Fulminant Evolution of Creutzfeldt-Jakob Disease: Clinical and Radiologic Correlation

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Abstract

Creutzfeldt-Jakob disease (CJD) is a spongiform encephalopathy that is clinically characterized by rapidly progressive dementia, usually accompanied by extra pyramidal motor symptoms (in varied degrees). Its pathophysiology involves changes in the structure of prion protein (acquired and familial forms). The definitive diagnosis requires histological analysis, whereas the probable diagnosis is based on a set of clinical, lab, electrophysiologic, and radiologic data.

The extension of brain damage is directly proportional to the clinical repercussions. It is, therefore, possible to establish a correlation between them through imaging tests, more specifically, through magnetic resonance imaging (MRI). This case report aims to describe the close correlation between the clinical presentation and the radiologic findings in the fulminant and fatal evolution of a patient diagnosed with probable CJD.

Introduction

Creutzfeldt-Jakob Disease (CJD) is one of the main causes of rapidly progressive dementia [1,2]. It results from changes in the structural arrangement of prion protein particles (PrP C, normal cell component), which are transformed into insoluble particles (PrP SC) and acquire pathologic potential. The pathophysiological mechanism triggered by these prion particles is not clear. The possibility of it resulting from an inflammatory process is challenged by several authors. However, by using histological analysis, recent studies have revealed an increase in microglia, astrocytes and apoptotic cells [3-6], as well as the release of several immune mediators, which corroborate the likelihood of an inflammatory substrate in the neural damage process.

The most common form of CJD is the sporadic one (85%) [2,5,6], but other forms (iatrogenic and familial), while less common, are also possible. In the present study, we shall describe a rapidly progressive case of a patient with a presumed diagnosis of spongiform encephalopathy (CJD) and the correlation between its clinical evolution and imaging signs on magnetic resonance imaging (MRI).

Case Report

A 62-year-old white female patient, born, raised and still living in the city of Maringá (Paraná, Brazil) with a history of systemic arterial hypertension and dyslipidemia (for which she was taking losartan 50 mg twice a day, amlodipine 5 mg/day, simvastatin 20 mg/day, AAS 100 mg/day), and depressive disorder (venlafaxine 50 mg/day), she had no other co-morbidities, history of travelling abroad, or similar family history or epidemiology for CJD/rapidly progressing dementia. A cesarean section was reported as her only previous surgery.

She was admitted to our center on 11/11/2014 after presenting dysarthria for a week. She had no other complaints. Clinical examination did not reveal abnormalities, except for high arterial pressure (AP) 180/100 mmHg. On neurological examination, the patient was lucid and orientated, with mild sporadic speech deficit (dysarthria), normal cranial nerves, no motor or sensitive deficit, normal deep tendon reflexes and no gait abnormality. Lab and cerebrospinal fluid (CSF) tests were normal and the computed tomography (CT) scan of the skull revealed a discrete cortical atrophy and no other abnormality. After two days of investigation, the patient was discharged for outpatient follow-up with neurology. On the MRI assessment (Figure 1), the echo-planar diffusion-weighted (DWI) sequence showed cortical signal changes affecting predominantly the left inferior parietal lobule (supramarginal and angular gyri), which were not identified on the other sequences. The FLAIR sequence showed hyperintensity foci in the white matter of the brain hemispheres, probably representing foci of gliosis related to microangiopathy usually seen in cases of dyslipidemia and systemic hypertension.

Figure 1: MRI of the skull: DWI (A and C) and FLAIR (B and D). There are signal changes affecting mainly the cortex of the left inferior parietal lobule (arrows) identified only on the diffusion sequence. Note the preservation of the basal nuclei and of the right cerebral hemisphere.
The patient returned a month after the onset of the symptoms with worsening of dysarthria accompanied by dysphagia to liquid and solid, and ataxia (unable to walk without support). She was conscious and oriented in time and space, though she had some periods of “alienation” at which she could not respond to commands and did not collaborate with the examination. There was also motor aphasia, accentuating the loss of bilateral visual acuity, but eye movement was not affected.

