A CREUTZFELDT-JAKOB DISEASE CASE PRESENTING WITH PSYCHIATRIC SYMPTOMS

Aşlı Akın Aslan¹, Arda Karagöl², Gökben Hızlı Sayar³, Ebru Bilge Dirik⁴

Abstract

Creutzfeldt Jakob Disease is an incurable and invariably fatal degenerative brain disease. Sporadic and variant forms of the disease can be observed among patients. We report on a patient for calling attention to clinical features and laboratory findings of Creutzfeldt-Jakob Disease and the psychiatric prodromal symptoms. This case demonstrates that psychiatric symptoms may also be a presenting symptom of Creutzfeldt-Jakob Disease and this diagnosis should be considered when rapid deterioration in cognition is observed with presence of psychiatric and neurological symptoms.

Keywords: Creutzfeldt-Jakob disease; diagnosis; psychiatric presentation

1. Introduction

Creutzfeldt-Jakob Disease (CJD) is an incurable and invariably fatal degenerative brain disease. It is a well-known cause of rapidly progressive dementia. Most victims die six months after initial symptoms appear, often of pneumonia due to impaired coughing reflexes. About 15% of patients survive two or more years (Puoti et al., 2012). Definite diagnosis of CJD requires tissue diagnosis showing spongiform degeneration, astrocytic gliosis, amyloid plaques and lack of inflammatory response (Ozen, 2007). The symptoms of CJD are caused by the progressive death of the brain’s nerve cells, which is associated with the build-up of abnormal prion proteins forming amyloids (Poser et al., 2000). It is not feasible to conduct a tissue biopsy in all suspected cases so various diagnostic criteria have been proposed (Newey, Sarwal, Wisco, Alam, & Lederman, 2013).

CJD is the most common prion disease with an incidence of about 1-2 persons/million people/year (Branden, Salomon, Capek, Vaillant, & Alpérovitch, 2009). Sporadic (85% of cases), genetic (10-15%) and variant (iatrogenic and acquired, more likely to be acquired, result from transmission of causative agent by contaminated surgical equipment or as a result of cornea, dura mater transplants or administration of human derived pituitary growth hormones) forms exist (Irons, Ritchie, & Head, 2005). We would like to report the clinical characteristics of a “probable” CJD case to demonstrate the diagnostic workup and to call attention to clinical presentation with early psychiatric symptoms.

2. Case

A 60-year-old male, married, farmer, referred by a general practitioner with a two months history of agitation, restlessness, increased speech, distractibility, insomnia and increased self-esteem. According to his family, several months before the other complaints, he suffered from personality changes, insomnia and talkativeness. For the last 10 days, he had severe insomnia, increased sexual arousal, transient disorientation, short term memory impairment and confabulation. He presented grandiose and paranoid delusions as fear of being killed by the ones jealous of his work. He didn’t have any history of smoking or alcohol/substance abuse. He didn’t have any medical history and there were not any psychiatric or neurological disease in his family.

¹Uz. Dr. Başkent Üniversitesi Zübeyde Hanım Hastanesi, Psikiyatri Anabilim Dalı, İzmir
²Uz. Dr. Atatürk Eğitim ve Araştırma Hastanesi, Psikiyatri Kliniği, Ankara
³Yrd. Doç. Dr. Üsküdar Üniversitesi, NPIstanbul Hastanesi, İstanbul
⁴Uz Dr Atatürk Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, Ankara
Corresponding Author: Gökben Hızlı Sayar E-mail adress: gokben.hizlisayar@uskudar.edu.tr
His family stated that he was diagnosed as "anxiety disorder" and was put on citalopram 20 mg/day treatment 4 weeks ago. But after a week, due to failure in improvement of his complaints, general practitioner referred him to psychiatric unit. Psychiatric examination revealed increased psychomotor activity, pressured and increased speech, labile affect, grandiose thoughts and overinvolvement of routine daily events. Computerized tomography of brain and EEG revealed normal findings. His Mini Mental Test score was 15. He was prediagnosed as "Bipolar affective disorder, manic episode" and a treatment of olanzapine 10 mg/day was initiated. Olanzapine dose was increased to 20 mg/day soon after. Unfortunately, the complaints did not relieve. His neurological symptoms, such as disorientation, bilateral dysmetria and cerebellar ataxic gait added to clinical presentation so he was hospitalized in neurology department to investigate the etiology. Quetiapine dose was increased to 900 mg/day as there was no significant reduction of agitation and insomnia at the end of the first week.

