CASE REPORT

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Parkinsonism as an atypical primary presentation of sporadic Creutzfeldt-Jakob disease

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ABSTRACT

BACKGROUND

Creutzfeldt - Jakob disease (CJD) is a rare prion-related neurodegenerative disease with a rapid progression and almost definitely fatal outcome. The most common manifestation is rapidly progressive dementia with gait ataxia and visual disturbance. However there are a few reports of patients with atypical features as the initial presentation that later developed to typical characteristics in the course of the disease. Additionally there are variants of CJD in which the primary manifestation might be challenging as the ones presenting with psychiatric complaints accompanied by sensory impairment. To our knowledge, the prognosis in the classical form of the disease is poorer with a rapid deterioration leading to death. Here we aimed to focus on the diverse presentations of sporadic CJD (sCJD) especially in the early stages which might cause a conflict for proper diagnosis.

CASE DESCRIPTION

The patient was a 62-year old man presenting to our referral clinic with progressive gait disturbance and bradykinesia. Based on the initial examination, atypical parkinsonism was diagnosed. However, over two weeks the patient developed an acute confusional state with involuntary movement. The second examination was highly suggestive of sCJD which was confirmed by the paraclinical assessments.

CONCLUSION

Sporadic CJD is a rare neurodegenerative disease with distinctive characteristics. However, there are reports of various manifestations of the disease. The present report indicates the diverse presentations of sCJD.

Keywords: CJD, parkinsonism, dementia, abnormal movement

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INTRODUCTION

Creutzfeldt-Jakob disease (CJD) is a rare prion-related neurodegenerative disease with a rapid progression which results almost definitely in death over a year.[1] Worldwide, the annual incidence of CJD is about 1–2 cases per 1 million people.[2]

Although it seems that the prevalence of the disease is insignificant, the importance of the burden of disease and the consequent effects on the social life of the patients' family makes the appropriate diagnosis a critical matter. Additionally, there are a few acquired forms of the disease which might lead to an epidemic if the underlying cause is not resolved. To date, about 260 cases of variant CJD (vCJD) mostly in the United Kingdom have been reported relating to consumption of infected beef. Other possible reported causative animals are elk, deer, sheep and goats.[2,3] Another challenge is the limitation to organ donation in these patients as there is the possibility of disease transmission through corneal or dura matter grafts.[4]

CJD usually appears in later life typically at about age 60. The most frequent form of CJD is the sporadic form (sCJD) accounting for about 85 % of all cases without a known cause in which the infected prions are believed to be made by an error of the cell machinery for making proteins.[3] The mean onset age of sCJD is 65 years.[5,6]

The main clinical features include a rapidly progressive dementia, myoclonus, visual disturbances, and cerebellar and pyramidal/ extrapyramidal signs. The confusional state might not be the first initial sign, however in the terminal stages, a severe dementia and akinetic mutism will develop.[5-7] On the other hand, to the best of our knowledge, parkinsonism is a rare primary manifestation of sCJD.[3]

It should be considered that the definite diagnosis of CJD is based on histopathological confirmation. A considerable limitation of brain biopsy is the risk of being accidentally infected by self-inoculation as there is no cure for the disease. Additionally the tissue biopsy is not always obtained from the affected part of the brain.[8]

There are other paraclinical tests providing easier ways to diagnosis as it can be supported by the presence of protein 14–3–3 in the cerebrospinal fluid (CSF), generalized fast periodic sharp wave complexes in the EEG, magnetic resonance imaging (MRI) abnormalities as alteration on diffusion weighted images (DWI) or fluid attenuated inversion recovery images (FLAIR) in caudate nucleus and/or putamen and in at least two cortical regions.[9,10]

Currently, there is neither curative nor modifying treatment. All the therapeutic methods are confined to make the patient comfortable as possible.[8] Here we aimed to describe a case of sCJD presenting with asymmetric parkinsonism which developed to the typical presentation of the disease over a month and eventually died over the course of nine months.

CASE REPORT

The patient was a 62-year old man presenting with a history of a month of progressive gait difficulty, bradykinesia and right-hand tremor. There were no complaints of early falls, ophthalmoplegia, sphincter impairment or dementia. His past medical history was unremarkable.

On examination, the patient was able to complete the Mini-Mental State Examination (MMSE) with a score of 28. He had a mask-like face. The motor system revealed generalized rigidity on the right side. Pill-rolling tremor was detected in the right hand. The gait was severely impaired due to short steps and flexed posture. Other examination outcomes were normal.

