

## SPORADIC CREUTZFELDT-JAKOB DISEASE IN A PATIENT WITH EPISODES OF NONCONVULSIVE STATUS EPILEPTICUS: CASE REPORT

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**SUMMARY** – Creutzfeldt-Jakob disease is the most common form of human prion diseases. A 57-year-old woman was transferred to our Department from a local hospital, where she had been treated for two weeks due to consciousness disorders and convulsive epileptic attacks that progressed to refractory status epilepticus. Electroencephalography showed diffuse spike-wave complex discharges and development of nonconvulsive status epilepticus. The causes of metabolic encephalopathy and paraneoplastic syndrome were ruled out. A combination of clinical features and findings of diagnostic procedures including electroencephalography, biomarkers in the cerebrospinal fluid and magnetic resonance imaging suggested with great probability that the patient was affected with sporadic Creutzfeldt-Jakob disease.

**Key words:** *Prion diseases; Creutzfeldt-Jakob disease, sporadic; Creutzfeldt-Jakob disease, diagnosis; Status epilepticus, nonconvulsive*

### Introduction

Prion diseases are a large group of transmissible neurodegenerative disorders that affect both animals and humans. All of them have long incubation and fatal outcome. They are unique in that they can be inherited, occur sporadically, or be infectious<sup>1</sup>. The most common human prion disease is sporadic Creutzfeldt-Jakob disease (sCJD). It is found worldwide, with an incidence of about 1 case *per* million in general population<sup>2</sup>.

The main pathogenic mechanism is conversion of the native cellular prion protein (PrP) into a pathologic, abnormal isoform that has a tendency to accumulate and form deposits in the brain<sup>3,4</sup>.

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### Case Report

A 57-year-old woman was transferred to our Department from a local hospital, where she had been treated for two weeks due to the state of confusion accompanied by vomiting and headache, and consciousness disorders. Vomiting and headache had lasted for two days, after which she became disoriented. On two occasions, partial motor and secondarily generalized tonic-clonic seizures appeared and progressed to status epilepticus that was partially persistent on all antiepileptic drugs administered. The patient was treated with levetiracetam 1000 mg three times a day and phenytoin 400 mg twice daily. Diagnostic work-up and multi-slice computer tomography (MSCT) of the brain undertaken in the local hospital did not determine the cause of the encephalopathy.

The patient's medical history revealed cirrhosis and bleeding from esophageal varices, which oc-



*Fig. 1. EEG (at admission to our Department) showed diffuse spike-wave complex discharges at a rate of 2-3 Hz.*

curred three years prior to the present hospitalization. In the past year, she was treated by a psychiatrist for an anxious-depressive syndrome. A year before, she underwent surgery because of basal cell carcinoma of the mandible.

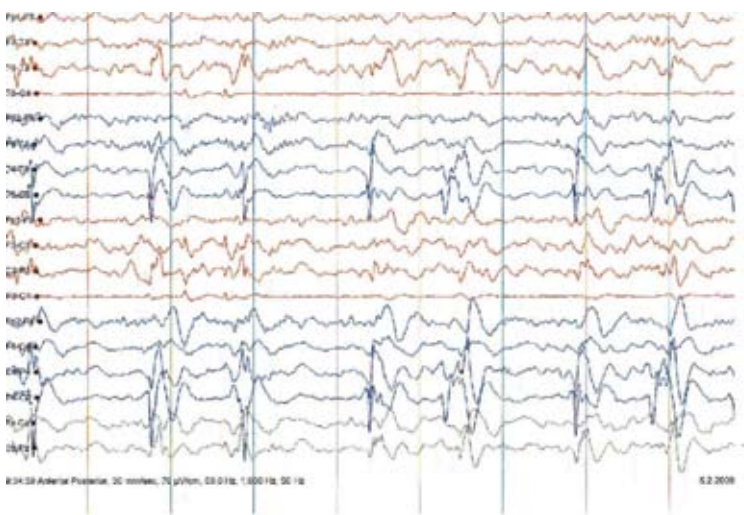
At admission to our Department, she was conscious, Glasgow Coma Scale (GCS) 10; she could spontaneously open her eyes, but verbal contact was not possible, she was unable to follow motion with her gaze and uncooperative for instructions given on neurologic examination. Her pupils were of equal shape, with normal response to photostimulation, and there were occasional myoclonic jerks on the right side of the head. All four extremities were falling to the ground, while the upper extremities showed high

