



# Creutzfeldt-Jacob's Disease Presenting with Psychiatric Symptoms and Severe Itching

## *Psikiyatrik Semptomlar ve Kaşıntı ile Prezente Olan Creutzfeldt-Jakob Olgusu*

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### Summary

Creutzfeldt-Jacob's disease is a rare and fatal neurodegenerative disease characterized by the accumulation of abnormal prion-like proteins in the central nervous system. Clinical features, electroencephalography (EEG), magnetic brain resonance imaging (MRI) and protein 14.3.3 is used in diagnosis. Protein 14.3.3 may be negative in the early or late stages of the disease. Presentation with psychiatric symptoms and itching is not typical in the onset of the disease. Here we present a patient who was first admitted to the pschiatry clinic due to his psychiatric symptoms and had severe itching resistant to antihistamine treatment. (Turkish Journal of Neurology 2013; 19:25-7)

**Key Words:** Creutzfeldt-Jacob's Disease (CJD), pruritus, psychiatric symptoms

### Özet

Creutzfeldt-Jakob Hastalığı, nadir görülen, fatal nörodejeneratif bir hastalık olup santral sinir sisteminde patolojik prion proteinlerinin birikimi ile karakterizedir. Hastalığın tanısı klinik, elektroensefalografi (EEG), kraniyal MRG ve 14.3.3 proteini incelemeleri ile konur. Protein 14.3.3, hastalığın erken veya geç fazında negatif olabilmektedir. Psikiyatrik bulgular ve kaşıntı ile klinik başlangıç hastalık için tipik değildir. Bu yazıda psikiyatrik bulguları nedeniyle psikiyatri kliniğine yatırılan ve antihistaminik ile tedaviye dirençli kaşıntı şikayeti olan bir hasta sunulmuştur. (Türk Nöroloji Dergisi 2013; 19:25-7)

**Anahtar Kelimeler:** Creutzfeldt-Jakob Hastalığı (CJD), kaşıntı, psikiyatrik belirtiler

### Introduction

Creutzfeldt-Jacob's disease (CJD) is a rare and fatal neurodegenerative disease characterized by the accumulation of abnormal prion-like proteins in the central nervous system (CNS). CJD is the most frequently seen type of prion disease. In the early stages of the disease, patients may have memory impairment, behavioural changes, lack of coordination and visual disturbances. As the illness progresses, mental deterioration becomes pronounced and involuntary movements, blindness, weakness in extremities and coma may be seen. Definitive diagnosis is made by periodical spikes in electroencephalography (EEG), cortical signal alterations during diffusion weighted magnetic resonance imaging (DW-MRI) studies, detection of protein 14.3.3 in cerebrospinal fluid (CSF) and with histological examination of brain biopsy or autopsy materials.

Sporadic CJD is the most common form of the human prion diseases and psychiatric symptoms may usually accompany the neurological findings. Although pruritis is a common feature in animal prion diseases, it has rarely been reported in humans with CJD, especially in the sporadic form.

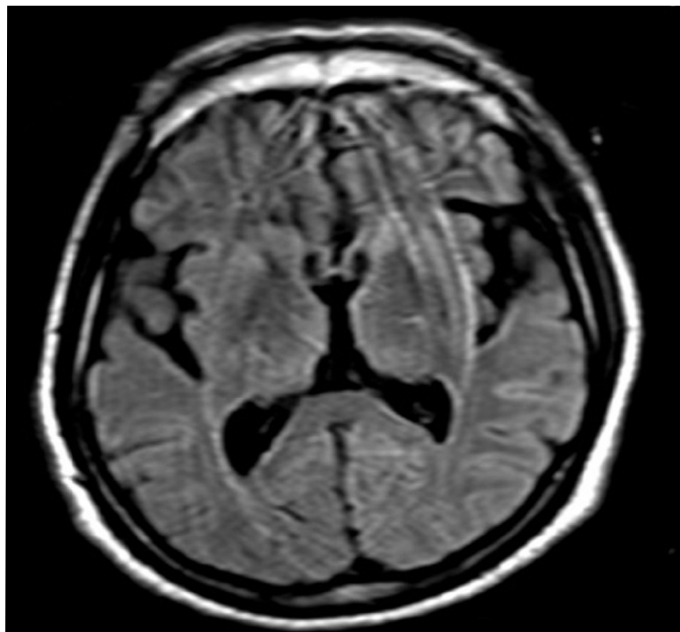
### Case Report

A previously highly functioning 56-year old male physics teacher experienced complaints including personality changes, insomnia, extreme anxiety, locking himself in his room, difficulty in writing, speaking, and reading, gait imbalance, frequent falls, irritability, difficulty in recognizing his wife and other relatives, poor concentration, progressive memory loss and itching. His itching was resistant to antihistamine treatment and was not of allergic nature. Three months after the onset of his symptoms,