All requested paraclinical examinations such as brain MRI and biochemistry were unrevealing. Given concern for atypical parkinsonism, treatment with Madopar 125 mg in divided dosage was started.

Two weeks later, the patient was admitted due to progressive agitated confusional state. The

second neurologic evaluation disclosed additional findings consisting of an MMSE score of 18, ataxic gait and frequent myoclonus on right shoulder.

A comprehensive assessment ruled out symptomatic encephalopathy secondary to infectious, endocrine, and metabolic disorders and auto-immune encephalopathy. Cerebrospinal fluid analysis was positive for 14-3-3 protein. Brain imaging revealed restricted cortical diffusion in the cingulate gyrus and thalami (Figures 1 and 2). The EEG showed diffusely slow background activity without periodic discharges.

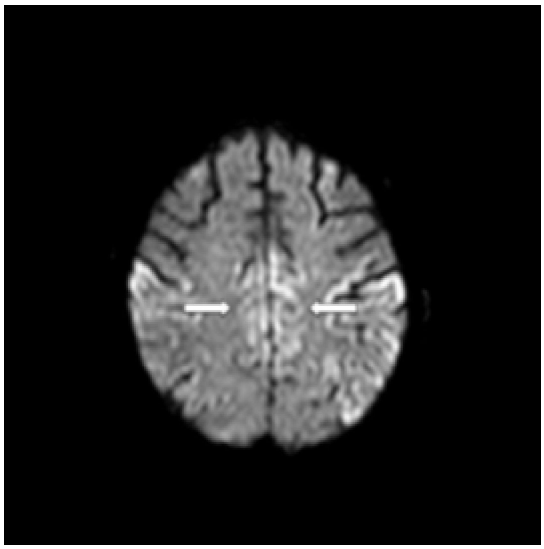

Figure 1. Hyperintense signal in the MRI diffusion-weighted images showing in the cingulate gyrus

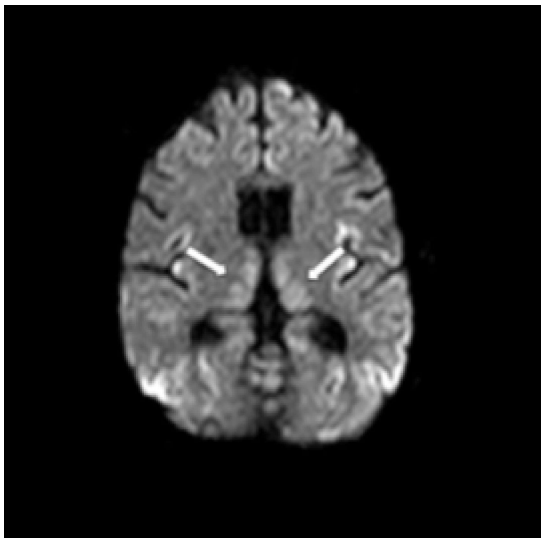

Figure 2. Hyperintense signal in the MRI diffusion-weighted images showing in bilateral thalami

Taking into account the total findings, the patient was diagnosed with sCJD. The family was consulted on the nature of the disease and the patient was discharged for home care. He progressively deteriorated and died 8 months after the onset. The patient's family did not give consent for autopsy. Informed consent was obtained by the patient for publication of the case report.

DISCUSSION

Creutzfeldt-Jakob disease (CJD) is a rare fatal neurodegenerative disorder which belongs to transmissible spongiform encephalopathy or prion disease.

It typically manifests with rapidly progressive dementia, visual disturbance and cerebellar ataxia which ultimately leads to death. As the disease progresses, the confusional state becomes more pronounced accompanied by frequent involuntary movements and eventually coma will occur. The disease affects about one person in one million per year worldwide which usually appears in the late years. However the variant forms in which atypical presentation as psychiatric symptoms are prominent, tend to occur at a younger age with a slightly longer duration.[1-4]

CJD captured public attention in the 1990s when there were reports of patients in the United Kingdom with variant CJD secondary to exposure to infected beef. [3] It might be primarily misdiagnosed as other dementias, such as Alzheimer's disease. However CJD has unique features on brain biopsy. Additionally its course tends to lead to more rapid deterioration than in other types of dementia.[11]As mentioned, there are three major categories of CJD in which sporadic CJD is the most common form accounting for at least 85% of cases.

