Sporadična Creutzfeldt-Jacobova bolezen – prikaz primera

Sporadic Creutzfeldt–Jacob Disease: A case report

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Izvleček

Namen: *Creutzfeldt-Jacobova bolezen (CJB) je redka progresivna nevrodegenerativna bolezen, ki je obenem najpogostejša prionska bolezen. Obstajajo 4 tipi: sporadični (sCJB), familiarni, iatrogeni in variantni. Klinične značilnosti sCJB so demenca, mioklonus, motnje vida, cerebelarna ataksija ter piramidni ali ekstrapiramidni znaki. Diagnozo postavimo na osnovi klinične slike, elektroencefalograma, preiskav likvorja in sprememb na magnetni resonanci možganov.*

Poročilo o primeru: *V poročilu predstavljamo primer 81-letne bolnice s progresivno demenco, značilnim izvidom elekroencefalograma in magnetne resonance.*

Zaključek: *Za postavitev diagnoze sCJB ni diagnostičnega testa. Kadar*

Abstract

Purpose: *Creutzfeldt–Jacob Disease (CJD) is a rare progressive neurodegenerative disorder and the most common form of prion disease. CJD is categorized into four subtypes: sporadic (sCJD), familial, iatrogenic, and variant. The clinical presentation of sCJD is characterized by progressive dementia, myoclonus, visual disturbances, cerebellar ataxia, and pyramidal and/or extrapyramidal signs. Diagnosis is based on clinical presentation, and the results of an electroencephalogram, cerebrospinal fluid analysis, and cranial magnetic resonance imaging.*

Case report: *The case of an 81-year-old woman with progressive dementia and typical electroencephalogram and magnetic resonance imaging findings for sporadic is presented.*

Conclusion: *No single diagnostic*

sumimo na sCJB, je najprej potrebno izključiti vzroke reverzibilnih demenc, kot sta encefalitis ter kronični meningitis.

test for sCJD is available. In suspected sCJD, the first priority is to exclude treatable forms of dementia, such as encephalitis or chronic meningitis.

INTRODUCTION

Creutzfeldt–Jacob Disease (CJD) is a rare progressive neurodegenerative disease, which was first described by Creutzfeldt and Jakob in the early 1920s. CJD is the most common form of prion disease (1). As with other subacute spongiform encephalopathies, CJD is thought to be caused by infectious agents termed prions. Prions are glycoproteins, which are present in normal human and animal cells. The gene for prion protein is located on chromosome 20. Research has shown that a polymorphism at codon 129 of this gene is implicated in CJD susceptibility (2). Defective folding of normal prions results in a post–translational infective prion protein (PrPSc). Intracellular accumulation of these abnormal prions leads to spongiform vacuolar degeneration (2).

This report describes the case of a female patient with sporadic CJD. The clinical diagnosis was based on medical history, clinical presentation, magnetic resonance imaging (MRI), electroencephalography (EEG), and cerebrospinal fluid (CSF) analysis, and was confirmed via a post–mortem neuropathological examination.

CASE REPORT

An 81–year–old right–handed woman with a history of chest pain and dizziness was brought to the Emergency Deparment by her husband. Her husband stated that in the last 10 days, she had been confused and had had speech difficulties. Her past medical history was non–contribitory. In 2006, she had had a myocardial infarction, and been diagnosed with atrial fibrilation and arterial hypertension. On clinical examination, the patient was disorientated, and displayed motor aphasia and dyscalculia. Cranial computer to-

