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A Difficult Diagnosis in Emergency Department: Creutzfeldt–Jakob Disease

Acil Serviste Zor Bir Tanı: Creutzfeldt-Jakob Hastalığı

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ABSTRACT

Introduction: Prion diseases are a group of diseases that affect the human brain tissue and cause characteristic spongiform changes. Creutzfeldt-Jakob Disease (CJD) is the most common type of this group of diseases. The diagnosis of CJD is very difficult particularly in emergency department (ED) settings and is mainly based on the exclusion of the other causes of ongoing mental status changes.

Case Report: We present the case of a 77-year-old female as a sporadic CJD patient who was consulted with the preliminary diagnosis of CJD in ED. The patient was brought to ED with complaints of being unable to get out of bed and urinary and fecal incontinence. Remarkable physical findings included poor general condition, the lack of verbal response, oromandibular dystonia, eye opening and flexor responses of upper extremities to painful stimuli, and choreoathetosis. All findings including progressive neurological symptoms, brain magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, and electroencephalography (EEG) were considered together, and the patient was diagnosed with CJD.

Conclusion: Even if an ED physician could not diagnose CJD in first hand, he/she should keep the level of additional imaging (MRI, CSF analysis, and EEG) and consultation threshold low, particularly in patients with ongoing mental status changes, jerking movements, and dementia.

Keywords: Creutzfeldt-Jakob Disease, prion diseases, dementia, emergency medicine

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ÖZET

Giriş: İnsan beyin dokusunu etkileyerek karakteristik süngerimsi değişikliklere neden olan bir grup hastalık prion hastalıkları olarak bilinir. Creutzfeldt-Jakob hastalığı (CJH), bu grup hastalıkların en sık görülen tipidir. Özellikle acil servis (AS) şartlarında bu hastalığın tanısını koymak çok zordur ve tanı, temel olarak devam eden bilinç durum değişikliğinin diğer nedenlerinin ekartasyonuna dayanır.

Olgu Sunumu: AS'de sporadik CJH ön tanısı ile değerlendirilen ve konsülte edilen 77 yaşında kadın bir hastayı sunuyoruz. Hasta AS'ye yataktan kalkamama ve idrar ve gayta inkontinansı şikayetleri ile getirildi. Hastanın fizik ve nörolojik muayenesinde öne çıkan bulgular arasında; kötü genel durum, sözel yanıtsızlık, oromandibular distoni, ağrılı uyaran verilmesi ile üst ekstremitelerde fleksör yanıt, ağrılı uyaranla göz açma ve koreatetotik hareketler mevcuttu. Hastanın devam eden nörolojik semptomları, beyin manyetik rezonans görüntüleme (MRG), beyin omurilik sıvısı (BOS) analizi ve elektroensefalografi (EEG) sonuçları birlikte değerlendirildiğinde, hastaya CJH tanısı kondu.

Sonuç: Her ne kadar AS hekimi CJH tanısını hastayı ilk değerlendirmesinde koyamayacak olsa da, özellikle devam eden mental durum değişikliği, miyoklonik hareketler ve demansı olan hastalarda ek görüntüleme (beyin MRG, BOS analizi, EEG gibi) seçeneklerini kullanma ve konsültasyon eşiğini düşük tutmalıdır.

Anahtar Kelimeler: Creutzfeldt-Jakob hastalığı; prion hastalıkları; demans; acil tıp (MeSH Database)

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Introduction

Prion diseases constitute a group of neurodegenerative diseases and have three main features: rapid progression, long incubation period, and generally fatal outcome (1). Prions can be defined as pathological protein particles, and accumulation of these particles in the brain tissue ultimately cause proliferation of glial cells and neuronal loss. As a result of these characteristic neuropathological changes, the brain tissue undergoes a spongiform degeneration (1).

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Creutzfeldt-Jakob Disease (CJD) is the most common form of human prion diseases. The annual incidence of this disease is 1/1,000,000 worldwide (1, 2). Sporadic, familial, iatrogenic, and variant forms are currently identified as four forms of the disease. Sporadic cases accounts for the majority of the patients (85-95%) (2, 3).