Although the definite diagnosis is based on immunohistochemical evidence, the diagnosis could be suspected based on the CDC [12] criteria for sporadic CJD which categorize sCJD as:

1. Definite, in case of detection of protease-resistant prion protein or scrapie-associated fibrils.
2. Probable, in case of no alternative diagnoses and progressive dementia with at least 2 of (i)-(iv) and at least one of (a)-(c).
3. Possible, in case of no alternative diagnosis and progressive dementia with duration of less than 2 years and with at least 2 of (i)-(iv) and at least one of (a)-(c).

(i) Myoclonus
(ii) Visual or cerebellar problems
(iii) Pyramidal or extrapyramidal features
(iv) Akinetic mutism
(a) Periodic sharp wave complexes on electroencephalography
(b) Positive 14-3-3 protein in the cerebrospinal fluid with a disease duration of less than 2 years
(c) High signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR) MRI

There is no cure for the disease heretofore. However studies of a variety of drugs are now in progress. Currently the therapeutic approaches are confined to controlling the symptoms to make the patient as comfortable as possible.[8]

Although the prevalence of the disease is insignificant, it is of paramount importance to detect suspected patients as there are acquired cases which might lead to a disaster in case of distribution of the underlying cause such as infected beef.[4]

Furthermore there is always a fear for the family of the patient to become affected. Recent studies suggest that while there may be prions in the blood of individuals with vCJD, this is not the case in patients with sCJD. Taking into account all the considerations, it is crucial to make an appropriate diagnosis to determine both the prognosis and the possibility of transmission of the disease. As the typical presentation might be absent in the primary stages of the disease, it is critical to keep in mind a precise history and vigilant observation in the approach to patients with a confusional state.[9]

There are a few reports of atypical preliminary presentation of sCJD in the literature. Taillefer et al.[13] reported a 74-year old man who was admitted due to confusional state following urinary tract infection. The patient was initially treated for delirious state. However, with development of visual impairment and rapidly progressive cognitive impairment during hospitalization, CJD was suggested and confirmed by post-mortem biopsy. Similarly, Dirzius et al.[14] reported a case of definite sCJD who first presented with posterior reversible encephalopathy. In this case the primary confusional state was attributed to a vascular event as the brain MRI was compatible with posterior reversible encephalopathy syndrome (PRES). However the development of memory impairment, ataxia, myoclonus and right-sided rigidity pointed to an alternative etiology. Re-evaluation of the paraclinical examination confirmed the diagnosis of CJD and the patient rapidly deteriorated leading to her death over 13 weeks.

Although extrapyramidal symptoms such as rigidity are common in the course of the disease, there is no report of parkinsonism manifesting with gait disturbance, one-sided tremor and rigidity as the primary presentation of sCJD in the literature so far. In the case we are describing, the patient initially presented with progressive right-sided rigidity and tremor, gait disturbance and bradykinesia which were not compatible with typical Parkinson's disease as the symptoms were rapidly progressive. In the following two weeks, the patient developed the classical symptoms of sCJD and was admitted to the emergency department with acute confusional state and involuntary movements. Regarding the new physical examination and history, the clinical scenario was more compatible with CJD. Eventually the patient was diagnosed with probable sCJD based on the CDC criteria. Similar to Taillefer's case the initial brain MRI was

Table 1. Characteristics of patients who were diagnosed with sCJD

Case	Age	Gender	Primary presentation	Other manifestation	Brain MRI	EEG	Course
Taillefer et al.[14]	74	Female	Delirium	UTI	Initially: Normal Eventually: Bilateral restriction in basal ganglia	Initially: Mild encephalopathy Eventually: Periodic discharge in frontal lobes	12 weeks
Dirzius et al.[15]	63	Female	Rapidly progressive dementia	Visual impairment, rigidity, ataxic gait, involuntary movement, akinetic mutism	Initially: PRES Eventually: Symmetric lesions in basal ganglia	Initially: Normal Eventually: Periodic sharp wave complexes in frontal lobes	13 weeks
Our case	52	Male	Parkinsonism	Dementia, myoclonus	Initially: normal Eventually: bilateral restriction in cingulate gyrus, thalami	Mild to moderate without encephalopathy	9 months

unrevealing but eventually showed bilateral thalamic restriction.

A summary of the characteristics of our patient compared to other atypical case reports is presented in Table 1.

CONCLUSION

Sporadic CJD is a rare neurodegenerative disease with distinctive characteristics. The most common manifestation is the rapidly progressive dementia with gait ataxia and visual disturbance. However there are a few reports of patients with atypical features as the initial presentation that later developed the typical characteristics in the course of the disease. The present report indicates the diverse presentations of sCJD.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interests.

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