During her stay, she developed intermittent myoclonus in the upper left limb, which spread progressively in association with gait ataxia with a tilt to the left side. Deep tendon reflexes and muscle strength were preserved.

A new MRI was performed (about one month after the first scan—Figure 2). The DWI sequence revealed a dramatic expansion of the cortical damage, with bilateral impairment (temporal, frontal and parietal opercula, and insular cortex) alongside deep grey matter (caudate nuclei) abnormality. General lab tests were normal as well as serum vitamin B12 level, thyroid hormones, and serology for HIV, herpes simplex and syphilis.

Electroencephalogram (EEG—Figure 3) showed periodic acute triphasic waves and diffuse background slowing with epileptiform discharges. Based on the patient’s clinical presentation (rapidly progressive dementia with motor impairment) in association with the imaging and EEG findings, the possibility of prion disease was considered, and that motivated the workup for Creutzfeldt-Jakob disease. Lumbar puncture for immunoblot analysis of reactivity to 14-3-3 proteins in CSF was performed and came out positive.

Other tests (such as transthoracic echocardiogram and carotid Doppler ultrasound) did not present significant findings. In addition to the support therapy, the patient received enteral nutrition via nasogastric tube, and was medicated with depakene and fenobarbital, which promoted partial improvement of myoclonus foci. She evolved with diarrhea and urinary tract infection, which were treated successfully.

On 01/07/2015, the patient was discharged and returned three days later with edema of face and glottis requiring orotracheal intubation, mechanical ventilation and admission to the ICU. She developed infectious complications with urinary and pulmonary foci and died in the end of the month.

Discussion

CJD is a spongiform encephalopathy that develops with rapidly progressing dementia of undetermined etiology. Although the possibility of an inflammatory process has been ruled out by some authors, others defend this hypothesis due to an increase in inflammatory cells in the central nervous system (microglia), and an increased expression of m-RNA for inflammatory mediators (such as IL-1) [3,4,7].

In terminal stages, the patient may present akinetic mutism [5,6]. The development of myoclonus usually coincides with the emergence of EEG findings [5], consisting of periodic sharp wave complexes, which is seen in 66% of patients with a specificity of 74% [5,8].

CSF tests detected the presence of 14-3-3 proteins, which is detected in approximately 90% of patients [5,8]. It is worth mentioning that this is not a pathognomonic finding of CJD [5,6], being seen in other conditions such as encephalitis, hypoxic injury, alzheimer disease, and intracranial hemorrhage [5].

On the CT and MRI scans, atrophy may be seen, but these tests may also present without any abnormality [5], especially during the initial stages of the disease. However, there are MRI findings that, when associated with other components of the diagnostic criteria defined by the WHO, enable physicians to diagnose probable CJD with high accuracy [1,8,9].

Many authors have come to the conclusion that the most sensitive MRI sequence is DWI, with correspondence on the ADC map [2,8]. These abnormalities can also be seen on FLAIR and T2 sequences as hyper intense signals [2,5,6,9]. The abnormalities on the DWI sequence may be seen even before the appearance of myoclonus and of EEG findings [5]. However, in more advanced stages, the findings are less visible on DWI and more evident on FLAIR [5].

In addition to atrophy, other signs that may be revealed by MRI affect the cortex and basal ganglia, more specifically the putamen and caudate nucleus, as well as the thalamus [2,6,8,9]. The most frequent site, however, is the basal ganglia [2]. The evolution in the clinical presentation of the disease may be accompanied by a progression of the abnormalities seen in imaging tests.
A study reported that most patients present hyperintense signals in at least three of these four areas: insula, cingulated gyrus, superior frontal gyrus and occipital gyrus [2,5]. Thus, the involvement of these structures in conjunction with a compatible clinical presentation should raise suspicion of CJD.

Conclusion

The clinical case reported above meets the diagnostic criteria defined by the WHO for probable sporadic Creutzfeldt-Jakob disease. A definitive diagnosis was not achieved, as the family did not authorize a necropsy. The rapid clinical evolution to this fatal outcome had precise correlation with the appearance of new imaging findings (MR-diffusion). These are, therefore, potential predictors of disease evolution.

References