The prognosis is extremely poor and CJD currently has no known effective treatment. Treatment options are very limited and mainly based on only symptom relief. Death usually occurs within the first year from symptom onset and median disease duration is approximately six months (4-6). The diagnosis is very difficult especially in the emergency department (ED) settings due to the non-specific neurological and psychiatric complaints (7). Patients with CJD may have been admitted to EDs several times before a definitive diagnosis is established (7). Here we report a 77-year-old female as a sporadic CJD patient who was consulted with the preliminary diagnosis of CJD and had been misdiagnosed with osteoarthritis at another hospital.

Case Report

A 77-year-old female patient admitted to ED with complaints of loss of speech, difficulty in walking, and urinary and fecal incontinence. Patient's relatives stated that these symptoms started six months ago. New complaints, such as pale expressions, slow physical movements, lack of attention to daily activities, jerky movements, and loss of speech while communicating with other people, added progressively to this clinical status during the last three months. The patient experienced several falls inside her home and outside because of dizziness and loss of balance. She was admitted to and discharged from another hospital with the diagnosis of osteoarthritis a week ago. The patient was brought to our ED with complaints of inability of getting out from the bed and urinary and fecal incontinence. She had a medical history of diabetes mellitus and took oral antidiabetic drug. The patient had no recent travel history but had lived in Germany for many years. Physical examination revealed normal vital signs. Remarkable physical and neurological examination findings included poor general condition, lack of verbal response, oromandibular dystonia, eye opening and flexor responses of upper extremities to painful stimuli, choreoathetotic movements, especially in the upper extremities and trunk, and flexor plantar reflexes. The neck was supple without signs of meningismus. There was no pathological reflex. Sensory and cerebellar examination could not be evaluated. Bedside fundus examination with a direct ophthalmoscope revealed no papilledema. Laboratory evaluation including complete blood count, liver, kidney, and thyroid function tests, serum electrolyte and hemostasis levels, electrocardiogram, computed tomography of head and urinalysis revealed no abnormality. During her ED admission, magnetic resonance imaging (MRI) (Philips Infinion 1.5 Tesla; Amsterdam, Netherlands) with diffusion-weighted images (DWI) of the brain revealed high signal intensity predominantly in the bilateral caudate nucleus, putamen, posteromedial thalamus, and frontal cortex (Figure 1a, 1b). Neurology department was consulted with the preliminary diagnoses of dementia, demyelinating disease, viral encephalitis, and prion disease. After consultation, the neurology service admitted the patient for further evaluation. During her hospital admission, lumbar puncture revealed elevated 14-3-3 protein level in cerebrospinal fluid (CSF). Other results of CSF analysis were completely normal. On second day of admission, an electroencephalogram (EEG) showed persistent rhythmic triphasic sharp wave activity and disseminated severe deceleration cerebral bioelectric activities. All these findings including progressive neurological symptoms, findings of MRI, CSF analysis, and EEG were considered together, and the patient was diagnosed with CJD. During follow-up, the patient developed myoclonic seizures and deceased on 40th day of admission. Written informed consent was obtained from the patient's son for this case report.

Discussion

There are five prion diseases affecting the human brain that are currently identified in the literature. These diseases are CJD, variant CJD, kuru, fatal familial insomnia, and Gerstmann-Sträussler-Scheinker syndrome (1). The common characteristic feature of all these disorders is progressive death of neurons. Amyloid deposits produced by the abnormal prion proteins are the main reason of this neuronal death (1). CJD accounts for the majority of the spongiform encephalopathies and may be sporadic, hereditary, or acquired (iatrogenic and variant) (2, 3). Sporadic CJD is the most common type of the disease, but the exact cause is unclear (2, 3). The mean age for the onset of the symptoms of CJD is between 57-62 years (2).

