

# Creutzfeldt-Jacob Disease with psychiatric onset: a case report

*Malattia di Creutzfeldt-Jacob con presentazione psichiatrica: un caso clinico*

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## Summary

### Introduction

*Creutzfeldt-Jacob Disease (CJD) is a neurological degenerative prion disease with a long incubation period but a rapidly progressive course after the onset of symptoms. Clinical onset is characterized in most cases by neurological symptoms, while in a much smaller percentage by signs of mental deterioration and psychiatric symptoms.*

### Case report

*We describe the case of an elderly female patient who presented with psychotic symptoms in the absence of neurological signs and symptoms, and after systematic diagnostic evaluation eventually turned out to be a sporadic CJD case.*

### Conclusions

*In clinical practice CJD should not be neglected as differential diagnosis in elderly patients with negative psychiatric history referring to psychiatrists for recent onset and rapidly progressing symptoms as behavior changes, anxiety, irritability, mood deflection, insomnia and poor response to treatment. In the case we reported, indeed, the symptoms necessary to diagnose a possible sporadic form of CJD, as focal neurological deficits or apraxia, emerged only belatedly, at a final stage, while symptoms at onset appeared to be purely psychiatric.*

### Key words

Creutzfeldt-Jacob Disease • Prion • MRI • Delusions

## Introduction

Creutzfeldt-Jacob Disease (CJD) is a neurological degenerative prion disease with typical neuropathological (spongiosis, neurogliosis, neuronal loss in absence of inflammation), molecular and genetic alterations<sup>1</sup>. CJD has a long incubation period but a rapidly progressive course after the onset of symptoms<sup>2</sup>. Diagnostic criteria to make a diagnosis of probable sporadic CJD (UCSF, 2007)<sup>3</sup> include: (1) rapid cognitive decline; (2) at least two of the following 6 symptoms: myoclonus, pyramidal/extra pyramidal, visual, cerebellar, akinetic mutism, other focal higher cortical sign (e.g., neglect, aphasia, apraxia, acalculia); (3) positive EEG (periodic epileptiform discharges) or positive MRI (either sub-cortical hyperintensity or cortical gyral hyperintensity [cortical ribboning] on DWI and preferably restricted diffusion on ADC map) or both; (4) routine investigations do not suggest an alternative diagnosis. Clinical onset is characterized in most cases by neurological symptoms, while in a much smaller percentage by signs of mental deterioration and psychiatric symptoms. Nonetheless, the diagnostic hypothesis of CJD should not be neglected in psychiatric settings when assessing elderly patients with no

psychopathological history presenting with recent onset and rapid progression of behavioral changes, anxiety, irritability, mood deflection, and insomnia. The differential diagnosis of psychosis in elderly patients includes delirium, dementia and primary psychiatric disorders<sup>4</sup>. A careful assessment is crucial to make the proper diagnosis. We describe the case of an elderly female patient who presented with psychotic symptoms in the absence of neurological signs and symptoms, and after systematic diagnostic evaluation eventually turned out to be a sporadic CJD case.

## Case report

P.R. is a 69-year-old woman, married, retired female nurse, who was referred for urgent psychiatric consultation by her General Practitioner for “psychomotor agitation”. The personal and family psychiatric history of the patient was unremarkable. No organic comorbidity was highlighted. The recent history was collected by the patient’s relatives (husband and sister), who reported that in the last 2-3 months the patient had shown behavioral changes, amnesia, suspiciousness and verbal aggressiveness toward her husband. The patient’s functioning had recently

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declined, and to date she had been able to manage her daily activities and shown a good social functioning. At first psychiatric evaluation, the patient was cooperative and helpful, alert but confused, not oriented in time, partly oriented towards space and self. The attention span was brief, with easy distractibility. It was possible to appreciate qualitative disorders of memory (false recognition) and medical history reported amnesia of fixation. Her speech was fluid and abundant with colorful tones and over-confidence, rich in confabulations. Formal thought disorders, such as perseverance and circumstantiality, were also evident. Thought content was focused on delusional persecutory issues about her husband's behaviour. The patient's mood was dysphoric and her attitude fatuous and disinhibited.