Contrasted cerebral MRI in T2 sequences showed frontal periventricular ischemic-gliotic areas and bilateral hyperintensity in caudate and putaminal nuclei. Moreover, diffusion MRI revealed hyperintensity right lentiform nucleus. In EEG tracing bilateral periodic sharp wave complexes observed. The laboratory workup did not show any autoimmune, metabolic or infectious etiology. Complete blood count, thyroid function tests, complete urine analysis, tumor markers including PSA, CEA, CA 19-9, CA-125, CA 15-3, hepatitis markers, anti HIV, VDRL, TPHA, Anti dsDNA, antcardiolipin IgM and IgG, mycobacterium PCR, CSF culture and Wright staining did not reveal any significant results as well. In cerebrospinal fluid (CSF) screening was also normal and tested negative for the P 14.3.3 protein. Gram staining, mycobacterium PCR, CSF culture and Wright staining did not reveal any significant results as well.

During the tenth day of the hospitalization he experienced generalized sudden jerks provoked by sounds and soon after sounds and soon after he had a focal motor seizure observed as tonic clonic contractions in his left upper extremity while he was asleep. His left arm while asleep. He presented ataxia, which worsened in a week. Visual hallucinations, akinetic mutism, urinary incontinence were added to the clinical course. At the end of the third week of hospitalization; cardiac failure occurred. Hepatic and renal function tests rapidly deteriorated. Unfortunately he died on the 32nd day of hospitalization in a state of akinetic mutism.

Patient’s symptoms, laboratory findings and clinical diagnosis in different phases of the disease were presented on Table 2.

### 3. Discussion

The clinical features of this case were consistent with previous descriptions of CJD. The final diagnosis was "probable sporadic CJD" according to the WHO and European MRI-CJD consortium criteria (WHO, 1998; Zerr et al., 2009). MRI-CJD consortium criteria for sporadic CJD are given on Table 1. Psychiatric symptoms, mainly depression and anxiety, occur in the clinical course in about one third of cases of sporadic CJD (Kurne et al., 2005). Rapidly progressing neurological symptoms including ataxia, myoclonus, cognitive impairment and akinetic mutism might be presented after the psychiatric symptoms. Clinical reports have described the early appearance of psychiatric symptoms in sporadic CJD, including paranoid psychosis (Dunn, Alfonso, Young, Isakov, & Lefer, 1999), mania (Lendvai, Saravay, & Steinberg, 1999), and depression (Jardri, DiPaola, Lajugie, Thomas, & Goeb, 2006). Schizophreniform disorders have been described during the clinical course, with auditory and visual hallucinations and paranoid delusions (Ali, Baborie, Larner, & White, 2013).

### Table 1. MRI-CJD Consortium criteria for sporadic CJD

<table>
<thead>
<tr>
<th>III. Clinical Signs</th>
<th>I. Clinical Signs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>dementia</td>
<td>• dementia</td>
<td></td>
</tr>
<tr>
<td>cerebellar or visual</td>
<td>• cerebellar or visual</td>
<td></td>
</tr>
<tr>
<td>pyramidal or extrapyramidal</td>
<td>• pyramidal or extrapyramidal</td>
<td></td>
</tr>
<tr>
<td>akinetic mutism</td>
<td>• akinetic mutism</td>
<td></td>
</tr>
<tr>
<td>II. Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>periodic sharp wave complexes in EEG</td>
<td>• periodic sharp wave complexes in EEG</td>
<td></td>
</tr>
<tr>
<td>14-3-3 detection in CSF (in patients with a disease duration of &lt; 2 years)</td>
<td>• 14-3-3 detection in CSF (in patients with a disease duration of &lt; 2 years)</td>
<td></td>
</tr>
<tr>
<td>high signal abnormalities in caudate nucleus and putamen or at least two cortical regions</td>
<td>• high signal abnormalities in caudate nucleus and putamen or at least two cortical regions</td>
<td></td>
</tr>
</tbody>
</table>