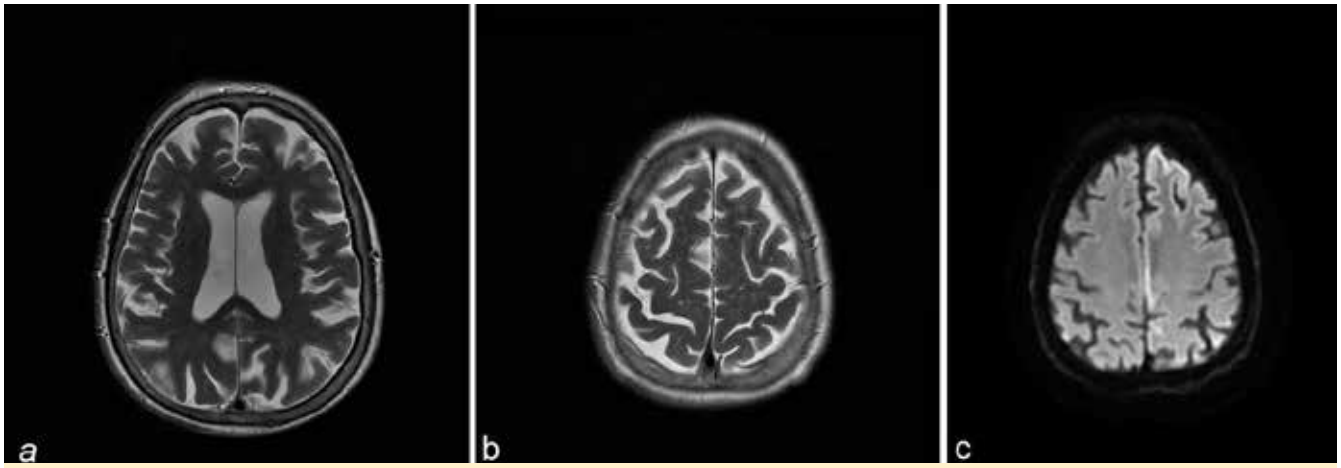

Figure 1. *a, b T2-weighted MRI showing dilatation of the lateral ventricle, diffuse cerebral atrophy, and high-intensity areas in the cerebral white matter. c DWI indicates high signal intensity areas, particularly in the frontal, parietal, and occipital cortices.*

mography was reported as normal. CSF analysis was unremarkable, with no detection of 14–3–3 protein. Over the three subsequent weeks, the patient's condition deteriorated. She displayed increasing confusion and speech difficulties, as well as feeding and dressing difficulties secondary to apraxia. A cranial MRI scan was therefore performed. T2 weighted and FLAIR imaging revealed marked diffuse cerebral atrophy and ventricular enlargement, while DWI MRI showed high signal intensity areas (cortical ribboning) across the cortex (Figure 1). An EEG was performed, which showed irregular normal activity disrupted by slow delta waves in the frontal lobe. The control EEG has shown three–phasic waves that appear periodically (Figure 2). A month later, the patient developed dysphagia and myoclonus. The patient died two and a half months after symptom onset. The cause of death was reported as aspiration pneumonia. Postmortem neuropathological examination revealed spongiform degeneration in sections of the hippocampus, amygdala, putamen, mesencephalon, cerebellum, and neocortex, as well as significant gliosis and neuronal loss in the occipital lobe. Histopathological examination also revealed the presence of PrPSc in the cerebral cortex and subcortical gray matter.

DISCUSSION

CJD is categorized into four subtypes: sporadic, familial, iatrogenic, and variant. Sporadic CJD accounts for approximately 80% of all CJD cases. Epidemiological studies indicate that the annual global incidence of sporadic CJD is approximately 1 case per million individuals (3). Over the 19–year period between 1985 and 2003, 39 cases of suspected CJD were referred to tertiary neurological services in Slovenia, and 22 of these were confirmed at post–mortem (4). Most cases of sCJD occur between the ages of 60 and 69 years, and an equal sex incidence has been reported (1).

Clinical findings in sCJD include rapidly progressive dementia, myoclonus, visual disturbances, cerebellar ataxia, and pyramidal and/or extrapyramidal signs. No specific symptoms occur at disease onset. However, personality changes, sleep disorders, and changes in weight are common. In most patients, key symptoms are an impairment of cognitive function and behavioral abnormalities. Our patient developed many of the characteristic neurological deficits of sCJD progression, which include worsening dementia, cerebellar dysfunction, myoclonus, pyramidal and/or extrapyramidal signs, and akinetic mutism(5). Death

