Case Report

Creutzfeldt-Jakob Disease: An Unusual Long Follow-Up

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Abstract

Introduction: Prion diseases are a group of neurodegenerative disorders of the nervous system caused by a conformational change of an endogenous protein. The sporadic form of Creutzfeldt-Jakob disease (CJD) is responsible for the majority of cases. Despite advances in diagnosis, the absence of effective treatment makes this disease rapidly progressive and invariably fatal.

Case presentation: A 56-year-old man presented with subjective cognitive complaints without important impact on daily activities, including professional duties. Significant cognitive deterioration occurred three years after the first symptoms and progressed to dementia in about four months. Magnetic resonance imaging showed hyper intensities in multiple cortical regions. The EEG revealed a slow basal activity, with inscription of bilateral periodic activity. The 14-3-3 protein assay in the CSF was positive. In the final phase the patient was in akinetic mutism with myoclonus. The diagnosis of probable CJD was made.

Discussion: This case presents an atypical evolution of the sporadic form of CJD, known for median survival of less than six months after the appearance of the first symptoms.

ABBREVIATIONS

CJD: Creutzfeldt-Jakob disease; MRI: Magnetic Resonance Imaging; CSF: Cerebrospinal Fluid; EEG: Electroencephalogram; DWI: Diffusion-Weighted Imaging; MMSE: Mini-Mental State Examination

INTRODUCTION

Prion diseases are a group of neurodegenerative disorders caused by the transformation of an endogenous protein (PrPc) into an abnormal conformation (PrPsc), with further accumulation in the central nervous system [1]. Creutzfeldt-Jakob disease (CJD) is the most frequent of the human prion diseases, although it is still rare. Sporadic, familial, iatrogenic, and variant forms of CJD are all recognized. The sporadic form is responsible for about 85% of cases of prion diseases in humans [2]. It occurs throughout the world, with an annual incidence of one case per million. The risk of developing the disease increases with age, reaching a peak between 60 and 74 years (six cases per million) [3].

Spongiform changes with neuronal loss and abnormal protein accumulation are the main histopathological features [1]. However, the clinical presentation and the typical findings in electroencephalography, magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) are in most cases sufficient to establish the CJD as probable [4].

The clinical picture is characterized by a rapidly progressive evolution of cognitive, behavioral and personality changes, difficulties with movement and coordination, visual and constitutional symptoms. Myoclonus is typical later in the clinical course. The end stage is usually a kinetic-mute state [2].

An electroencephalogram (EEG) characteristic of CJD shows sharp or triphasic waves (periodic sharp wave complexes). This finding is highly specific (91%), but not so sensitive (61%) [5]. Unfortunately, the EEG is often typical only late in the course of CJD [6]. Although somewhat controversial, CSF biomarkers, namely the 14-3-3 protein, may be useful in reducing diagnostic uncertainty [7].

The MRI has shown high sensitivity and specificity for the diagnosis of CJD. The most typical changes involve the cortex and the deep grey matter (striatum and/or thalamus), particularly noticeable on FLAIR and diffusion-weighted imaging (DWI) [6].

Despite advances in diagnosis, the absence of effective treatment makes this disease invariably progressive and rapidly fatal. In variant CJD survival is usually more prolonged than in sporadic CJD, but considerable variation is seen within all subtypes of human transmissible spongiform encephalopathies, namely in genetic and iatrogenic forms. In a case series of M. Pocchiari et al., sporadic and genetic CJD had the shortest median survival times of less than six months; while variant CJD had median clinical durations of approximately 1 year [8].

CASE PRESENTATION

We present the case of a fifty-six-year-old man with the fourth grade, right-handed and working as a goldsmith with a past...
medical history of hypertension, dyslipidemia and an intestinal surgery for obstruction. He was referred to the neurologist observation in November 2009, after an episode of anal pain with change in strength/sensitivity affecting the left side of the body; no clear etiology was found, but there was spontaneous and complete resolution in few weeks. Since then he started complaints of difficulty concentrating, will-lessness, irritability, decreased libido and easy fatigue. He had started fluoxetine by his family physician, but did not improve. The neurological exam was normal.

In April 2010, he had more difficulty in keeping regular tasks at work and remembering recent events, was more distracted and undecided and more dependent on his wife. He scored 28/30 in the mini-mental state examination (MMSE); the clock-drawing test was perfect and the remainder neurological exam was normal. The brain MRI and the neuropsychological assessment were normal too.

In August 2010, he was maintaining the same complaints, but kept his professional activity, which involved long trips on his own. In March 2011, mnesic complaints were getting worse, but the patient continued his activities at work.

He was more or less the same until February 2012; at this point he showed a quick cognitive decline, in about four months. He was hospitalized in June of the same year for further diagnostic investigation. At that time he was listless and inattentive, without verbal or motor initiative, with puerile behavior, unable to perform the MMSE. He presented mixed aphasia. The muscle tone was normal and there were no motor deficits; the deep tendon reflexes had a symmetrical brisk response. There were no signs of cerebellar dysfunction, namely appendicular dysmetria. He was able to walk, but with an abnormal posture, catatonic-like. There were no frontal release signs or myoclonus. At this stage, he still maintained normal sleep and eating patterns. He already needed some guidance to dress and to manage personal hygiene.

Brain MRI showed restricted diffusion in the parieto-occipital, temporal, parasagittal frontal and insular cortex (Figure 1). The EEG revealed a slow basal activity, irregular and symmetrical, with inscription of periodic activity, characterized by biphasic wave complexes and slow wave, with right and left anterior hemispheric predominance; no myoclonus was detected. The 14-3-3 protein assay in the CSF was positive. The immunological study was negative and other infectious causes were not identified. Thyroid function was normal and the vitamin assays showed no deficits. The diagnosis of probable sporadic CJD was made.

In the last quarter of 2012, he was described as bedridden, dependent for all activities of daily life, fed by nasogastric tube, with myoclonus and in akinetic mutism. He died in March 2013.

**DISCUSSION**

The patient presented does not follow the typical pattern of rapid evolution of CJD: during four years, there were only subjective cognitive complaints without important impact on daily activities, including professional duties. Significant cognitive deterioration occurred only three years after the first symptoms and progressed to dementia in about four months. In the final phase the patient was in akinetic mutism with myoclonus, typical characteristics of the advanced stage of this disease.

**REFERENCES**