CASE REPORT

A patient with a 'typical presentation' of Wernicke encephalopathy was found to have sporadic Creutzfeldt-Jakob disease

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ABSTRACT

Creutzfeldt-Jakob disease (CJD) has a significant degree of clinical heterogeneity that is especially found in the features at onset. Here we present a patient with the sporadic form of CJD mimicking Wernicke encephalopathy. We first treated him with a high dose of thiamine; however, the vitamin B1 levels proved to be normal, which ruled out Wernicke encephalopathy. Meanwhile, his clinical condition progressively worsened and he developed a rapidly progressive cognitive disorder, mutism and myoclonus of the muscles. At this point, the diagnosis of CJD was most likely. The patient died two months after the first symptoms. Autopsy showed prion-protein depositions in several regions. Genetic analysis was negative for familial CJD. Those findings confirmed the diagnosis of 'sporadic Creutzfeldt-Jakob disease'. CJD presents in a wide range of sequences and clinical symptoms. Therefore, recognition in the early stage can be difficult.

KEYWORDS

Creutzfeldt-Jakob disease, Sporadic, Wernicke encephalopathy

What is known on this topic?
Creutzfeldt-Jakob disease (CJD) has a significant degree of clinical heterogeneity that is especially found in the features at onset. Recognition of the disease is exceedingly difficult.

What does this add?
It is not uncommon that an alternative diagnosis is suspected. The disease CJD can mimic acute Wernicke encephalopathy, which was the case with our patient. We call attention to the importance of recognition of sporadic CJD.

INTRODUCTION

Creutzfeldt-Jakob disease (CJD) is a neurodegenerative disorder. It is a transmissible prion disease whereby incorrectly folded prion proteins are formed.[1,2] There are several forms of the disease, depending on the prion subtype. Recognition of the disease is exceedingly difficult.[3,4] We describe a 65-year-old man with the sporadic form of CJD mimicking Wernicke encephalopathy.

CASE REPORT

A 65-year-old man was referred to the department of internal medicine by the general practitioner due to complaints of progressive cognitive impairment, which consisted of memory loss, loss of organisation and disorientation. He also had a drunken man's gait and double vision. These complaints had been present for approximately four weeks.

The medical history revealed a myocardial infarction and chronic obstructive pulmonary disease. The patient was not on any medication. He drank 6 units of beer a day. Previously, his alcohol consumption had been considerably higher.

The general physical examination showed no abnormalities. On neurological examination he had nystagmus, a paresis of the right lateral rectus muscle of

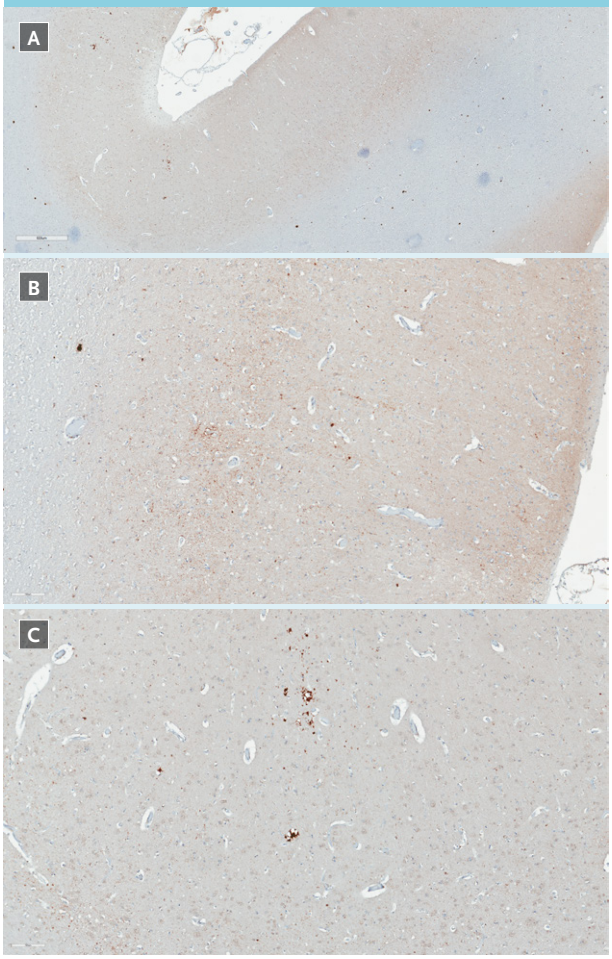
the eye and a wide gait. Additional laboratory tests and a CAT scan of the brain showed no abnormalities. The most obvious diagnosis was acute Wernicke encephalopathy. We treated the patient immediately with thiamine 500 mg three times a day. After two days the paresis of the lateral rectus muscle showed some improvement. We sent the patient home with the advice to take 100 mg thiamine a day. His wife was involved in the care and checked the correct intake of medications.

