

Creutzfeldt-Jacob Disease with Presence of Psychomotor Agitation

Yasin Hasan Balcioglu¹,
Mucahid Erdogan²,
Cengiz Dayan²,
Hayrunisa Dilek Atakli²

¹Bakirkoy Training and Research Hospital for Psychiatry
Neurology, and Neurosurgery, Department of
Forensic Psychiatry, Istanbul - Turkey

²Bakirkoy Training and Research Hospital for
Psychiatry Neurology, and Neurosurgery, Department
of Neurology, Istanbul - Turkey

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Address reprint requests to / Yazisma adresi: Yasin Hasan Balcioglu, Bakirkoy Training and Research Hospital for Psychiatry Neurology, and Neurosurgery, Department of Forensic Psychiatry, Dr Tefik Saglam St. 34147, Zuhuratbaba, Bakirkoy/Istanbul, Turkey

Phone / Telefon: +90-212-409-1515/2490

E-mail address / Elektronik posta adresi: yasinhasanbalcioglu@bakirkoyruhsinir.gov.tr

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Dear Editor,

Creutzfeldt-Jacob Disease (CJD) is a rare, prion-associated neurodegenerative disorder characterized by rapidly progressive dementia and neuropsychiatric symptoms. The main clinical presentations are cognitive decline, myoclonus, cerebellar ataxia, visual symptoms, and pyramidal/extrapyramidal signs. Psychiatric symptoms are prominently and frequently manifest in the symptomatology of CJD. Such symptoms were reported to manifest in up to 90% of the patients, with agitation being the most common symptom (64%) (1). Conditions like confusion, mood and behavioral disturbances, psychosis, or depression were also reported with CJD (2). We want to draw attention to the late onset of psychomotor agitation in a patient with CJD and discuss the appropriate

management of psychiatric symptoms. We also aim to discuss possible underlying neural mechanisms of psychomotor agitation in CJD.

A 62-year-old female patient presented approximately one year after sudden onset of lack of memory and blurred speech. She had been followed up with a diagnosis of dementia by our outpatient clinic. Six months after initial symptoms, a mild behavioral disturbance began. Other than a 10mg/daily dose of memantine for the memory deficits, no medication had been initiated for the behavioral problems. The patient was brought to the emergency room by her relatives because of a progressive increase in her uncontrolled behaviors and loss of communication for approximately one and a half months. She did not use any regular medication. In the mental state examination, typical symptoms of organic

brain disease were revealed. She was awake but not alert. Speech output was severely decreased and blurred speech was noted. Her orientation could not be evaluated due to incomprehension. She was not responding to verbal commands. She was immobile, and ophthalmological examination revealed mildly impaired vision, but the remaining cranial nerve examination was not significant. There was no lateralizing sign. Cranial magnetic resonance imaging (MRI) showed a bilateral diffuse, cortical diffusion restriction and bilateral increased signal of putamen and caudate (Figure 1). There was no other medical condition in the history that would explain the symptoms. Preliminary diagnosis of CJD was made and the patient was admitted to the inpatient clinic for further evaluation. No myoclonus was seen while the

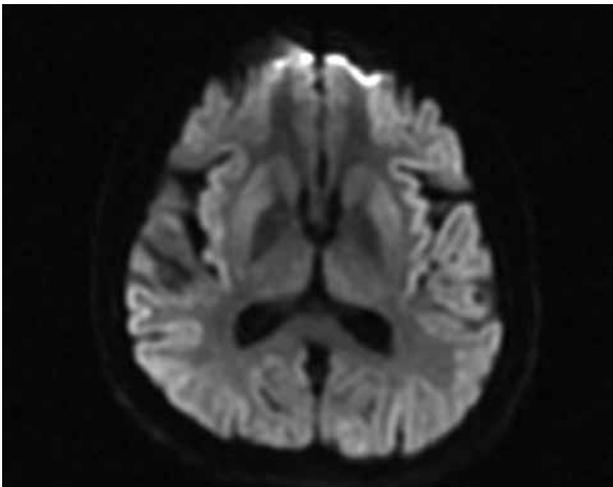


Figure 1: Bilateral diffuse cortical diffusion restriction and bilateral increased signal of basal ganglia in the MRI



Figure 2: Generalized periodic sharp wave complexes recurring in 1-2 seconds frequency on the EEG

patient was in the clinic. She showed psychomotor and vocal agitation during most of the days, and risperidone 2mg/day was initiated. In routine laboratory tests, folate and vitamin B12 deficiency were found and treatment was given. Paraneoplastic panels, neuron-specific enolase (NSE), and protein 14-3-3 tests were done. Further talk with her relatives revealed a history of myocloni appearing a few months ago. The electroencephalogram showed generalized periodic sharp wave complexes occurring every 1-2 seconds (Figure 2). The NSE level was elevated and protein 14-3-3 was negative. The behavioral disturbance resolved with low-dose risperidone. The patient was discharged with memantine and risperidone 2mg/day and she was offered close follow-ups.

Neuropsychiatric symptoms of CJD have effects on the prognosis. Rapidly progressive cognitive deterioration is the main neuropsychiatric symptom of CJD and may even lead to death. Behavioral disturbances such as agitation and aggression are frequently described in dementia with the presence of psychotic features; however, non-psychotic psychomotor disinhibition disturbances have also been recognized in different dementia syndromes (3). Agitation and repetitive vocalizations are commonly considered as startle response in CJD and often coexist with stimulus-sensitive myoclonus, particularly in the later stages of the disease (2). A 25-year analysis of CJD patients reported agitated behavior with a prevalence of 37.3%, similar to other types of dementia (4). Our patient manifested a late-onset behavioral disturbance, which might be deemed unusual for the typical disease course. Psychiatric symptoms are mostly found already at disease onset; however, they might emerge at any time of the illness course (5). While our patient was diagnosed with sporadic CJD, psychiatric symptoms are reported to be less frequent in sporadic CJD than in variant CJD (1). Structural and functional deficits in the specific brain regions and related impaired serotonergic and dopaminergic transmission and receptor activity are blamed for agitated behavior. Serra et al. (6) asserted that cortical gray matter atrophy in the anterior cingulate would be related to agitation

in dementia. In our CJD case, restricted diffusion of cortical structures (ribbon-like) including the cingulate cortex might explain behavioral disinhibition. In a large cohort, greater atrophy of frontal, insular, amygdala, cingulate, and hippocampal regions were associated with the severity of agitation (7). In the management of higher-order loss of behavioral control in CJD, such as psychomotor agitation, irritability, and aberrant vocalizations, the symptomatic approach has been advised. Antipsychotics are known to have apparent clinical benefits (2). We initiated low-dose risperidone, and improvement in psychomotor hyperactivity was seen without any side effects. It is important to consider CJD in differential diagnoses of

new-onset dementia and behavioral disturbances. Abudy et al. (8) showed that 44% of the CJD patients had been misdiagnosed with a psychiatric disorder at the beginning of the illness (8). Psychiatric symptoms such as behavioral disturbances are the major entities that reduce life quality in CJD. Therefore, the early and accurate detection of psychiatric symptoms is essential in patients with CJD, as appropriate management of the symptoms would relieve their distress and lessen the burden on caregivers and healthcare professionals. Further studies with large groups of dementia syndromes are required to demonstrate possible neuroanatomical aspects of behavioral disturbances.

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