Probable CJD: two out of I and at least one out of II
Possible CJD: two out of I and duration less than 2 years

In this case in the prodromal phase psychiatric symptoms of the CJD (pressured speech, increased sexual arousal, increased energy, and decreased sleep) are prominent. Although there is only one CJD patient in the literature that was presented with manic symptoms, Lendvai et al suggested that familial predisposition could be the cause

### Table 2. Patient’s symptoms, laboratory findings and clinical diagnosis in different phases of the disease

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prodomal</th>
<th>Early phase</th>
<th>Late phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety disorder</td>
<td></td>
<td>Insomnia, increased speech and sexual arousal, transient memory impairment</td>
<td>Rapid progressive dementia, disorientation hallucinations</td>
</tr>
<tr>
<td>Bipolar affective disorder, manic episode</td>
<td>Ataxia</td>
<td>Myoclonic jerks urinary incontinence, akinetic mutism</td>
<td></td>
</tr>
<tr>
<td>CJD</td>
<td>Normal Brain CT, Normal EEG</td>
<td>Brain MRI: hyperintensity of putamen EEG: Periodic sharp wave complexes</td>
<td></td>
</tr>
</tbody>
</table>
of manic presentation on that case (Lendvai, Saravay, & Steinberg, 1999).

Our patient did not have any depressive or manic episode history; so his mood state was considered as secondary mania. Secondary mania can occur with physical illness; medications (e.g., bronchodilators, corticosteroids); metabolic disturbances (e.g., vitamin B12 deficiency, thyrotoxicosis); neoplasms, central nervous system diseases (e.g., Parkinson disease, cerebritis due to lupus, multiple sclerosis, epilepsy, cerebrovascular accident); and infections (e.g., neurosyphilis, HIV, influenza) (Price, & Marzani-Nissen, 2012). Nakimu-Mpngu et al. reported that in the majority of HIV-positive patients presenting with mania, the mania is secondary to HIV infection and that its presentation and correlates differ from those of HIV-negative patients with primary mania (Nakimu-Mpngu, Musisi, Mpungu, & Katabira, 2006).

Although the 14-3-3 test negativity did not support our diagnosis, it is suggested to evaluate the test with clinical correlation since the test can be false negative or false positive and cannot rule out the CJD (Cuadrado-Corales et al., 2006). EEG is the best available auxiliary means of diagnosing sporadic CJD, with a reported sensitivity of around 60% (Collins et al., 2006). The typical EEG in sporadic CJD is characterized by periodic or periodic/periodic sharp wave complexes. These complexes tend to arise in the middle and late stages of disease; diffuse slowing and frontal rhythmic delta activity are often recorded in early stages (Hansen, Zschocke, Stürenburg, & Kunze, 1998). The finding of asymmetric hyperintensity on diffuse weight imaging in at least three cortical non-contiguous gyri or in the striatum (caudate and rostral part of the putamen), or both, is highly suggestive of sporadic CJD. On the basis of these criteria, MRI has proven to be an accurate diagnostic test (1).

This case reminds us that sporadic CJD patients may initially present with psychiatric symptoms. Clinicians should pay attention to subtle neurological signs in patients with atypical mood disorder. Utilizing investigations including EEG, 14-3-3 protein detection in CSF and MRI could help clinicians to make more precise and earlier diagnosis of CJD.

4. Conclusion

The first symptoms of this patient were purely psychiatric and difficult to distinguish from common psychiatric disorders. As sporadic CJD can present with psychiatric symptoms, this diagnosis should be considered when there is rapid deterioration in cognition with fleeting psychiatric symptoms and the presence of neurological symptoms.

References


