mrs. D develops a low-grade fever. Although the physician does not suspect an infection, he prescribes a prophylactic course of levofloxacin, 500 mg/d. After 2 days of monitoring and assessments, the psychiatrist attributes Mrs. D's presentation to depression, prescribes bupropion, 100 mg/d, and zolpidem, 5 mg at bedtime, and refers her for psychiatric follow-up.

Six days after discharge, Mrs. D's family brings her to the psychiatric emergency room. They report that since discharge she has remained fatigued and seems confused intermittently. Her depressive symptoms—decreased appetite, anhedonia, poor sleep, and agitation—persist, and her personal care has deteriorated.

Dr. Saragoza is a third-year psychiatry resident and Dr. Maixner is assistant professor of psychiatry, University of Michigan Medical School, Ann Arbor.

Mrs. D's symptoms suggest which diagnosis?

a) major depression with psychosis
b) somatization disorder
c) seizure disorder

The authors' observations

The psychiatrist attributes Mrs. D's declining functioning to a worsening mood disorder. Major depression with psychotic features can include:

- fearfulness
- suspiciousness
- delusions of poverty.

Others felt her presentation could be psychogenic. However, somatization disorders usually manifest before age 30 and rarely develop late in life.[1] Also, this type of diagnostic reasoning blames the patient for a neuropsychiatric condition that clinicians might not yet have identified.

Mrs. D's cognitive and behavioral status fluctuated during her initial medical hospitalization, and on 1 occasion she required intubation. Her confusion worsened after discharge. These aspects of her history, along with worsening psychosis, can indicate seizures.

Psychiatric manifestations of seizures have been recognized for centuries. Partial complex seizures—one of the most common seizure types—have been called "psychosensory" or "psychomotor" seizures because they often include psychiatric symptoms.[1]

Psychiatric symptoms most often occur with seizures involving the temporal lobe, and limbic system activation adds an affective dimension to perceptual data processed by the temporal neocortex.[2] Frontal and parietal lobe seizure foci also are associated with behavior change.

Psychiatric manifestations of seizures can include:

- cognitive problems
- anxiety
- mood/affect, psychotic, and dissociative symptoms
- personality changes (***Table 1, page 70***).[2-6]

These symptoms can occur during seizure auras, the seizure itself, or postictal or interictal periods.

As many as 30% of patients with seizures experience prominent psychiatric symptoms.[7] Approximately one-half have comorbid psychiatric syndromes.[8]

EVALUATION Continuing decline

The emergency room staff learns Mrs. D has a history of vague auditory hallucinations and has developed more overt paranoia, including thoughts that police may be out to harm her. She has difficulty responding to questions and can not offer details of her history; her speech is soft and her thought process appears slowed.

Mrs. D is admitted to the inpatient psychiatry service. Her family reports that she has episodes of disorientation, poor memory, staring, and paranoia about the police that last minutes to 1 hour.

On initial examination, she is poorly oriented. MMSE is 12/30, indicating a dramatic change in cognition from a week ago, and language impairment severely affects bedside cognitive testing. Her speech is perseverative: she repeats the phrase, "yes, very good, uh hum." Later, she has difficulty speaking clearly. She attempts to answer questions but her speech is garbled. She can follow commands but cannot speak or do verbal repetitions.

On a subsequent examination 1 hour later, her speech difficulties are variable. She cannot speak fluently, has limited ability to repeat phrases, and cannot follow simple verbal commands. These symptoms persist only minutes. Mrs. D slowly becomes more conversant but appears tired. During the next few hours she is disoriented and tries to walk into the nursing station. Other repetitive activity includes putting on/taking off multiple layers of clothing.

What further testing would you order?

a) repeat MRI
b) electroencephalography (EEG)
c) lumbar puncture

continued

Clinical Point

Although Mrs. D's symptoms might be psychogenic, somatization disorders rarely develop late in life

Table 1

Seizure-related psychiatric symptoms: What to look for

Symptom type	Characteristic features with seizures
Cognitive: intellectual function, memory, orientation	Episodic, fluctuating course of changes Amnesia occurs with complex—but not simple—seizures
Anxiety	Occurs most often with temporal lobe seizures May appear as full-blown panic attack Agoraphobia is rare Associated seizure features may include disturbed consciousness, automatisms, and hallucinations
Mood and affect	Change in affect is often episodic and profound, without many other symptoms associated with major depression or mania
Psychotic	Usually manifests as a single symptom, often described as incongruous, fragmentary, or out of context[2] Occurs most often with temporal lobe seizures[3] Delusions (paranoid, grandiose), forced thinking Hallucinations: auditory, visual, olfactory, tactile, gustatory Negative symptoms (emotional withdrawal, blunted affect) may be more common in frontal lobe seizures[4]
Dissociative: depersonalization, déjà vu, jamais vu	Symptoms tend to be less extreme than in patients with dissociative identity disorder or PTSD May occur more often in context of panic symptoms with temporal lobe seizures[5]
Personality changes (in epilepsy)	May be due to underlying frontal or temporal lobe damage Includes anancastic personality, emotionally unstable personality, and Geschwind syndrome (hypergraphia, hyperreligiosity, hyposexuality, and viscous personality style—perseverative and difficult to disengage from conversation)[6]

