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Case Report

A Case of Sporadic Creutzfeldt-Jakob Disease Mimicking Variant Form

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Abstract

Creutzfeldt-Jakob Disease (CJD) is a rare neurodegenerative disease that causes a rapidly progressive dementia, and it can be classified as sporadic, heritable, and variant (acquired). In this paper, we report a case mimicking variant CJD, with phenotypic presentation and findings. A 44-year-old man was admitted to the emergency department with progressive neuropsychiatric symptoms and myoclonus. Signal hyperintensity in the bilateral basal ganglia and thalamus was detected via fluid attenuated inversion recovery (FLAIR) sequence and diffusion weighted magnetic resonance. 14.3.3 protein in cerebrospinal fluid was negative, and electroencephalography was atypical for sporadic CJD. After the diagnostic tests and follow-up, the patient was diagnosed with probable sporadic CJD, based on the World Health Organization's (WHO) diagnostic criteria. His health deteriorated rapidly, and the patient died 2 months after the diagnosis. In this paper, we point out the differences between and the signs of variant CJD and sporadic CJD. When pathological confirmation is not possible, as in case of our patient, it is very helpful to consider the WHO diagnostic criteria. Variant CJD is a disorder that has not been reported in Turkey yet. Its diagnosis and reporting require direct interventions by the health and veterinary authorities.

Keywords: Prion, variant Creutzfeldt-Jakob Disease, pulvinar sign

Introduction

Creutzfeldt-Jakob disease (CJD) is a rare, rapid, and progressive fatal human prion disease, affecting annually 1-2 persons per million worldwide. In addition to abnormal protein accumulation, CJD is characterized by neuronal loss, gliosis, and spongioform changes. CJD is classified as sporadic, genetic, iatrogenic, and variant CJD (1). In this report, we will discuss a patient on phenotypic expression of sporadic and variant CJD.

Whereas the majority of CJD cases (about 85%) occur as sporadic disease, clinical presentation of sporadic CJD is highly variable. CJD shows a broad range of symptoms, but the disease begins with cognitive and cerebellar symptoms in most of cases. Visual changes and extrapyramidal and pyramidal signs are less frequently seen as initial manifestations (1, 2). Myoclonus occurs during the clinical course in approximately 90% of cases, and the disease eventually progresses to akinetic mutism in all patients. In most of cases, the disease lasts less than a year, but the course of sporadic CJD depends on polymorphisms in PRNP codon 129 and the type of protease-K resistant prion (3).

Variant CJD was identified in 1996 attracting attention as a casually link to bovine spongioform encephalopathy (4). Variant CJD is still the only example of an infectious disease crossing from bovines to humans. In contrast to the sporadic CJD, clinical presentation of variant CJD is unique almost in all cases, and diagnosis could be predicted confidently by clinical findings and neuroimaging (5). Persistent sensory symptoms, early psychiatric symptoms, chorea, and upgaze paresis are much more common in variant CJD, whereas early forgetfulness and ataxia are relatively uncommon (6).

Case Report

A 44-year-old man was admitted to our emergency department complaining of dizziness, fatigue, and difficulties at walking. The history revealed complaints that started 2 months before. Dizziness and behavioral symptoms started 2 weeks after the upper-respiratory-tract infection. There were occult behavioral symptoms present, including agitation, anxiety, and bizarre new ideas, and there was not past psychiatric disorder history. Patient had been using ketiapin 200 mg/day for a week, as recommended by a psychiatric specialist, and he was admitted to our hospital due to worsening of symptoms, as proposed by a psychiatrist. There was no past illness history and family history of dementia or a neuropsychiatric disease. During the neurologic examination,

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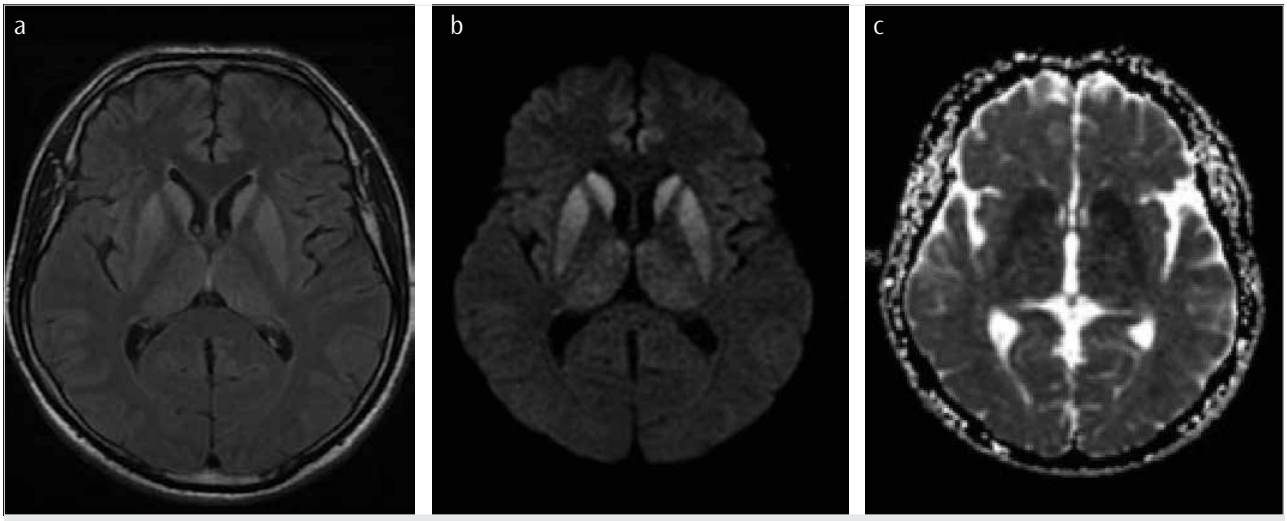

