Creutzfeldt-Jakob's Disease – Case Report With Emphasis on the Electroencephalographic Features

Patrícia Coral*,**, Francisco M. B. Germiniani*, Carlos E. Silvado*,**,***

Epicentro – Centro Integrado de Atendimento de Epilepsia, Curitiba, PR

ABSTRACT
Creuzfeldt-Jakob's Disease is a rare neurodegenerative disorder that is included among the transmissible spongiform encephalopathies. The clinical features are those of a rapid progressive dementia with myoclonic jerks, which progresses to death in less than one year. We report the case of a 79 years old woman, with initial complaints of vertigo, visual and gait compromise, with an initial brain MRI, EEG and CSF that had no specific features of CJD. After 12 days she was again admitted to the hospital with a worsening of her symptoms, along with global spasticity, inability to walk and a further deterioration of speech and swallowing. A new EEG disclosed periodic triphasic complexes, typical of the disease. CSF had a positive 14-3-3 protein. She later evolved with myoclonic jerks, coma, multiple infectious complications and, ultimately, death 45 days after her second admission. We focus on the role of the EEG as an adjunctive electrophysiological tool for the presumptive in vivo diagnosis of the disease.

Key words: dementia, Creutzfeldt-Jakob's Disease, prion.

RESUMO
Doença de Creutzfeldt-Jakob – Relato de caso com enfoque nos aspectos eletronecefalográﬁcos
A Doença de Creuzfeldt-Jakob é uma rara desordem neurodegenerativa, que faz parte das encefalopatias espongiformes transmissíveis. Apresenta-se com um quadro de demência rapidamente progressiva, associada a mioclonias, que geralmente leva ao óbito em menos de um ano. Apresentamos um caso de uma mulher, 79 anos, com quadro inicial de vertigem, alteração visual, dificuldade de marcha. Inicialmente foram realizados ressonâncias magnéticas do crânio, EEG e liquor que não evidenciaram alterações específicas da doença. Após 12 dias reintervém com piora do quadro, espasticidade nos quatro membros, não deambulava, emitia sons incompreensíveis e não se alimentava. Novo EEG revelou os complexos de ondas trifásicas periódicas típicos da doença. A pesquisa da proteína 14-3-3 no líquor foi positiva. A paciente evoluiu com mioclonias, coma e múltiplas complicações infecciosas, vindo a óbito 45 dias após a internação. O presente artigo dá ênfase ao valor do armamentário eletrofisiológico (EEG) no contexto que leva ao diagnóstico presuntivo da doença in vivo.


Creutzfeldt-Jakob's Disease (DCJ) is a rare, neurodegenerative disorder that is part of a larger group of transmissible spongiform encephalopathies. It was first described by Gerhard Creutzfeldt and Alfons Jakob in Germany last century, during the twenties. It was initially believed to be an infectious disease caused transmitted by an unconventional virus, which was later termed "prion" (proteinaceous infectious particle) by Prusiner in 1982. Nowadays, four different forms of the disease are recognized:
Electroencephalographic changes also vary along with the different stages of the disease, with the characteristic periodic pattern occurring in as much as 75 to 94%, even tough it might only be found in the later stages (up to 12 weeks)\(^{(7)}\).

We report a case of probable sporadic Creutzfeldt-Jakob’s Disease with emphasis on the EEG findings.

CASE REPORT

A 79 years old white woman first presented to a medical visit complaining of vertigo – like symptoms that started about 45 days prior to her visit. She first consulted with an otorhinolaryngologist who found no abnormalities in his examination and prescribed anti-vertiginous medications. She then had a progressive worsening of her symptoms, associated with bilateral visual impairment, gait compromise and child-like behaviour. Her medical history was unremarkable, except for controlled arterial hypertension, cardiac arrhythmia and a prosthetic replacement of her left knee as a result of severe arthrosis.

On examination the patient was disoriented in both time and space, had a gait ataxia, increased deep tendon reflexes and horizontal nystagmus. A previous resonance imaging study had only disclosed a minor volumetric reduction of her brain, which was considered within normal limits for her age. She was then admitted for investigation, during which an EEG was performed as part of the routine evaluation. Her EEG was strikingly abnormal, with high amplitude, generalized delta waves occurring in rhythmic bursts, with a duration of up to 4 seconds, most prominent over the anterior regions, a pattern that was compatible with FIRDA (Frontal Intermittent Rhythmic Delta Activity). A spinal tap was performed, but her spinal fluid had cytological and biochemical findings within normal ranges. No metabolic abnormalities were found. She was then discharged without a clear diagnosis, with planned outpatient visits.