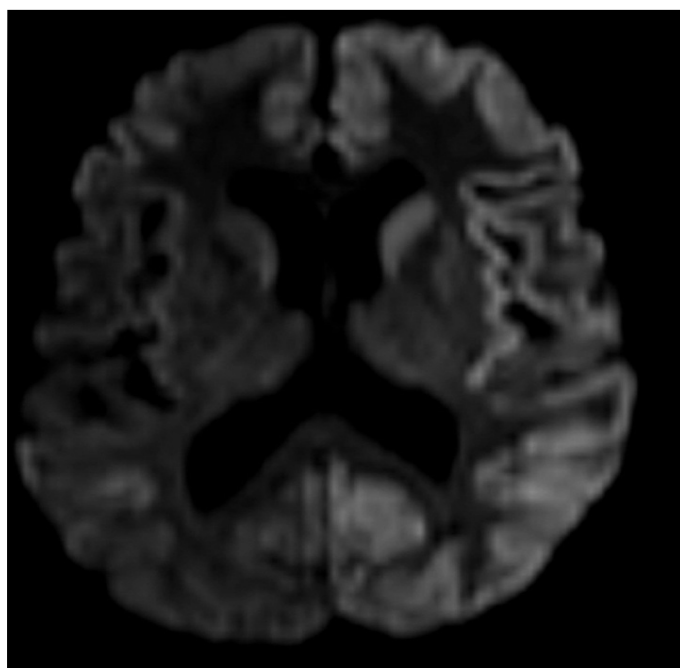
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he had urinary and fecal incontinence, emotional lability such as laughing and crying without reason, startling easily, and rigidity in the trunk and extremities and he became aphasic and bedridden. Two days prior to his admission to our clinic and 3 months after the onset of the initial symptoms he had a tonic-clonic seizure. He had a history of hypertension requiring antihypertensive drugs, but no history of alcohol or drug abuse, suspect sexual intercourse,

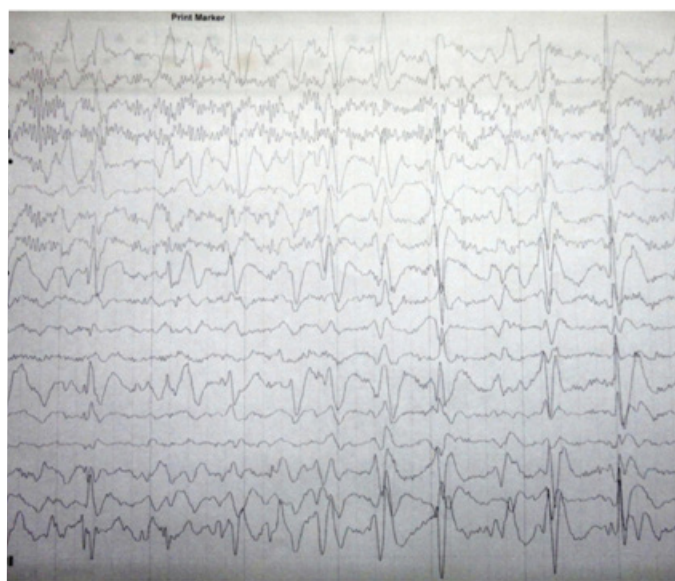


**Figure 1:** Diffuse cerebral and cerebellar atrophy, generalize cortical and bilateral caudate nuclei, putamen hyperintensity are seen on FLAIR MRI of the patient.



**Figure 2:** "cortical ribboning sign" on diffusion MRI of the patient.

or intake of unpasteurized dairy products. There was no other family member with similar complaints. Initial hypothesis was a neurodegenerative disease. Differential diagnosis included catatonic depression, CNS infection, Hashimoto encephalopathy, Lyme Disease, or paraneoplastic syndrome. An EEG and brain MRI was performed and no specific findings were observed. Protein 14.3.3 was found to be high in the CSF of the patient with raised protein (85 mg/dl [normal range 15-45 mg/dl]) and normal glucose and electrolyte levels. He was initially admitted to a psychiatry clinic and treated with risperidone, lorazepam, haloperidol without any benefit. Physical examination was significant for disorientated male with flat affect who did not follow simple commands, had rigidity in all four extremities, a startle response to touch, spontaneous and provokable myoclonic movements and was aphasic. He could move all four extremities equally. There were wide spread abrasions on the skin, especially on the trunk due to generalized severe itching. Routine haematology and biochemistry tests were normal. Hepatitis markers, Anti-HIV, borrellia IgG and IgM, anti-TG, anti-TPO, tumour markers were either normal or negative. An MRI of the brain demonstrated diffuse cerebral and cerebellar atrophy, mild cortical hyperintensity at the bilateral frontal, temporal, occipital and parietal cortex, bilateral caudate nuclei and putamen on fluid attenuation inversion recovery (FLAIR) and T2-weighted images, and increased signals in the same regions, especially in the left hemisphere in diffusion weighted images (Figures 1, 2) suggestive of CJD. A second lumbar puncture was performed, with protein of 49 mg/dl (normal range 15-45 mg/dl), normal glucose and electrolyte levels, no pleocytosis was found and viral markers, TBC PCR, borrellia IgG or, IgM, and 14.3.3 protein was negative. EEG showed moderately severe abnormalities of background rhythm with bilateral periodic sharp wave activity (Figure 3). The patient died 5 days after being discharged from the hospital and 3 months from the onset of the disease. His relatives did not consent to an autopsy.