Resim 1. a-c. Brain magnetic resonance imaging (MRI) shows bilateral striatal and thalamic hyperintensities. (a) Fluid attenuated inversion recovery (FLAIR) sequence and, (b) diffusion weighted imaging show bilateral striatal and thalamic hyperintensities, (c) apparent diffusion coefficient map shows striatal and mildly thalamic hypointensity. Also note that anterior putamen and caudate are more hyperintense than the thalamus

cooperation and orientation were normal, marked photophobia was present, whereas cranial nerve examination showed bilateral upper-gaze palsy and prominent truncal ataxia. Myoclonic jerks were present in the upper extremities and facial muscles, particularly periocular muscles, nearly continuous. The patient was hospitalized, and magnetic resonance imaging (MRI) and laboratory tests were performed. MRI diffusion weighted and fluid attenuated inversion recovery (FLAIR) sequence showed hyperintensity at symmetrically bilateral thalamus, and caudate and lentiform nucleus (Figure 1). Laboratory findings, including serum biochemistry, hemogram, liver and kidney function test, thyroid function test, vitamin B12 and folate levels, were within the n ormal limits. Electroencephalography (EEG) showed alpha and tetha rhythm and generalize slowing, and there was no periodic sharp continuous wave activity and/or other epileptiform discharge. Lumbar puncture was performed; cerebrospinal fluid (CSF) opening pressure, glucose, and protein levels were within a normal range, and 14.3.3 protein was negative. Patient's condition deteriorated rapidly, and at the 2-month follow-up, akinetic mutism developed. The patient was fed through percutaneous endoscopic gastrostomy catheter. Two weeks later, the patient was transferred to the intensive care unit because of a respiratory failure, and he died 2 months later. Written consent was obtained from patient's relatives.

Discussion

Our goal was to discuss this case in the light of phenotypic characteristics and features that distinguish sporadic CJD from variant CJD. The young age at onset, early presentation with psychiatric disturbances, upgaze paresis, atypical EEG, negative 14.3.3 protein in CSF and MRI diffusion hyperintensities at thalamus, and caudate and lentiform nucleus alerted us for variant CJD probability. To our knowledge, there is only one probable case of variant CJD in Turkey reported in 2011 without pathological confirmation (7). We did not consider the MRI of our patient to be concordant with variant CJD. The WHO listed diagnostic criteria for variant CJD in 2001 (6). In this report, definite variant CJD diagnosis is based on a progressive neuropsychiatric disorder and pathologic confirmation. Variant CJD diagnosis is probable if (a) the illness lasts longer than 6 months and other typical clinical signs for variant CJD occur; (b) EEG does not show the clinical characteristics of sporadic CJD; and (c) MRI shows bilateral symmetrical pulvinar high signals. The most important segment of the MRI criteria is "pulvinar sign." Although other conditions may also cause thalamic and other gray matter hyperintensities, in variant CJD, the highest signal is always in the pulvinar of the thalamus, and this is an essential distinguishing feature. The pulvinar sign has a 90% sensitivity for the diagnosis of variant CJD, and the specificity of the pulvinar sign is over 95%. The pulvinar sign is the best noninvasive in vivo diagnostic test for variant CJD. Will R. G. reported that all the cases fulfilling these criteria, including MRI features for probable variant CJD, have been confirmed pathologically as variant CJD (4). Although there is one case of probable variant CJD reported in Turkey (7), the MRI did not show the characteristic "pulvinar sign." Will RG (8) also discussed this report and assumed that this case cannot be regarded as variant CJD unless there is a neuropathological verification. Thus far, Turkey is geographically regarded as variant-CJD unreported area.

With regard to our case, we assumed that it was sporadic CJD with some peculiar findings. These findings could be attributed to young-age onset or a molecular subtype based on the polymorphisms in PRNP codon 129 (2). We could not perform autopsy because the family did not approve it. We did not plan tonsil biopsy because neuropsychiatric complaints lasted less than 6 months, although other clinical findings, EEG and CSF, were atypical for sporadic CJD.

Conclusion

It is important to diagnose and report variant CJD in our country if it exists, because even one case of this infectious lethal disease would require a prompt action by state health and veterinary authorities. Ultimately, we believe and point out that when it is not possible to perform biopsy, like in case of our patient, the WHO diagnostic criteria could prevent misdiagnosis of variant CJD. Diagnostic criteria are especially important in countries where performing an autopsy is challenging.

Informed Consent: Written informed consent was obtained from the relatives of the patient who participated in this study.

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