The Psychiatric Presentation of Creutzfeldt-Jakob Disease

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Creutzfeldt-Jakob disease (CJD) is a rapidly progressing prion disease. It has various etiologies (sporadic, iatrogenic, acquired, and variant) and a worldwide incidence of about 1 in 1 million per year.[1] Most patients with CJD have psychiatric and behavioral symptoms, and the efficacy of symptomatic treatments is limited.[1,2]

Case Report

A patient in her 60s with a history of congestive heart failure, pulmonary embolism (on anticoagulation), and peripheral vascular disease was sent to the emergency department (ED) by her neurologist due to 1.5 months of visual hallucinations. The hallucinations abruptly started while she was driving. She was initially evaluated by an ophthalmologist who ordered a brain magnetic resonance imaging (MRI) scan and referred her to neurology. The MRI showed increased restricted diffusion involving bilateral occipital/parietal cortices, raising suspicion for CJD. In the ED, she exhibited photophobia, headache, neck spasms, visual hallucinations, myoclonus, and psychomotor agitation.

Computed tomography of the abdomen and pelvis showed a lung nodule concerning for a paraneoplastic syndrome. The patient was admitted with a provisional diagnosis of acute encephalopathy. The differential diagnosis included CJD, a paraneoplastic syndrome, and autoimmune processes. An electroencephalogram (EEG) showed nonepileptic bursts of moderate- to high-voltage generalized polymorphic sharp waves. Lacosamide was started. A lumbar puncture was completed, and cerebrospinal fluid (CSF) was sent for testing. After 48 hours, the patient had worsening myoclonic jerks, visual hallucinations, and psychomotor agitation.

She was started on quetiapine 12.5 mg every 12 hours. On day 5, pulmonology was consulted for the lung nodule. Bronchoscopy with interventional radiology (IR)–guided biopsy showed necrotizing granulomas with yeast forms consistent with histoplasmosis and was negative for malignancy. To treat the infection, intravenous fluconazole was started. On day 6, methylprednisolone was started but was ineffective. On day 13, fluconazole was replaced by itraconazole, and quetiapine was increased to 25 mg each morning and 50 mg nightly. CSF was negative for cryptococcus, cytomegalovirus, enterovirus, *Haemophilus influenzae*, human herpesvirus 6 (HHV-6), xanthochromia, fungus, acid-fast bacilli, and herpes simplex virus types 1 and 2. The *N*-methyl-D-aspartate test was negative. CSF cultures showed no growth. On day 16, CSF was positive for real-time quaking-induced conversion (RT-QuIC), elevated T-tau, and elevated 14-3-3 protein. Symptoms were unchanged. The patient's family opted for comfort measures on day 17. The patient transitioned to palliative care and died soon after.

Discussion

CJD is a rapidly progressing neurodegenerative condition with variable presentation. The most common form is sporadic CJD with a mean age of onset at 55–75 years.[1] Definitive diagnosis requires neuropathological testing. A probable diagnosis can be given for a neuropsychiatric disorder plus CSF positive for RT-QuIC or rapidly progressive dementia plus 2 of the following: visual or cerebellar signs, myoclonus, pyramidal or extrapyramidal signs, or akinetic mutism. Probable diagnosis also requires 14-3-3 protein in CSF, an EEG with polymorphic sharp wave complexes, or MRI with abnormal hyperintensity in at least 2 cortical regions on diffusion-weighted imaging or fluid-attenuated inversion recovery.[1,3] Neurological symptoms typically appear first with behavioral and psychiatric symptoms following, but psychiatric symptoms appear first in up to 20% of patients. Most patients have psychiatric symptoms within 100 days of onset.[4] Symptomatic treatments include selective serotonin reuptake inhibitors for depression, acetylcholinesterase inhibitors for hallucinations, benzodiazepines for agitation, and atypical antipsychotics for agitation, mood, and psychosis.[1] These treatments are marginally successful. No medication class shows improvement in greater than 60% of patients.[2]

This case highlights the difficulty in controlling the symptoms. The patient received increasing doses of quetiapine for agitation and visual hallucinations with limited results. Her myoclonus also worsened. In a large UK study, quetiapine was the most prescribed antipsychotic, and antipsychotics had the most clinical benefit for agitation.[2,5] They are less effective for hallucinations.[2] Given the prevalence and severity of psychiatric and behavioral symptoms in CJD, further research into effective symptomatic treatment is imperative.

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