tone. Periodically she moved all four limbs to a lesser extent. Babinski's sign was positive on the left leg. She was of normal cardiorespiratory status, normotensive, afebrile.

Electroencephalography was performed repeatedly. In the beginning, it showed continuous pointed waves temporally on the right, and on the next day diffuse spike-wave complex discharges at a rate of 2-3 Hz were recorded (Fig. 1). Throughout the recording, the patient was in nonconvulsive status epilepticus. An epilepsy specialist was consulted and switching of antiepileptic drugs gradually led to deceleration of brain activity, appearance of delta waves and discharge of spike-wave complex with periodic triphasic complexes<sup>5</sup>. Phenytoin was gradually replaced by valproic acid 500 mg three times a day and levetiracetam dose was reduced from 3000 mg to 2500 mg daily (Fig. 2).

Magnetic resonance brain images (FLAIR and DWI) revealed high signal abnormalities in the insular cortex bilaterally and in the right temporal region (Figs. 3 and 4).

Paraneoplastic antibodies (Anti Yo, Anti Hu and Anti-Ri) in the serum were negative. Serologic findings on viral causes of encephalitis were negative. Lumbar puncture was performed and a clear, colorless cerebrospinal fluid with 1/3 cells and 0.28 proteins was obtained. The finding of biomarkers in cerebrospinal fluid showed positive protein 14-3-3, TauAg (6250.0 pg/mL; ref. 80.0-149.8) and NSE (20.5 µg/L; ref. 0.0-15.5 µg/L).



*Fig. 2. EEG detection of delta waves and discharge of spike-wave complex with periodic triphasic complexes.*