Some significant features that may be considered as a risk factor for sporadic CJD cases are as follows: history of psychosis, multiple surgical procedures, having lived for more than 10 years on a farm, and presence of family history of CJD (8, 9). The presented patient did not have these risk factors, but had lived in Europe for many years. The two major clinical features of CJD are myoclonus and rapidly progressive deterioration of mental status. The most important components of mental status deterioration are dementia, behavioral abnormalities, and higher cortical dysfunctions. Dementia causing loss of memory, personality changes, and hallucinations is usually the first symptom of the disease. Disturbances in gait, posture, balance, and coordination are also among the common symptoms. On an average, death usually occurs a year after the onset of symptoms (4). The symptoms of our patient started within 6 months and were consistent with the literature.

It is difficult to diagnose CJD at ED settings. The differential diagnostic list is long and comprises toxic and metabolic encephalopathies, central nervous system infections, including menengitis or encephalitis, seizure disorders and status epilepticus, demyelinating diseases, dementia, central nervous system vasculitis, and psychiatric disease, including depression (5). Although initial laboratory and imaging results revealed no pathology in ED, our patient underwent MRI due to ongoing disturbances of consciousness, which revealed the characteristic pathologic findings.

The gold standard diagnostic test for CJD is performing a brain biopsy. However, brain biopsy is not a widely used diagnostic tool in our country and is often associated with post-mortem processes. The patient presented here also did not undergo brain biopsy. However, a number of clinical and laboratory features are potentially