On the basis of this clinical picture, the patient was admitted to our Psychiatric ward. The physical and neurological examination performed upon admission to the ward and routine blood tests and ECG showed no pathological alterations.

According to the clinical picture, negative psychopathologic history and the rapid progression of presenting symptoms, an organic substrate for psychiatric symptoms was hypothesized. Systematic diagnostic evaluation began with an EEG and a CT yielding inconclusive results because of nonspecific reports (Tab. Ia for details).

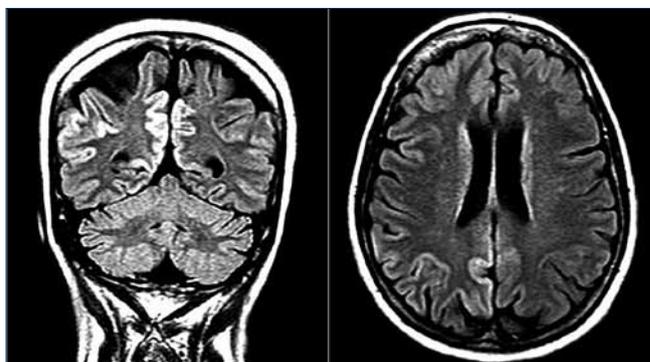
To manage the worsening of symptoms which emerged during hospitalization with worsening confusion, thought disorganization, well-organized visual hallucinations and illusions, alternating drowsiness and psychomotor agitation, therapy was initiated with atypical antipsychotics (quetiapine up to 200 mg/day) and benzodiazepines (initially with 250 cc saline + lorazepam 4 mg/day i.v., and then gradually decreased to 1 mg/day administered orally). Since in similar cases definite guidelines are lacking as far as pharmacotherapy is concerned, we chose an atypical antipsychotic with a sedative effect but with little collateral effects on movement.

According to the rapid evolution of symptoms, it was possible to exclude common forms of dementia, such as Alzheimer's disease<sup>5</sup>. An unresponsive to treatment dementia that evolves rapidly, is associated with motor symptoms, and leads to death in a few months average, is typical of a prion disease<sup>6</sup>.

Afterwards, the patient's symptoms worsened, with a deterioration in mental status, opposition to feeding and mobilization; neurological symptoms eventually turned evident with apraxia and focal neurological deficits (myoclonus, pyramidal and akinetic mutism). Given the poor response to treatment and the non-specificity of the results of instrumental tests so far, MRI was performed (Tab. Ib and Fig. 1). MRI showed a picture compatible, as first hypothesis, with neural degenerative cortex alterations of possible prion disease.

**TABLE I.**Results of instrumental tests. *Referti test strumentali.*

Test	Report: salient data
EEG a	Widespread brain electrical signs of suffering more evident in bilateral fronto-temporal quadrant
CT a	Absence of any solid or haemorrhagic lesion
MRI b	Grey matter cortical ribboning of: right parietal lobe cortex, homolateral cingulate gyrus, right prefrontal dorso-lateral cortex, left temporo-parietal cortex, left dorso-lateral prefrontal cortex
EEG c	Severely abnormal triphasic periodic waves characterized by diffuse projection

**FIGURE 1.**  
MRI.

The patient was then transferred to the Neurology department. A second EEG showed, this time, severely abnormal triphasic periodic waves characterized by diffuse projection (Tab. Ic).

It was then necessary to perform tests on CSF in order to confirm prion disease. Lumbar puncture showed the presence of protein 14/3/3 and high Tau protein levels (16.383 pg/ml). Genetic analysis showed homozygosity for Met/Met gene. At this time, it was possible to diagnose CJD, sporadic form.

In our clinical case, motor symptoms become evident lately. Finally, the patient died after seventy days of hospitalization, according to normal evolution of the disease, where death occurs after an average of four months since symptoms onset<sup>7,8</sup>.