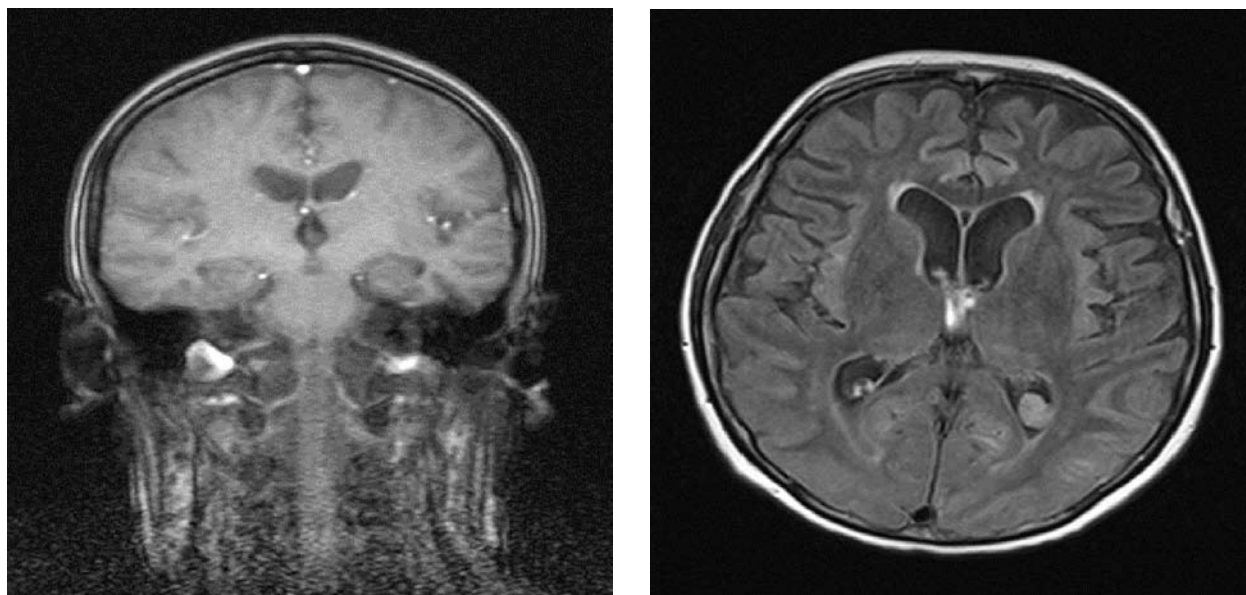


Fig. 3. MRI brain images (FLAIR and DWI) revealed high signal abnormalities in the insular cortex bilaterally and in the right temporal region.

Six months after admission, the patient died in the state of akinetic mutism.

## Discussion

The clinical picture in patients with sCJD is mostly characterized by rapidly progressive dementia and cognitive decline, movement disorders, myoclonic jerks, visual disturbances and cerebellar ataxia<sup>6,7</sup>. Focal and generalized seizures are uncommon symptoms of this prion disease<sup>7,8</sup>. Also, nonconvulsive status epilepticus has been described in several reports as a rare presentation of sCJD<sup>9-12</sup>.

Definitive diagnosis of CJD can only be made by brain biopsy (neuropathology). In 2009, Zerr *et al.* published amendments to the clinical diagnostic criteria for sCJD, based on their results obtained in a multicenter international study. The new clinical criteria for premortem diagnosis of sCJD include the following: I clinical signs: 1) dementia, 2) cerebellar or visual, 3) pyramidal or extrapyramidal, and 4) akinetic mutism; and II tests: 1) EEG detection of periodic sharp wave complexes, 2) elevated levels of 14-3-3 protein in cerebrospinal fluid, and 3) high signal abnormalities in caudate nucleus and putamen or at least two cortical regions (temporal-parietal-occipital) either on DWI or FLAIR<sup>6</sup>.

We report on a 57-year-old woman admitted to our Department because of confusion, alteration of mental state and seizures that occurred for the first time in her life. The initial clinical findings were compatible with nonconvulsive status epilepticus. The changing of antiepileptic therapeutics led to deceleration of brain activity<sup>5</sup>. A combination of clinical features and findings of diagnostic procedures including electroencephalography, biomarkers in the cerebrospinal fluid and MRI suggested with great probability that the patient was affected with sCJD.

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### Sažetak

#### SPORADIČNI OBLIK CREUTZFELDT-JAKOBOVE BOLESTI U BOLESNICE S ISPADIMA NEKONVULZIVNOG EPILEPTIČNOG STATUSA: PRIKAZ SLUČAJA

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Creutzfeldt-Jakobova bolest je najčešći oblik prionske bolesti u ljudi. Prikazuje se slučaj bolesnice koja je prevezena u našu Kliniku iz manje bolnice, gdje je bila liječena dva tjedna zbog poremećaja stanja svijesti i konvulzivnih epileptičnih napadaja koji su progredirali do epileptičnog statusa koji je bio refraktoran na primijenjenu terapiju. Elektroencefalografija je prikazala difuzna izbijanja kompleksa šiljak-val i razvoj nekonvulzivnog epileptičnog statusa. Koristeći kombinaciju kliničkih značajka i nalaza dijagnostičkih pretraga uključujući elektroencefalografiju, biomarkere u cerebrospinalnoj tekućini i nalaze magnetske rezonance zaključeno je s velikom vjerojatnošću da se radi o sporadičnom obliku Creutzfeldt-Jakobove bolesti.

*Ključne riječi: Prionska bolest; Creutzfeldt-Jakobova bolest, sporadični oblik; Creutzfeldt-Jakobova bolest, dijagnostika; Epileptični status, nekonvulzivni*