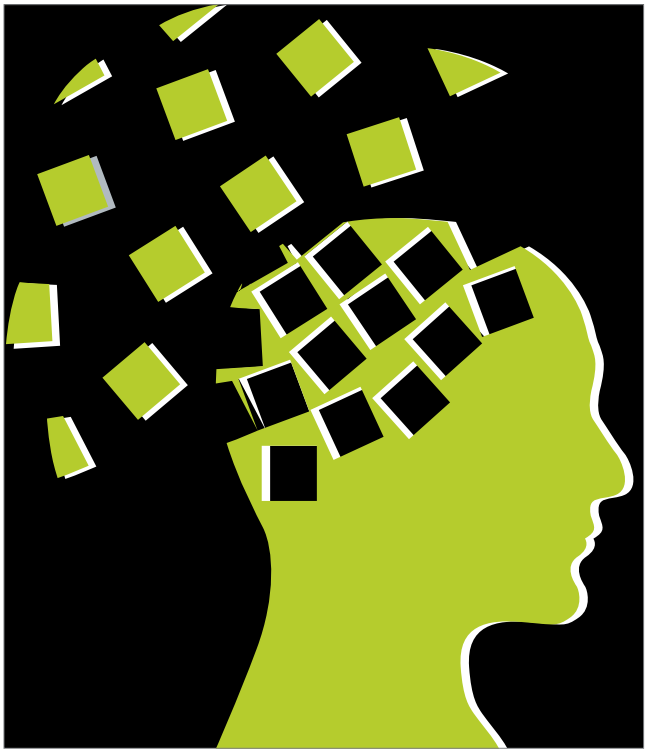
Current PSYCHIATRY

# Evaluating for conversion disorder: When to suspect Creutzfeldt-Jakob disease



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**Jane P. Gagliardi, MD**
Assistant Professor of Psychiatry and Behavioral Sciences
Assistant Professor of Medicine
Duke University School of Medicine
Durham, NC

## Consider this rare disorder in patients with rapid-onset neurologic symptoms

Ms. J, age 63, is admitted to Neurology with progressive dizziness and cognitive impairment. She had developed word-finding difficulties, weakness, memory problems, and an episode of arm shaking, which prompted referral for inpatient workup. Ms. J has a history of hypertension, palpitations, and diabetes mellitus.

Her neurologic examination is variable; some examiners find pronounced aphasia and right-sided weakness, whereas others document a nearly normal examination. Lumbar puncture (LP) shows normal cell count, glucose, protein, and negative Gram's stain; MRI of the brain is normal. Enterovirus polymerase chain reaction, cryptococcal antigen, and Lyme antibody are negative. Electroencephalography (EEG) demonstrates diffuse slowing. The primary team requests psychiatric consultation to assess for conversion disorder.

Ms. J is cooperative with psychiatric evaluation. She denies current or past psychiatric symptomatology and does not meet criteria for major depression, dysthymia, adjustment disorder, anxiety disorder, psychosis, or mania. She denies personal or family history of suicidal or homicidal ideation, intent, or plan. Her youngest son died 5 years earlier; she is financially secure and her 40-year marriage is stable. Ms. J denies having a history of substance use, physical or sexual abuse, or trauma.

In the Cardiology clinic 2 months ago, Ms. J denied having neurologic symptoms and was noted to be doing well. Her neurologic symptoms began shortly after that visit and steadily progressed. She is unable to identify an inciting event or stressor. Ms. J worked until 2 weeks before this admission. Neurologic examination at the time of psychiatric consultation

is notable for waxing and waning expressive aphasia, right homonymous hemianopsia, and mildly decreased strength in the left biceps and forearm.

Ms. J presented to her cardiologist reporting dizziness and blurred vision 6 weeks ago, and she was observed in the hospital 3 weeks earlier for further evaluation. Laboratory testing during that hospitalization included blood counts, basic metabolic panel, thyroid function studies, erythrocyte sedimentation rate, thiamine, folic acid and vitamin B12, rapid plasma reagin and human immunodeficiency virus antibody, and LP, all reported as within normal limits.

Thorough review of Ms. J's medical records reveals abnormalities that would be difficult to ascribe to conversion disorder. Specifically, 6 weeks ago, MRI of the brain demonstrated restricted diffusion in the left occipital lobe, and cerebrospinal fluid (CSF) neuron-specific enolase was moderately elevated at 34 ng/mL. The psychiatric consultant discusses these findings and concern for possible rapidly progressive dementia or Creutzfeldt-Jakob disease (CJD) with the primary team, Ms. J, and her family.

Ms. J is discharged with testing for CSF protein 14-3-3 pending and medical follow-up in 10 days. At follow-up 1 week later, her symptoms are worse; she is completely aphasic and wheelchair-bound. Antithyroglobulin and antimicrosomal thyroid antibodies and paraneoplastic antibody panel return normal. CSF protein 14-3-3 ultimately returns positive, supporting a clinical diagnosis of CJD. Ms. J dies shortly after hospital follow-up, less than 4 months after her first complaint of neurologic symptoms. No autopsy is performed.

