Acute presentation of rapidly progressive probable Creutzfeldt–Jakob disease

Introduction

This article presents the case of a 68-year-old man admitted with a 3-week history of cognitive deterioration and progressive gait disturbance. Before presentation the patient had worked normally as a chemical research scientist. Examination revealed myoclonic jerks and a right-sided homonymous hemianopia.

Initial investigations did not elucidate the aetiology of the disease. However, characteristic findings on CSF analysis and electroencephalography were highly suggestive of a diagnosis of sporadic Creutzfeldt–Jakob disease. This case represents a less common presentation of sporadic Creutzfeldt–Jakob disease because of the rapidity of decline, with progression to akinetic muteness and ultimately death within 6 weeks. It also highlights the importance of CSF analysis, with 14-3-3 protein detection, and electroencephalography analysis for the pre-mortem diagnosis of Creutzfeldt–Jakob disease.

Discussion

Creutzfeldt–Jakob disease is an incurable and invariably fatal neurodegenerative disease. The pathological process involves replication of misfolded prion proteins, which spread throughout the brain tissue causing it to become sponge-like in texture. This causes a progressive dementia often associated with personality disturbance, along with physical signs including myoclonus, speech disturbance and ataxia. The disease is rare with a reported incidence of one case per million each year.

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The median length of survival from diagnosis in sporadic Creutzfeldt–Jakob disease is considered to be 4–5 months, with around 65% of cases having a disease course of less than 6 months. Variant Creutzfeldt–Jakob disease, however, normally has a longer disease duration, with a median life expectancy of 14 months (Centers for Disease Control and Prevention, 2012).

The differential diagnosis of sporadic Creutzfeldt–Jakob disease includes a large number of neurological and psychiatric diseases, of which the most important in elderly patients is Alzheimer's dementia. Other forms of dementia, including Lewy body and vascular subtypes, are also frequently found. In younger patients inflammatory processes of the CNS, such as encephalitis, are more likely differentials.

As the age of onset in variant Creutzfeldt–Jakob disease is generally lower, a slightly different group of differentials exists, including vitamin B_{12} deficiency, cerebrovascular disease, Wilson's disease and cerebral vasculitis. However, the most common differentials for this condition remain Alzheimer's dementia and sporadic Creutzfeldt–Jakob disease (Zerr and Poser, 2002).

This case demonstrates an important differential diagnosis in patients presenting with a rapidly progressive deterioration in cognition. Creutzfeldt–Jakob disease, although rare, is extremely significant because of the incurable and invariably fatal nature of the condition, and a significant proportion of cases occur in those over the age of 65 years. Investigations, primarily with magnetic resonance imag-

Case Report

A 68-year-old chemical research scientist was admitted acutely to a care of the elderly ward in a district general hospital with a 3-week history of unsteady gait and loss of balance. His family described a 2-week history of rapid deterioration in cognitive function and disorientation. Before this, the patient had been functioning normally at work, which involved complex mathematical equations. Of note, 2 weeks previously he had been seen by an optician who had detected a right-sided homonymous hemianopia on visual field testing, and had referred him on to a neurologist. The day before admission family members noticed the onset of myoclonic jerking.

On admission the patient was disorientated in time and place and had a Mini-Mental State Examination score of 11/30. Examination showed evidence of myoclonic jerks and a degree of expressive dysphasia. Cranial nerve examination confirmed a right-sided homonymous hemianopia. Further physical examination was unremarkable.

Blood tests were all within normal ranges and imaging, including a computed tomography brain scan and two magnetic resonance imaging brain scans, was reported as normal (*Figures 1* and *2*). Electroencephalography testing, however, displayed abnormal findings of frequent asymmetrical sharp waveforms occurring in a repetitive manner and fluctuating in nature. In addition, the CSF immunoassay performed by the National Creutzfeldt–Jakob Disease Research and Surveillance Unit was positive for 14-3-3 protein. Many processes leading to rapid neuronal destruction can cause elevated 14-3-3 levels. Furthermore, CSF s-100b levels, a low molecular weight calcium-binding protein associated with CNS damage in Creutzfeldt–Jakob disease, were elevated at 4.1 μg/ml (normal range <0.2 μg/litre).