Twelve days later she was once again admitted with a significant worsening of her symptoms, which then included spasticity of all four limbs, an inability to walk and a worsening of her dementia with inability to swallow or talk, emitting only incomprehensible mumbled sounds. A second EEG disclosed periodic triphasic wave complexes, repeating every 0.5 to 1 second, of moderate amplitude, generalized delta waves occurring in rhythmic bursts, with a duration of up to 4 seconds, most prominent over the anterior regions, a pattern that was compatible with FIRDA (Frontal Intermittent Rhythmic Delta Activity). A spinal tap was performed, but her spinal fluid had cytological and biochemical findings within normal ranges. No metabolic abnormalities were found. She was then discharged without a clear diagnosis, with planned outpatient visits.

A new diffusion brain MRI study showed no significant changes when compared with her previous exam. A new spinal tap was performed and a CSF sample was sent to laboratory analysis for 14-3-3 protein and specific-enolase enzyme detection. The former was positive, while the latter was negative. A peripheral blood sample was collected and sent for detection of the mutation of the gene for the PrPC protein, but no such DNA mutation was found.
Figure 1. Periodic generalized triphasic wave complexes, moderate amplitude, repeating every 0.5 to 1 second. First EEG, during second hospital admission, day -40.

Figure 2. Periodic generalized triphasic wave complexes, moderate amplitude, during repetitive photic stimulation. Evolutive EEG, day-33.

Figure 3. Periodic generalized triphasic wave complexes, moderate amplitude, at rest. Last EEG day-25.
During her hospital stay she evolved with coma with frequent mioclonic jerks and rare tonic-clonic seizures. Subsequent EEGs had the same typical pattern, sometimes mixed with diffuse voltage depression. She had several urinary and pulmonary infectious complications during her stay and finally died after 45 days as a result of respiratory insufficiency.

DISCUSSION

EEG studies play an important role in the investigation and diagnosis of CJD when specific findings are found, thus allowing the clinician to progress in the investigation from a suspected case of CJD to a probable diagnosis status, which also has epidemiological repercussions. Typical EEG findings of CJD are generalized complexes, either biphasic or triphasic, lasting for 100 to 300 milliseconds, with a mean amplitude of 300 µV and an interval among repetitions of 0.5 to 1.5 seconds. May proposed, in 1968, a clinical staging for the disease, with a good correlation with EEG evolution. In the prodromic phase the clinical symptoms are somewhat vague, such as headache, vertigo, confusion and syncope. In this stage the EEG shows a slowing of background activity, with both theta and delta waves with a generalized bilateral distribution, sometimes predominating over one hemisphere or the other. Also, physiological sleep graph elements are lacking.

At the beginning of the proper disease phase, another pattern can be found, known as FIRDA (frontal intermittent rhythmic delta activity), which is characterized by high amplitude, 100 a 150 µV, rhythmic delta waves, most prominent over the anterior regions of the scalp, that present in an intermittent fashion. This pattern is by no means specific, as it can also be found in metabolic encephalopathies and even in patients with focal lesions of the Central Nervous System. Later, during this same stage, the typical pattern described is time-locked to the mioclonic jerks, as they occur a few milliseconds before or after the electrical discharges. The evolution of FIRDA to periodic complexes might take from 1 to 3 weeks. This pattern is better defined when the patient is more alert, and is less defined during sleep.

Another feature of the periodic complexes is that they can either be attenuated or disappear after intravenous use of Midazolam. Several different theories try to explain the origin of this pattern, which sometimes resembles some patterns that are generated in the thalamo-cortical axis, such as sleep graphs and 3 Hz spike-waves in absence epilepsy. However, this periodic pattern can vary in both shape and interval in the same patient.

Finally, in the terminal stage the patient develops an akinetic mutism, evolving further to coma and a reduction of the mioclonic jerks; concomitantly, the EEG has a reduction of the periodic complexes until they are no longer visible and are replaced by a diffuse depression of background voltage.

The typical pattern can be found in as many as 75 to 94% of all patients, and according to Steinhoff, who reported in 2004 a series of 150 patients who underwent necropsy, the EEG has a sensitivity of 64%, specificity of 91%, a positive predictive value of 95% and a negative predictive value of 49%. In those patients who had a false positive EEG, the autopsy diagnosis were of Alzheimer’s Disease in 4 cases and vascular dementia in one case. In another study, Zerr et al found a sensitivity of 66% and a specificity of 74%.

In 1929 Heidenhain described a variant form of the disease that had initially predominant visual symptoms followed by a rapid evolution. The EEG of such patients had the periodic complexes localized more predominantly over the posterior regions bilaterally.

Our case illustrates both clinical and electroencephalographic features typical of this rare and fatal disease, with the EEG playing a large role in the diagnosis. We highlight the need for serialized recordings in a suspected case, due to the different evolutive stages of EEG findings and clinical symptoms.

REFERENCES


Mande seu caso para:  
JECN – A/c. de ANDRÉ PALMINI  
Av. Montenegro, 186 sala 505 – Petrópolis  
CEP 90460-160, Porto Alegre, RS, Brasil ou  
pelo e-mail: jecnpoa@terra.com.br