Patients with conversion disorder may present with neurologic symptoms such as blindness, seizures, paralysis, or sensory loss with no identifiable anatomical or medical explanation.[1] Conversion seizures—also known as pseudoseizures or nonepileptic seizures—may be clinically indistinguishable from generalized tonic-clonic seizures, but no EEG correlate can be identified.[1,2] Conversion disorder is conceptualized as an unconscious manifestation of psychological conflict or stress—patients are not aware they are producing symptoms—and has been associated with emotional, sexual, and physical trauma.[3,4]

**Table 1**

## Differential diagnosis of rapidly progressive dementia

| |
|---|
| Celiac disease |
| Central nervous system vasculitis |
| Creutzfeldt-Jakob disease |
| Delirium (numerous possible etiologies) |
| Focal status epilepticus |
| Hashimoto's encephalopathy |
| Infection<br>• viral (HSV, EBV, enterovirus, West Nile virus, rabies virus, JC virus, BK virus, HIV)<br>• bacterial (bartonella, mycobacteria, mycoplasma, Whipple's disease)<br>• syphilis<br>• Lyme disease<br>• fungal/parasitic (cryptococcus, trypanosome, malaria, ameba) |
| Intoxication<br>• heavy metal intoxication (arsenic, mercury, aluminum, lithium, lead)<br>• bismuth intoxication |
| Limbic encephalopathy from paraneoplastic antibody syndrome |
| Lymphomatoid granulomatosis |
| Malignancy<br>• central nervous system lymphoma<br>• intravascular lymphoma<br>• gliomatosis cerebri |
| Porphyria |
| Progressive supranuclear palsy |
| Psychiatric disorder<br>• conversion disorder<br>• dementia (Alzheimer's dementia, diffuse Lewy body dementia, frontotemporal dementia with motor neuron disease)<br>• malingering<br>• pseudodementia related to depressive disorder<br>• psychosis |
| Sarcoidosis |
| Stroke |
| Vitamin deficiency (vitamin E, thiamine) |

EBV: Epstein-Barr virus; HIV: human immunodeficiency virus; HSV: herpes simplex virus

**Source:** References 7,8,12

Conversion disorder is a diagnosis of exclusion and requires thorough evaluation to rule out neurologic or medical etiologies. The differential diagnosis for conversion disorder includes the broad medical differential diagnosis for the symptom, whether it be paralysis, seizures, sensory loss, or other presenting symptoms. Therefore, when evaluating patients for conversion disorder, be

**Clinical Point**

**When evaluating for conversion disorder, be vigilant to the possibility of undiscovered medical or neurologic illness**

**Creutzfeldt-Jakob disease**

## Clinical Point

**A rapidly progressing neurodegenerative disorder, CJD is characterized by gait disturbances, akinetic mutism, and myoclonus**

Table 2

### Distinguishing features of Creutzfeldt-Jakob disease

| | Sporadic CJD | AD | DLBD | FTD-MND |
|---|---|---|---|---|
| **Time course** | Rapid progression (median survival 4 to 5 months) | Insidious onset; progressive decline | Insidious onset; progressive decline | May experience rapid course to death |
| **Age at onset** | Age 50 to 70 | Incidence increases with age (usual onset age 65 to 85) | Older (age ~80) | Young age at onset |
| **EEG findings** | Periodic atypical triphasic waves; GPEDs | Normal or diffuse abnormalities | Rarely atypical triphasic waves | Increased slow activity, decreased fast activity |
| **MRI findings** | Restricted diffusion | Generalized atrophy | Generalized atrophy | Frontal atrophy |

AD: Alzheimer's disease; CJD: Creutzfeldt-Jakob disease; DLBD: diffuse Lewy body dementia; EEG: electroencephalography; FTD-MND: frontotemporal dementia with motor neuron disease; GPEDs: generalized periodic epileptiform discharges

**Source:** References 7,8,19

vigilant to the possibility of not only underlying psychological stress or trauma but also undiscovered medical or neurologic illness.

In Ms. J's case, the primary team began to suspect there was no organic cause of her neurologic symptoms. However, psychiatric evaluation revealed that Ms. J had no history of stress or trauma that typically would be associated with conversion disorder, nor did she manifest other psychiatric symptoms, except waxing and waning mental status, which raised concerns for possible delirium or encephalopathy. Additionally, slowing on EEG was a nonspecific but abnormal finding that made conversion disorder unlikely. The consulting psychiatrist discussed this slowing, in conjunction with the abnormal MRI and elevated CSF neuron-specific enolase, with members of the referring Neurology service, who ordered additional testing of CSF for protein 14-3-3.