PTSD: posttraumatic stress disorder

Clinical Point

A normal EEG does not guarantee the absence of recent seizures

The authors' observations

Although EEG is important for distinguishing an atypical psychiatric presentation from seizures, carefully consider the patient's history and symptoms before you look to the EEG for diagnosis because:

- A normal EEG does not guarantee the absence of recent seizures; a standard scalp EEG can miss epileptiform changes that may occur earlier in the ictal phase.[9]
- EEG abnormalities may occur in normal subjects.

O'Sullivan[10] recommended performing an EEG only in the presence of an "organic factor," such as a recent known or suspected convulsion, recent head trauma with more than momentary loss of consciousness, or a known CNS disorder. Exam findings that warrant EEG include:

- visual, olfactory, or tactile hallucinations
- mutism
- catatonia
- poor memory not due to inattention
- episodic aphasia, apraxia, or agnosia.

Because only 50% to 70% of patients with recurrent seizures will have epileptiform activity on a single interictal EEG,[11] repeat studies are useful, especially if they include activation procedures and sleep deprivation.

Mrs. D's confusion level and speech abnormalities varied over time. Her speech arrest early in the admission appeared to be a Broca's or expressive aphasia because she comprehended commands but was unable to speak. Later, her speech exhibited a mixed transcortical aphasia pattern—she was unable to speak or comprehend, but retained some ability to repeat. The changing

continued on page 73

continued from page 70

aphasia patterns and the often abrupt starting and stopping of these symptoms were the clues that an active process was occurring, suggesting that seizures should be considered.

DIAGNOSIS Irrefutable EEG evidence

Mrs. D receives another neurology consult. An EEG shows spike and wave discharges in both frontal lobes consistent with nonconvulsive status epilepticus (NCSE). During these bursts, the neurologist notes speech arrest and altered alertness. Phenytoin loading is administered as a single 800-mg oral dose followed by 100 mg twice daily, and Mrs. D is transferred to the neurology unit for further stabilization.

What features suggest a seizure disorder?

a) brief spells of symptoms
b) abrupt onset
c) stereotypical episodes with highly similar symptoms
d) automatisms: automatic, simple or complex movements
e) all the above

The authors' observations

When evaluating whether a psychiatric presentation reflects an underlying general medical or neurologic disorder—including seizures—consider the clinical features outlined in ***Table 2***.[12]

In Mrs. D's case, several factors supported the diagnosis of depression. She had numerous depressive symptoms, including depressed mood, social withdrawal, low energy, poor sleep, and "scattered mind," which the psychiatrist interpreted as poor concentration. Interestingly, she attributed her dramatic episode of mutism and unresponsiveness in the hospital to being depressed. Mrs. D also had a personal and family history of depression; she had experienced a possible major depressive episode in her late 20s but was never treated, and her brother had depression.

Several features of her presentation were atypical, however, and suggested a medical etiology. Her family described the onset of her symptoms as abrupt, and she declined rapidly. Mrs. D's concern about her estate had no connection with reality, and she became more psychotic. The dramatic episode of decreased responsiveness that led to her intubation was both peculiar and brief.

Following the initial neurologic consultation, the medical team did not carefully consider seizure because Mrs. D appeared depressed. The neurology team was quick to ascribe her episodes as psychosomatic and mood-related after an episode occurred in the presence of Mrs. D's daughter. The psychiatry consultants did not uncover major conflicts or psychological crises that could explain her presentation but also focused heavily on her depressive history.

Mrs. D's symptoms had an episodic quality with sudden onset, were repeatedly associated with aphasia, and included some automatic behavior (including dressing and undressing) suggestive of seizures. Symptoms of depression should not be surprising in this context because depression may

Table 2

Is the patient's disorder psychiatric or medical/neurologic?

Are the symptoms typical of a psychiatric disorder, including the severity?
Are the onset and course of symptoms usual?
Does the patient have risk factors for psychiatric illness, such as a personal or family history of psychiatric illness?
Are psychiatric symptoms responding poorly to treatment?
Does the patient have a general medical or neurologic condition commonly associated with psychiatric symptoms?
Does the patient exhibit abnormal cognitive functioning, including memory impairment or altered level of consciousness?
Did the psychiatric symptoms emerge after an abrupt change in personality?