**Figure 3:** Bilateral periodic sharp waves activity on EEG.

## Discussion

CJD is the most frequently seen type of prion diseases. It occurs in inherited, variant, iatrogenic and sporadic forms. Sporadic CJD (sCJD), mostly affecting individuals between 50 and 70 years old, represents 90% of all cases. Personality changes, visual symptoms, ataxia, akinetic mutism may also be seen. CJD is a neurodegenerative disease, leading to spongiform changes of the brain, neuronal loss and deposition of an abnormal prion protein (PrP) in tissues. All prion diseases are brain diseases typically leads to fatal rapid progressive dementia and presently there is no cure (1,2). The duration of the disease can vary between weeks and several years (3).

Variant CJD has been related with psychiatric symptoms (4). Psychiatric manifestations include sleep disturbances, such as insomnia and hypersomnolence, psychotic symptoms, depressive symptoms, irritability, agitation, catatonia, tactile hallucinations, panic attacks, apprehension, wandering, confusion, emotional lability, increased guilt, anhedonia, decreased libido, apathy, loss of appetite, or being tearful (5,6). Clinicians must consider sCJD as a differential diagnosis in patients with new onset dementia, particularly when accompanied by psychiatric symptoms that persist and worsen, despite psychiatric treatments as many of the patients have initially been admitted to psychiatry clinics (6). Loss of appetite, irritability, antihistamine-resistant itching, apprehension, laughing and crying without reason, locking himself up in his room, startles, seizures, gait disturbances, rigidity and mutism were all symptoms that our subject experienced.

In all suspected cases, brain imaging, especially MRI should be performed. In sporadic CJD, certain characteristic MRI changes may be observed, particularly high signal changes in the anterior basal ganglia and cortex (7). Our patient's MRI showed hyperintense signal abnormalities in the bilateral frontal, temporal, parietal, left occipital cortex, left caudate nucleus and putamen.

CSF analysis for 14.3.3 proteins is not useful as a screening test in patients with dementia. However, in patients suspected of CJD, the presence of proteins is a reminder of the diagnosis and may rule out other differential diagnosis. 14.3.3 proteins are detectable in some patients at an early stage of the disease, preceding the typical EEG changes, suggesting that they may be an earlier disease marker than the EEG (8).

Zerr et al. found that the 14.3.3 protein is 94% sensitive and 84% specific for the disease (8). The 14.3.3 protein can also be identified in Hashimoto encephalopathy, metabolic encephalopathy and amyotrophic lateral sclerosis (8,9). A CSF sample taken very early or very late in the course of the disease has an increased probability of being false negative (9). Mollenhauer presents a case whose protein 14.3.3 was first positive and then negative in the CSF study repeated 4 months later. Since protein 14.3.3 is a neuronal protein as the progressive neuronal cell loss continues, the neuronal proteins are depleted and their levels decrease (10,12), protein 14.3.3, tested 1 month after the onset of the symptoms, was positive, whereas in the lumbar puncture performed 4 months after the onset of the symptoms, 14.3.3 was found to be negative.

Periodic sharp wave complexes are the hallmark EEG finding in patients with sCJD (5,11). Typical periodic EEG activity may not be seen in patients with sCJD, especially in early or terminal stages of the disease (2). In early stages of sCJD, EEG recordings may be characterized by nonspecific EEG patterns such as diffuse

slowing of background activity or focal slow activity (2,5). In our patient there were bilateral periodic sharp waves and slowing of the background activity in both hemispheres.

Pruritus is an unpleasant cutaneous sensation that causes the urge to scratch. Although it is a common feature of animal prion diseases, pruritus has rarely been reported in humans with CJD (12). The exact mechanism causing pruritus in CJD is still unknown, but a few hypotheses can be proposed, including deposition of the pathologic prion protein in the skin, dorsal root ganglia and peripheral nerves, or destruction of central pathways. In addition, Cohen et al. reported that pruritus was associated with imaging findings including diffusion changes in various sites in the brain (12). The lack of pharmacologic benefit of peripherally acting drugs in those patients might support the hypothesis of a central origin of pruritus (12,13). Our patient had antihistamine-resistant pruritus, causing skin abrasion, and no other aetiology was found to explain the pruritus.

In CJD, a positive 14.3.3 test strongly confirms the diagnosis, whereas a negative test does not exclude the diagnosis, especially in patients with long disease duration (10). CJD is a condition that should be considered in patients that have progressive psychiatric symptoms and neurologic symptoms, dementia and itching.

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