However, six weeks later the patient's cognitive function had regressed and he was totally dependent in his activities of daily living. He also had a dysarthric speech, nystagmus, ataxia and myoclonus of several muscle groups. The diagnosis of rapidly progressive dementia was made, with the differential diagnosis limbic encephalitis, malignancy or Creutzfeldt Jakob disease (CJD). Meanwhile, the results of the vitamin B1 level proved to be normal, whereupon the diagnosis of acute Wernicke encephalopathy was rejected. Tests for paraneoplastic antibodies were negative and the level of protein 14-3-3 in cerebral spinal fluid (CSF) was still pending. An MRI scan (with diffusion weighted imaging) of the brain gave no new insights. The EEG showed a diffuse encephalopathic pattern with delta waves parieto-temporally and sharp-slow waves without triphasic complexes, which made a neurodegenerative condition more likely.

During the following days there was a rapid progression of the symptoms, as well as hypertonia in the arms and legs. The patient could barely speak. The diagnosis of CJD was most likely and the infaust prognosis was shared with the family members. We contacted the physicians of the Registration Centre of Prion Diseases of the Department of Epidemiology, ErasmusMC Rotterdam, who informed the public health authorities. They contacted the family members to inform them about the importance of performing an autopsy.

The patient died the following day, two months after the first symptoms emerged. During the autopsy of the brain, deposits of prion proteins were found, both synaptic as well as perineural and perivacuolar (*figure 1*). The 14-3-3 protein was detected in CSF. Gene analysis was negative for the familial form of CJD. These findings confirmed the sporadic form of Creutzfeldt-Jakob disease.

Figure 1. *Staining with 3F4-anti-PrP. A. Overview of a sulcus with fine cortical synaptic pattern (brown, fine-grained haze) perivacuolar staining and plaque-like deposits in the white matter. B. Low perineural enhancement. C. Perivacuolar deposits*



Pathogenesis and clinic

CJD is a communicable and fatal neurodegenerative disease caused by accumulation of natural misfolded proteins (prion proteins) in the body, which will deform the central nervous system.[1,5] Neural loss, astrocyte proliferation, spongiform changes and deposition of proteins in the brain tissue will occur.

CJD is divided into multiple forms, depending on the cause and clinical pathological profile (*table 1*). The sporadic form occurs in 85% of all cases of CJD, with an annual worldwide incidence of 1-2 persons/million. It occurs particularly in people between the ages of 50-70 years.[4] The cause is unclear, but there may be a spontaneous change of the structure of prion protein or a spontaneous mutation in the PRNP gene encoding.

Individuals can present with the same symptoms in a different sequence, which makes the disease difficult to recognize in the early stages.[3,6,7] It is not uncommon that an alternative diagnosis is suspected, which was the case with our patient.