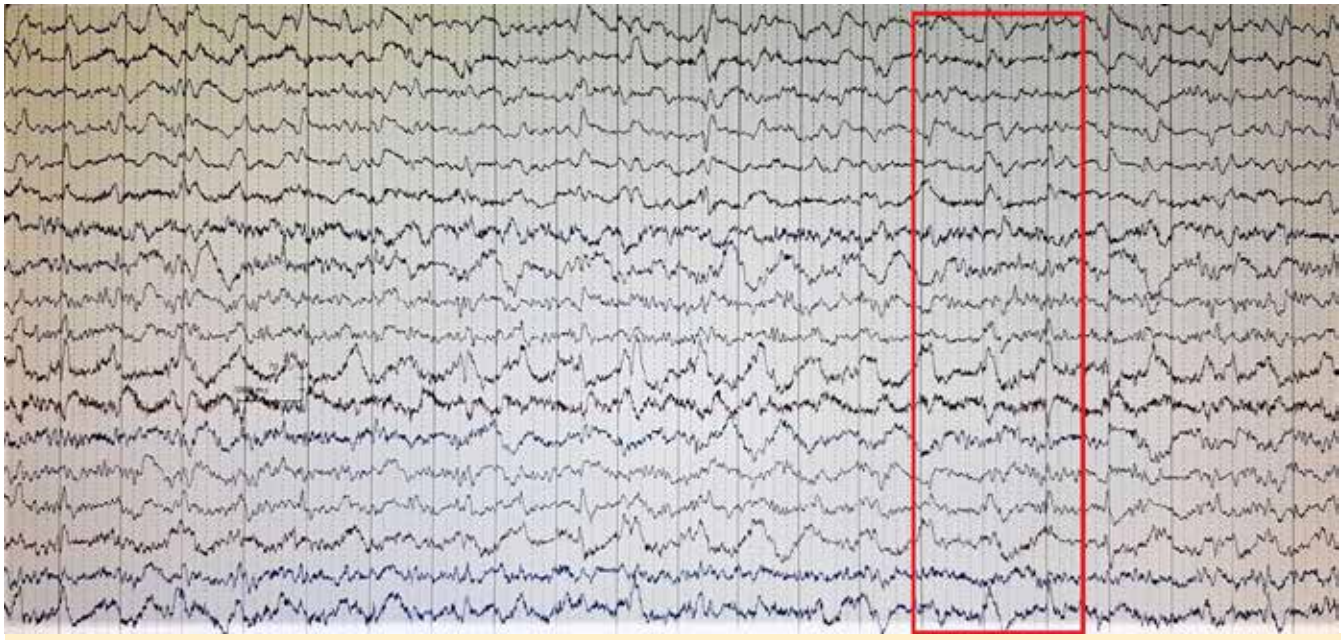

Figure 2. *EEG showing periodic tri-phasic waves.*

usually occurs 4 to 6 months after disease onset or even sooner as seen in our case (1). Zerr et al. reported that the detection of 14–3–3 protein in CSF using a modified western blot technique was highly sensitive (94%) and specific (84%) for diagnosis of sCJD (6, 7). The 14–3–3 protein is released by damaged neurons in the CSF, and is also detected in patients with herpes simplex encephalopathy, hypoxic brain damage, metabolic encephalopathy, and progressive dementia of unknown cause. Thus positive results must be interpreted within the given clinical context. CSF analysis has an important role in differentiating between diseases with a similar clinical presentation. In the present case, CSF analysis was performed to exclude an infection with a neurotropic virus or a bacteria, or a paraneoplastic syndrome. Moreover, cytological analysis of CSF has shown no signs of paraneoplastic syndrome. In sCJD, a characteristic electroencephalogram finding is the presence of periodic sharp waves. Initially, these may be focal or unilateral. In sCJD, the EEG exhibits characteristic changes depending on the stage of the disease, ranging from nonspecific findings as presented in the early stages to disease-typical periodic sharp wave complexes in the middle and late stages, as described in our case. The detection of these periodic sharp wave complexes in the EEG were shown in previous studies to have sensitivity of 66%, with a specificity of 74%. Despite the high specificity of EEG for the diagnosis of sCJD, some sCJD patients – in particular those with atypical, ataxic, or amyotrophic forms – may not show this characteristic periodic EEG pattern (7, 8). MRI abnormalities observed in sCJD patients include hyperintensity in areas of the thalamus, basal ganglia, and cerebral cortex. Recent studies have shown that even in the early phase of the disease, FLAIR and DWI imaging techniques have a sensitivity of 91% and specificity of 95% for the detection of pathological signs for sCJD (9). However, a definitive diagnosis of sCJD requires a neuropathological examination. In most patients with sCJD spongiform changes, astroglyosis, and neuronal loss are observed. The detection of PrPSc in the brain is an important tool in the molecular classification of human prion diseases, and has important implications for their definitive diagnosis (2).

CONCLUSION

No pathognomonic signs or tests are available for the diagnosis of sCJD. However, EEG analysis, CSF analysis, and cranial MRI findings can contribute to the clinical diagnosis of the disease. According to current diagnostic criteria, a definitive diagnosis of sCJD requires a post–mortem histopathological examination of brain tissue (9).

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