The National Creutzfeldt–Jakob Disease Research and Surveillance Unit were consulted once the diagnosis was questioned and a team visited to review the patient. Rapid deterioration became evident during his 3-week admission with progression to akinetic muteness, myoclonus and rigidity. Treatment was primarily supportive. A multidisciplinary approach was adopted throughout his care including early and extensive input from the palliative care team. The patient went from the initial development of symptoms to death within 6 weeks. In accordance with the family's wishes, a post-mortem examination was not performed.

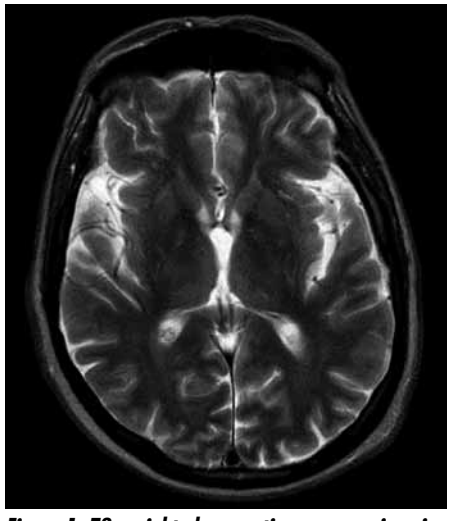

Figure 1. T2-weighted magnetic resonance imaging of basal ganglia showing normal appearance.

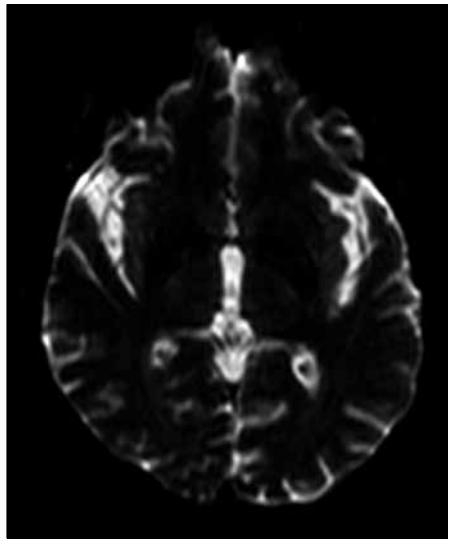

Figure 2. Diffusion-weighted magnetic resonance imaging of basal ganglia showing normal appearance.

ing, CSF analysis for 14-3-3 protein and electroencephalography testing, can allow a confident pre-mortem diagnosis.

Magnetic resonance imaging of patients with sporadic Creutzfeldt–Jakob disease often shows high signal in the head of the caudate nucleus and putamen on T2-weighted images. One study found these changes to have a reported sensitivity of 67% and a specificity of 93% for the diagnosis (Schroter et al, 2002). Variant Creutzfeldt–Jakob disease, meanwhile, classically shows bilateral increased signal in the pulvinar thalami, with a reported sensitivity of 78% and a specificity of 100% (Zeidler et al, 2002). It has been suggested that diffusion-weighted magnetic resonance imaging may be the best modality for early detection of sporadic Creutzfeldt–Jakob disease (Fujita et al, 2012).

Steinhoff et al (1996) found electroencephalography testing for periodic sharp complexes to have a sensitivity of 67% and a specificity of 86% for Creutzfeldt–Jakob disease. Furthermore, Lemstra et al (2000) analysed 14-3-3 protein levels in 110 patients suspected of having Creutzfeldt–Jakob disease, and found the test to have a specificity of 87% and a sensitivity of 97%. This has significant implications for management as timely diagnosis allows early palliative care input, provision of support for family and appropriate end-of-life care planning. BJHM

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LEARNING POINTS

- Creutzfeldt–Jakob disease is an incurable and invariably fatal neurodegenerative disease. When presenting as a progressive dementia, it can initially mimic more common causes of cognitive impairment in the elderly.
- The median length of survival from diagnosis is thought to be 4–6 months. However, this case demonstrates that deterioration can be more rapid with progression to death within 6 weeks of presentation.
- Pre-mortem diagnosis can be confidently made using magnetic resonance imaging, CSF analysis for 14-3-3 protein and electroencephalography testing.
- Timely diagnosis allows early palliative care input, provision of support for family and appropriate end-of-life care planning.