There are always signs of a rapidly progressive dementia, developing over a period of several weeks or months, in combination with other symptoms such as cerebellar ataxia, loss of vision and myoclonus. However, the disease can also present with isolated cerebellar ataxia or an isolated loss of vision. Characteristically the symptoms are rapidly progressive. The patient can deteriorate in a matter

Table 1. *CJD divided into multiple forms*

Forms of CJD	Cause	Features
Sporadic form	Unclear: probably a spontaneous mutation in the prion protein	• Occurs at middle-age • Cerebellar ataxia, loss of vision, myoclonus • Median duration of disease is 5 months
Genetic form	Mutations in PRNP gene	• Can mimic the other forms • Dementia often occurs late in the course of disease • Median duration of disease is several years • Family history can be negative • Can occur at younger ages • Often no detectable 14-3-3 proteins in CSF
Iatrogenic form	Iatrogenic transmission of prion protein by invasive medical treatment	• Similar features as the sporadic form
Variant	Ingestion of contaminated products with bovine spongiform encephalopathy	• Occurs at a young age (median age 26 years) • Presents with psychiatric symptoms such as depression, anxiety and social withdrawal • At later stadium there is ataxia, dystonia, chorea, myoclonus. • Median duration of disease is 14 months

of days. Classical symptoms at the end stage of the disease are akinetic mutism and myoclonus, which were present in our patient. The median duration of the disease is four months.[3]

Diagnosis and treatment

As previously described,[8] often the diagnosis cannot be made with certainty during the patient's life. To diagnose CJD with certainty examination of (post-mortem) brain tissue showing the presence of prion proteins in the brain tissues is required. In exceptional cases a brain biopsy is performed while the patient is still alive if there are clear MRI changes, which can be biopsied. The sensitivity of the detection of 14-3-3 protein in CSF (a nonspecific marker of rapid neuronal loss) is 94-97% and the specificity is 84-87%.[9,10] The sensitivity of detection of periodic sharp wave complexes in the EEG is 66% with a specificity of 74%. According to the diagnostic criteria, six weeks after presentation the probable diagnosis 'sporadic CJD' could have been made in our patient due to rapid progressive dementia, visual and cerebellar problems and myoclonus (*table 2*).[11]

To date, there is no curative treatment for this disease and the treatment is only supportive.

Pitfalls

CJD can mimic acute Wernicke encephalopathy with the classical triad of cognitive impairment, nystagmus and ataxia caused by a vitamin B1 deficiency, which is typically seen in malnourished patients, for example in alcohol abusers.[12] In our patient this triad was present. Combined with the alcohol abuse, the diagnosis was plausible. However, the non-significant improvement of the paresis of the lateral rectus muscle after supplementation with thiamine did not seem to support this diagnosis.

With the onset of new symptoms a few weeks later, the diagnosis of CJD became clear, enabling us to inform the family members of the situation.

CONCLUSION

The rarity of CJD and the diverse clinical symptoms make recognition of the disease extremely difficult. Rapid recognition of the disease is important so that the patient and relatives can be informed as early as possible during the course of the disease. It is essential to inform the relatives fully to create awareness that deterioration of their loved one can be expected within a period of weeks without possible treatment. Also of importance for the relatives is the information about whether the CJD is the familial form. Because the diagnosis can only be made with the examination of (post-mortem) brain tissue, family members should be extensively counselled about the importance of performing an autopsy.

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Table 2. *Diagnostic criteria for sporadic CJD (January 2017) adapted from the university of Edinburgh*[11]

A	Rapidly progressive cognitive impairment
B	– Myoclonus – Visual or cerebellar problems – Pyramidal or extrapyramidal features – Akinetic mutism
C	Typical EEG
D	High signal in caudate/putamen on MRI brain scan

Suspect cases can be diagnosed as 'sporadic CJD' as follows;

Possible
A and two items of B and duration < 2 years

Probable
A and two items of B and typical EEG*
OR
A and two items of B and typical MRI brain scan**
OR
A and two items of B and positive 14-3-3 protein in CSF
OR
Progressive neurological syndrome and positive 'real-time quaking-induced conversion (RT-QuIC)' in CSF or other tissues

Definite
Progressive neurological syndrome and
Neuropathologically or immunocytochemically or biochemically confirmed

*Generalised periodic complexes
**High signal in caudate/putamen on MRI brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR).

spelling. Furthermore we would like to thank the family of our patient for granting informed consent to publish this case report.

DISCLOSURES

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