## Creutzfeldt-Jakob disease

CJD is a rapidly progressive neurodegenerative disorder characterized by cognitive changes, behavioral changes, gait disturbances, akinetic mutism, and myoclonus.[5] CJD results from the transition of prion proteins, which are present in the normal human brain, to disease-associated forms that aggregate and propagate and result in neurotoxicity with spongiform changes in neurons.[6] The transition of normal prions to disease-associated prions may be hereditary, iatrogenic, infectious, or sporadic. Because the pathologic prion protein can be transmitted and normal sterilization procedures do not prevent the spread of CJD, special precautions should be taken to avoid contact with blood or CSF from patients suspected of having CJD.[5]

CJD most commonly occurs in the sporadic form, for which there are no identifiable risk factors, with an average age of onset between age 50 and 70. The disease affects women and men equally at a rate of 1 to 2 persons per million per year worldwide.[6,7] Most patients with CJD die within 12 months of diagnosis[8]; median survival is 4 to 5 months.[7,9] Although there is no approved or standard effective treatment for this uniformly fatal disease, research into the possibility of genetic or post-translational treatments is ongoing. One group reported inhibition of prion propagation by quinacrine and chlorpromazine in vitro.[10] Clinical studies of quinacrine have demonstrated tolerability but no impact on the course of CJD.[6]

**Clues to diagnosis.** Although there is no treatment for CJD, early diagnosis can help patients and families understand the relentless progression of symptoms and also

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**Creutzfeldt-Jakob disease**

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## Related Resources

- National Institute of Neurological Disorders and Stroke. Creutzfeldt-Jakob disease fact sheet. www.ninds.nih.gov/disorders/cjd/detail_cjd.htm.
- Centers for Disease Control and Prevention. About CJD. www.cdc.gov/ncidod/dvrd/cjd.

**Drug Brand Names**

Chlorpromazine • Thorazine, Largactil
Quinacine • Atabrine

**Disclosure**

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

**Clinical Point**

**Elevated levels of CSF neuron-specific enolase and protein 14-3-3 are fairly sensitive and specific for CJD**

permits end-of-life planning and palliative care.[11] Diagnosing CJD requires a high level of suspicion and traditionally has required brain biopsy or autopsy for conclusive diagnosis, although in some cases rare EEG findings of periodic sharp wave complexes or generalized periodic epileptiform discharges (GPEDs) have suggested the diagnosis.[7,8,12] Recently, specific MRI findings have been described with fluid attenuated inversion recovery (FLAIR) and diffusion sequences.[9,13,14]

Routine LP for CSF examination (including cell count, protein, and glucose) frequently is normal.[8] Specific testing to assess for CJD is required. Elevated levels of CSF neuron-specific enolase (normal <30 ng/mL) and protein 14-3-3 (normal <8 ng/mL) are fairly sensitive and specific for CJD when assessed in patients with the proper clinical history, although normal levels of these proteins have been detected in patients later confirmed to have CJD.[7,15] A large multinational collaborative study of confirmed CJD cases that evaluated diagnostic test characteristics recommended that because each test has limitations and can be falsely negative—even in a case of later-confirmed CJD—a rational approach to diagnosis includes brain MRI with diffusion-weighted imaging, CSF analysis for protein 14-3-3, and EEG to assess for periodic sharp wave complexes or GPEDs.[16]

Because CJD presentation varies widely, most clinicians will not consider the diagnosis until the disease has progressed or the patient has died. Patients who present with psychological symptoms or predominant language disturbances and dysphagia may be referred to a psychiatrist or an ear, nose, and throat specialist before seeing a neurologist.[9] Patients may be extensively evaluated and treated for conversion disorder when the correct diagnosis is CJD.[17]

Sporadic CJD traditionally is associated with neurologic presentations, whereas variant CJD is believed to present with psychiatric symptomatology. However, in a 25-year retrospective review of 126 patients with sporadic CJD, 80% of cases demonstrated psychiatric symptoms within the first 100 days of the disease course.[18] Of these, nearly 25% showed psychiatric symptoms at presentation, including sleep disturbances, psychotic symptoms, agitation, and anxiety.

Psychiatrists should be aware of distinguishing features of rapidly progressive dementias and CJD, especially in the setting of psychiatric consultation, to rule out somatic etiologies of unexplained neurologic symptoms. It is important to obtain a history of baseline functioning, duration of decline, and psychiatric symptomatology to differentiate between organic and somatic causes. Differential diagnosis for rapidly progressive cognitive impairment is broad and includes delirium from diverse medical causes; rapidly progressive dementia such as accelerated

# Bottom Line

Conversion disorder is within the differential diagnosis for rapidly progressive dementia but is a diagnosis of exclusion. Creutzfeldt-Jakob disease (CJD) is a rapidly progressive, fatal dementia that may be associated with normal cerebrospinal fluid studies and nonspecific electroencephalography slowing. MRI can be sensitive and specific for CJD if diffusion-weighted imaging and fluid attenuated inversion recovery (FLAIR) sequences are obtained. There is no treatment for CJD.

Alzheimer's disease, Lewy body disease, or frontotemporal dementia; and psychogenic causes, including conversion disorder ***(Table 1, page 79)***.[7,8,12] ***Table 2 (page 80)*** provides distinguishing features of CJD, Alzheimer's disease, Lewy body disease, and frontotemporal dementia with motor neuron disease.[7,8,19]

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**Clinical Point**

**Although there is no treatment for CJD, early diagnosis permits end-of-life planning and palliative care**