Source: Reference 12

Clinical Point

Changing aphasia patterns and abrupt starting/stopping of symptoms were clues that an active process was occurring

Related Resource

- Ettinger AB, Kanner AM, eds. *Psychiatric issues in epilepsy: a practical guide to diagnosis and treatment.* 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

Drug Brand Names

Bupropion • Wellbutrin
Ciprofloxacin • Cipro
Citalopram • Celexa
Levofloxacin • Levaquin
Olanzapine • Zyprexa
Phenytoin • Dilantin
Zolpidem • Ambien

Disclosures

Dr. Saragoza reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Dr. Maixner receives research/grant support from Neuronetics Inc., and is a speaker for Pfizer Inc., Bristol-Meyers Squibb, Janssen LP, and AstraZeneca.

Clinical Point

Depression may be the most common psychiatric comorbidity in elderly persons with epilepsy

be the most common comorbid psychiatric condition in elderly persons with epilepsy.[13] Indeed, Mrs. D's ultimate diagnosis—NCSE—is characterized by great variability in presentation, ranging from mildly impaired attention and orientation to mood disturbance, speech disturbance, and psychosis. All of these symptoms are seen with seizures.

Further, NCSE can have gradual or sudden onset, varying intensity and duration of symptoms, and fluctuating responsiveness.[14] At least 10% of patients presenting with NCSE have no history of seizures.[15] Precipitating factors include infection and drug toxicity.[14]

In reviewing Mrs. D's case, it is possible that she was in NCSE at her initial presentation, perhaps related to her recent sepsis and subsequent treatment with ciprofloxacin; fluoroquinolones can promote seizures, particularly among elderly patients.[15] By the time Mrs. D was readmitted, her seizures were more dramatic and possibly affected by another fluoroquinolone (levofloxacin) in combination with bupropion.

OUTCOME Dual treatment

During a one-week neurology hospitalization, Mrs. D continues to receive phenytoin. Long-term EEG monitoring reveals she is no longer in status epilepticus. The patient is prescribed citalopram, 10 mg/d, and olanzapine, 2.5 mg at bedtime, to resolve mild depressive symptoms and hallucinosis. Mrs. D is referred for both neurology and psychiatry outpatient follow-up.

References

1. Taylor M. *The fundamentals of clinical neuropsychiatry*. New York, NY: Oxford University Press; 1999:298-324.
2. Gloor P. The role of the limbic system in experiential phenomena of temporal lobe epilepsy. *Ann Neurol* 1982;12(2):129-44.
3. Scheepers M. Epilepsy and behaviour. *Curr Opin Neurol* 2003;16:183-7.
4. Adachi N. Inter-ictal and post-ictal psychoses in frontal lobe epilepsy: a retrospective comparison with psychoses in temporal lobe epilepsy. *Seizure* 2000;9:328-35.
5. Toni C. Psychosensorial and related phenomena in panic disorder and in temporal lobe epilepsy. *Compr Psychiatry* 1996;37(2):125-33.
6. Tucker G. Seizure disorders presenting with psychiatric symptomatology. *Psychiatr Clin North Am* 1998;21(3):626-35.
7. Onuma T. Classification of psychiatric symptoms in patients with epilepsy. *Epilepsia* 2000;41(suppl 9):43-8.
8. Marsh L, Rao V. Psychiatric complications in patients with epilepsy: a review. *Epilepsy Res* 2002;49(1):11-33.
9. Stern T, ed. *Massachusetts General Hospital handbook of general hospital psychiatry*. 5th ed. St. Louis, MO: Mosby; 2004:457-62.
10. O'Sullivan S. The role of the standard EEG in clinical psychiatry. *Human Psychopharmacol Clin Exp* 2006;21:265-71.
11. Gelb D. *Introduction to clinical neurology*. 2nd ed. London, UK: Butterworth Heinemann; 2000:133-4.
12. Marsh CM. Psychiatric presentations of medical illness. *Psychiatr Clin North Am* 1997;20(1):181-2.
13. Cloyd J, Hauser W, Towne A, et al. Epidemiological and medical aspects of epilepsy in the elderly. *Epilepsy Res* 2006;68(suppl 1):S39-48.
14. Riggio S. Nonconvulsive status epilepticus: clinical features and diagnostic challenges. *Psychiatr Clin North Am* 2005;28:653-64.
15. Mehlhorn AJ, Brown DA. Safety concerns with fluoroquinolones. *Ann Pharmacother* 2007;41:1859-66.

Bottom Line

Seizures can be mistaken for anxiety, mood, psychotic, and personality disorders. Be vigilant for the psychosensory symptoms associated with seizures, and consider seizures in the differential diagnosis of patients who present with abrupt onset of psychiatric symptoms.