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Two Forms of Presentation of Confirmed Sporadic Creutzfeldt-Jakob Disease

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Abstract

Prion diseases are a rare type of neurodegenerative disease, and the sporadic Creutzfeldt-Jakob subtype is the most common. The disease occurs worldwide with an incidence of 1 case per million population per year. Prion protein (*PrP*) gene polymorphism without genetic mutation results in an aberrant protein isoform being deposited intraneuronally, leading to spongiform neuronal degeneration. We report on two patients who were admitted to our Service with systemic and neurological disease, with fatal end after 14 and 9 months of follow-up, respectively. Diagnosis was confirmed by histologic examination of the brain.

Keywords: Dementia; Sporadic Creutzfeldt-Jakob disease; Prion diseases; Protein 14-3-3 protein; Constitutional syndrome

Introduction

Case report on two confirmed cases of sporadic Creutzfeldt-Jakob disease (CJD) diagnosed in our Internal Medicine Service, with different clinical patterns of presentation.

Case Report

Case 1

A 75-year-old woman with no relevant medical history was admitted to our Service for a systemic, organic disorder at two months' evolution. During the neurological examination, she presented a fine distal tremor in both hands and mild short-term memory loss, with no other symptoms of interest. The complementary tests that were initially carried out (blood test for tumour biomarkers, chest radiograph, cranial and chest-abdominal computerised tomography [CT] scan, mammography) were all normal. After seven months of follow-up, the patient

displayed more notable memory loss, involuntary choreic movements, generalised asymmetrical myoclonus (involuntary twitching), dysmetria and ataxia. Cerebrospinal fluid was positive for the 14-3-3 protein, and the nuclear magnetic resonance (NMR) imaging of the brain only showed chronic ischaemic lacunar lesions. Four months later, she presented with increased myocloni, visual hallucinations and worsened memory loss. The genetic study showed heterozygosity methionine/valine at codon 129, with no mutations in the prion protein gene (*PrNP*), which ruled out a genetic origin and suggested CJD. The electroencephalogram (EEG) had an abnormal appearance, with irregularities and slowness in the base activity and some sharp waves in both hemispheres. Fourteen months after initial clinical presentation, the patient died from respiratory sepsis. Following autopsy, the cerebropathological report described the deterioration of the spongiform in the grey matter, vacuolisation with more intense involvement of the caudate and putamen, considerable neuronal loss, marked astrocytic gliosis and prion protein (PrP) deposits. The definitive diagnosis was "spongiform encephalopathy, type CJD, with immunohistochemically positive deposits of PrP".

Case 2

A 79-year-old woman, with no relevant medical history and a Barthel Index of 100, who was admitted to our service due to progressive cognitive deterioration at 3-4 weeks' evolution, with episodic anterograde amnesia, temporal-spatial disorientation and progressive sensory dysfasia. There was no motor or sensory impairment, ataxia or sphincter incontinence. The clinical situation worsened rapidly, especially the higher cortical functions (severe transcortical sensory aphasia, motor aphasia, complete anterograde amnesia, attention deficit), with appearance of progressive myocloni of the laterocervical region and in the upper left limb.

The blood tests, tumor biomarkers, endocrinological (adrenocorticotrophic hormone [ACTH], thyroid stimulating

hormone (TSH), cortisol) and immunological (onconeural antibodies) studies, serology (syphilis and HIV) and the brain computerised axial tomography (CAT) scan were all normal. The NMR showed predominantly frontal diffuse cortical atrophy; disturbed cortical signal with bilateral diffusion restriction and parieto-occipital predominance; and signal alterations in the superior cerebellar mesencephalon/peduncle. There was no involvement of the basal ganglia. The EEG showed diffuse periodic short-interval diffuse discharges (PSIDDs), and the analysis of the cerebrospinal fluid was positive for the 14-3-3 protein. The brain SPECT showed diffuse cortical hypoperfusion, which was more severe in the left frontotemporal and bilateral parietal regions. The patient's condition worsened gradually over the next 5-6 weeks, when akinetic mutism and dysphagia to both solids and liquids appeared. The patient died from respiratory sepsis at three months. The neuropathological diagnosis confirmed the type CJD spongiform encephalopathy.

Discussion

CJD is a rare cause of dementia (incidence 1:1,000,000). It generally appears in the fifth or sixth decade of life, with no distinction between sexes. Among the associated risk factors, reports have described cases related to the administration of growth hormones and gonadotropin, the performance of cornea and liver transplants, and the use of contaminated materials in neurosurgery [1]. Several subtypes of CJD have been described: 85%-90% are sporadic, 5%-15% are hereditary and 1% are acquired. The typical clinical presentation is a rapidly progressive dementia with behavioural changes (particularly in younger patients), cortical impairments (aphasia, amnesia and attention deficit), myocloni, corticospinal tract alterations, and akinetic mutism (usually occurring in the final stages) [2]. At times, CJD can present as a progressive pseudodementia, secondary to a depressive syndrome, or rarely, as a systemic disorder (case 1) [3,4].

It is important to consider this disease within a differential diagnosis of rapidly progressive dementia. The brain NMR and EEG may suggest the probability of CJD. Similar findings in the NMR and EEG also appear in metabolic and toxic encephalopathies, viral encephalomyelitis (HIV and herpes virus) and paraneoplastic syndromes [5]. The positive identification of 14-3-3 protein in cerebrospinal fluid (sensitivity 92%, specificity 80%) is one of the most frequently used analytical methods for the diagnosis [6]. Mean survival usually ranges from six months to a year [7]. Definitive diagnosis is confirmed by pathological anatomy, but criteria for clinical suspicion have been described (presence of progressive dementia+two typical clinical symptoms [myoclonus, extrapyramidalism, cerebellar degeneration, akinetic mutism]+abnormal EEG or 14-3-3 protein in cerebrospinal fluid or suggestive findings on NMR (diffusion weighted imaging, DWI, or fluid-attenuated inversion recovery, FLAIR) [8-10].

The anatomopathological diagnosis by standardised autopsy should be mandatory in all cases where suspicion exists, with a particular importance given to identifying hereditary cases and other genetic prion disease (fatal familial insomnia and Gertsmann-Straussler-Scheinker disease). Currently, there is no

treatment for this disease, and the vital prognosis is ominous in the short term.

We want to highlight the need to consider this pathology, not only in the study of a patient with cognitive decline, but also in systemic syndromes associated with neuropsychiatric disorders. The diagnosis of suspicion should be made as soon as possible, as epidemiological and preventive measures must be foremost from the very beginning.

Conclusion

CJD is very rare form of rapidly progressive dementia that should be considered once the most frequent processes (Alzheimer's disease, Parkinson's disease, frontotemporal dementia, alcoholic dementia and Lewy body dementia) have been ruled out. Up to 90% of cases are sporadic, although clusters in incidence have been described (probably due to greater epidemiological vigilance). The diagnosis of suspicion is essential, keeping in mind the possibility of atypical presentation as a systemic syndrome.

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