## Discussion

Sporadic CJD (sCJD) is the most common form of spongiform encephalopathy. The mean age of onset is around 65 years of age with a median survival time of four months<sup>9</sup>. In sCJD, a variety of psychological and behav-

**TABLE II.**Potential causes of rapidly progressive dementias <sup>10-12</sup>. *Potenziali cause di demenza rapidamente progressiva* <sup>10-12</sup>.

Vascular	Ischemic or haemorrhagic stroke
Infectious	HSV, HIV, Syphilis, PESS, PML, aspergillosis
Toxic - Metabolic	Endocrine abnormalities – thyroid, parathyroid, adrenal disease -, electrolyte abnormalities, vitamin deficiency, uremia, Wilson's disease, hepatic encephalopathy, metal toxicity
Autoimmune	Hashimoto encephalopathy, PLE, VGKC, lupus, sarcoidosis, CNS vasculitis
Metastases - CNS neoplasm	
Iatrogenic	e.g. pituitary hormone recipients <sup>12</sup>
Neurodegenerative	Prion disease, AD, DLB, FTD, CBD, PSP
Systemic	Sarcoidosis, mitochondrial disease e.g. MELAS

our symptoms occur, such as changes in personality, insomnia, depression, behavioural dyscontrol and psychosis, and can precede neurological involvement, but only in a small percentage of cases. Cognitive impairment and ataxia could appear before myoclonic jerks, pyramidal and extrapyramidal symptoms. Rare presentations like occipital blindness, stroke-like onset and pure cerebellar syndrome have also been reported.

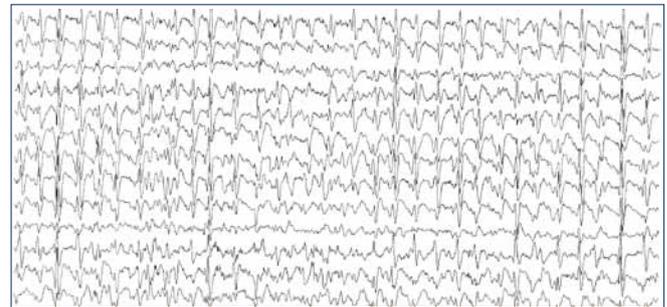
When suspecting sCJD it is necessary to evaluate potential causes of rapidly progressive dementia, as listed in Table II. Currently, therapies to cure or to delay the progression of the disease are not available, so the only therapeutic opportunity is symptomatic relief. There are no specific studies about the management of psychiatric illness in CJD. Anxiety, agitation, restlessness or aggression may be treated with benzodiazepines. Alternatively, second generation neuroleptics can be prescribed. An antidepressant might be effective for depressive symptoms <sup>13</sup>. The role of psychiatrists therefore is to set up a proper treatment and to assist patients, relatives and other clinicians in a liaison psychiatry setting.

## Conclusions

CJD should not be neglected as differential diagnosis in elderly patients with negative psychiatric history referring to psychiatrists for recent onset and rapidly progressing symptoms such as behavioural changes, anxiety, irritability, mood deflection and insomnia.

In the case we reported, the symptoms necessary to diagnose a possible sporadic form of CJD (UCSF, 2007) <sup>3</sup>, such as focal neurological deficits or apraxia, emerged only belatedly, at a final stage, while symptoms at onset appeared to be purely psychiatric.

In clinical practice, it is therefore important for psychiatrists to consider prion diseases among the possible differential diagnoses in late onset, non-responsive to treatment, psychotic symptoms.



**FIGURE 2.**  
EEG-c.

## Meetings

Poster: 15° congresso della Società Italiana di Psicopatologia, Vulnerabilità, esordi, intervento precoce, 15-19 febbraio 2011, Roma. E-poster: 19<sup>th</sup> European congress of Psychiatry – EPA 2011, 12-15 march 2011. Vienna, Austria.

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