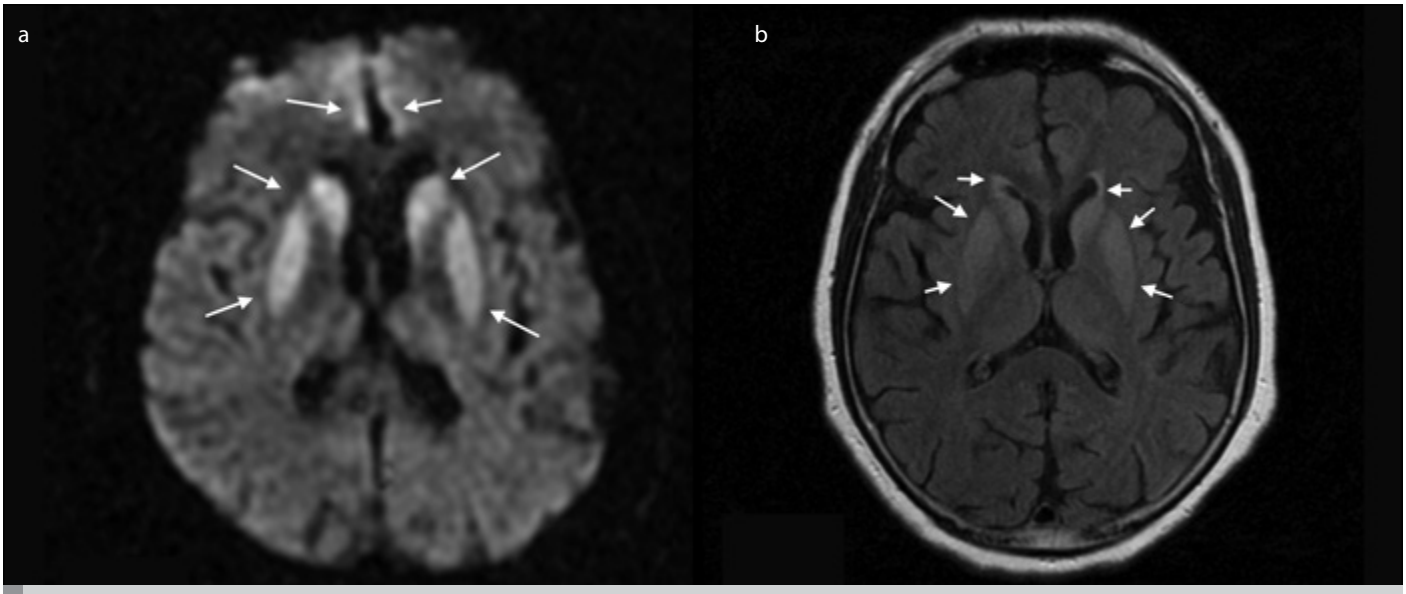

Figure 1. a, b. MRI of the brain with DWI sequences images show increased signal intensity predominantly in the bilateral caudate nucleus, putamen, posteromedial thalamus, and frontal cortex (a), MRI of the brain with FLAIR sequences images show increased signal intensity predominantly in the bilateral caudate nucleus, putamen, posteromedial thalamus, and frontal cortex (b)

available and accepted for probable diagnosis of sporadic CJD cases. These criteria generally include progressive dementia, atypical EEG findings, positive 14-3-3 protein levels in CSF analysis, high signal abnormalities in caudate nucleus and/or putamen on DWI or fluid attenuated inversion recovery MRI, and exclusion of potential alternative diagnoses (10). CJD is a highly fatal disease and currently has no known effective treatment (10). Our patient deceased shortly after approximately six months from the onset of the symptoms.

Conclusion

In conclusion, even if the ED physician does not diagnose CJD at first, he/she should keep the level of additional imaging and consultation threshold low, especially in patients with ongoing mental status changes, jerking movements (myoclonus), and dementia. CJD is a very rare cause of mental status deterioration in ED; however, we should consider that CJD may be the underlying etiology in patients who have unclear cause of mental status changes or have frequent hospital admissions before definitive diagnosis.

Informed Consent: Written informed consent was obtained from the patient's son who participated in this case.

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References

1. Puoti G, Bizzi A, Forloni G, Safar JG, Tagliavini F, Gambetti P. Sporadic human prion diseases: molecular insights and diagnosis. Lancet Neurol 2012; 11: 618-28. [CrossRef]
2. Ladogana A, Puopolo M, Croes EA, Budka H, Jarius C, Collins S, et al. Mortality from Creutzfeldt-Jakob disease and related disorders in Europe, Australia, and Canada. Neurology 2005; 64: 1586-91. [CrossRef]
3. Masters CL, Harris JO, Gajdusek DC, Gibbs CJ Jr, Bernoulli C, Asher DM. Creutzfeldt-Jakob disease: patterns of worldwide occurrence and the significance of familial and sporadic clustering. Ann Neurol 1979; 5: 177-88. [CrossRef]
4. Haywood AM. Transmissible spongiform encephalopathies. N Engl J Med 1997; 337: 1821-8. [CrossRef]
5. Heinemann U, Krasnianski A, Meissner B, Varges D, Kallenberg K, Schulz-Schaeffer WJ, et al. Creutzfeldt-Jakob disease in Germany: a prospective 12-year surveillance. Brain 2007; 130: 1350-9. [CrossRef]
6. Pocchiari M, Puopolo M, Croes EA, Budka H, Gelpi E, Collins S, et al. Predictors of survival in sporadic Creutzfeldt-Jakob disease and other human transmissible spongiform encephalopathies. Brain 2004; 127: 2348-59. [CrossRef]
7. Clendenin J, Lall M. Creutzfeldt-Jacob Disease: An Emergency Department Presentation. American Journal of Emergency Medicine (2014). [CrossRef]
8. Wientjens DP, Davanipour Z, Hofman A, Kondo K, Matthews WB, Will RG. Risk factors for Creutzfeldt-Jakob disease: a reanalysis of case-control studies. Neurology 1996; 46: 1287-91. [CrossRef]
9. Collins S, Law MG, Fletcher A, Boyd A, Kaldor J, Masters CL. Surgical treatment and risk of sporadic Creutzfeldt-Jakob disease: a case-control study. Lancet 1999; 353: 693-7. [CrossRef]
10. CDC's Diagnostic Criteria for Creutzfeldt-Jakob Disease (CJD), 2010 http://www.cdc.gov/ncidod/dvrd/cjd/diagnostic_criteria.html (Accessed on October 27, 2014).