The Heidenhain variant of Creutzfeldt–Jakob disease

Introduction

A 65-year-old man presented to the accident and emergency department with a 2-week history of acute onset rapidly progressive confusion with visual hallucinations and an unsteady gait. Heidenhain variant of Creutzfeldt–Jakob disease was diagnosed. He died 4 weeks after the initial onset of symptoms.

Discussion

Creutzfeldt–Jakob disease is a rare, rapidly progressive neurodegenerative disease caused by misfolded proteins known as prions, with an incidence of around one in 1 million worldwide (Ricketts et al, 1997). There are several types of Creutzfeldt–Jakob disease including sporadic, variant and familial, but they present in a similar manner. Sporadic Creutzfeldt–Jakob disease accounts for around 85% of cases while familial Creutzfeldt–Jakob disease is seen in around 15% and displays an autosomal dominant transmission (Hill et al, 2003). Creutzfeldt–Jakob disease presents with progressive dementia, cerebellar ataxia, myoclonus and eventually death, often in the absence of any systemic upset, with haematological and biochemical markers within normal ranges (Sikorska et al, 2012).

At present, there is no gold standard premortem clinical investigation for prion diseases as definitive diagnosis requires brain biopsy, although the presence of 14-3-3 proteins has been implicated in several neurodegenerative conditions such as Parkinson's disease, Alzheimer's disease and Creutzfeldt–Jakob disease (Foote and Zhou, 2012). Furthermore, a study by McGuire et al (2013) concluded that real-time quaking-induced conversion (RT-QuIC) analysis is highly sensitive and specific for the diagnosis of Creutzfeldt–Jakob disease. Brain magnetic resonance imaging scans showing cerebral cortical signal increases and high signal in the caudate nucleus have been shown to be significant in the pre-mortem diagnosis of Creutzfeldt–Jakob disease (Zerr et al, 2009).

In this case, the observed significant decline in the cognitive state associated with visual hallucinations first and foremost, combined with periodic sharp wave complexes on electroencephalogram, the positive findings on lumbar puncture and magnetic resonance imaging changes, reaffirmed the diagnosis of Creutzfeldt–Jakob disease.

Dr Alex Hunt, Foundation Year 2 Trainee, Department of Health and Ageing, Conquest Hospital, East Sussex Healthcare Trust, St Leonards-on-Sea, East Sussex

Dr Kasim Ibrahim, Specialist Trainee Year 3, Department of Health and Ageing, Conquest Hospital, East Sussex Healthcare Trust, St Leonards-on-Sea, East Sussex

Dr Muhammad JH Rahmani, Consultant Physician, Department of Health and Ageing, Conquest Hospital, East Sussex Healthcare Trust, St Leonards-on-Sea, East Sussex TN37 7RD

Correspondence to: Dr MJH Rahmani (m.rahmani3@nhs.net)

CASE REPORT

A 65-year-old man presented to the accident and emergency department with a 2-week history of progressive confusion with visual hallucinations. This began with symptoms of photosensitivity and the distorted appearance of objects and progressed to an unsteady gait and problems with spatial awareness. By the end of the second week he displayed evidence of cognitive impairment and was admitted to hospital.

On the day of his admission, he required the assistance of one person to mobilize and could converse, although he was not orientated to time or place. He began to display signs of frontal disinhibition becoming uncharacteristically aggressive and using foul language. On initial examination, he had no evidence of facial asymmetry, visual fields were intact, and his pupils were equal and reactive to light. Mild dysdiadochokinesia was noted, worse on the left, with mild dysmetria bilaterally. He had normal power and tone in all four limbs.

Blood tests including an autoimmune screen were unremarkable (haemoglobin 148 g/litre, white cell count 7.30x10^9/litre, platelets 259x10^9/litre, serum potassium 4.3 mmol/litre, serum urea 6.1 mmol/litre, serum creatinine 89 mmol/litre, serum bilirubin 9 umol/litre, serum alkaline phosphatase 56 U/litre, serum alanine transaminase 33 U/litre, plasma glucose 7.6 mmol/litre, serum vitamin B_{12} 193 ng/litre, serum folate 6.5 ug/litre, serum hepatitis Bs antigen negative, serum hepatitis C IgG antibody 1&2 negative, serum syphilis IgG/IgM negative, serum intrinsic factor antibody negative, serum cardiolipin screen negative, serum anti-neutrophil cytoplasm antibody negative, serum ANA immunoassay screen negative).

A lumbar puncture was performed and the samples were sent to the National Creutzfeldt–Jakob disease (CJD) Research and Surveillance Unit in Edinburgh. The findings were white cell count <5/mm^3, red cell count <100/mm^3, total protein 1.02 g/litre, glucose non-consumed, S100-b 0.54 ng/ml (reference range <0.41 ng/ml), and real time quaking induced conversion and protein 14-3-3 positive.

An electroencephalogram demonstrated characteristic features of Creutzfeldt–Jakob disease with diffuse slowing and periodic sharp wave complexes (*Figure 1*).

Magnetic resonance imaging of his brain showed increased signal restricted diffusion within the caudate nuclei bilaterally (*Figures 2a* and *b*) with further restricted diffusion of the cortex in the frontal, parietal and occipital lobes on the right (*Figures 3a* and *b*).

Diffusion-weighted magnetic resonance imaging has the highest diagnostic accuracy (~97%) (Osborn et al, 2015). In this case, the observed asymmetrical involvement predominantly of the occipital lobe on the right side on axial magnetic resonance imaging highlights the increased possibility of the Heidenhain variant of Creutzfeldt–Jakob disease.

During the following 10 days, his tone increased in all four limbs with hyperreflexia and associated dystonic posturing of both upper limbs. He had bilateral grasp reflexes and there were frequent myoclonic jerks of his upper limbs. He had a fixed gaze with a restrictive horizontal gaze. He was transferred to a hospice where his myoclonus and agitation were well-controlled by a phenobarbital infusion. He died 2 days after admission to the hospice.

Figure 1. An electroencephalogram demonstrated characteristic features of Creutzfeldt–Jakob disease with diffuse slowing and periodic sharp wave complexes.

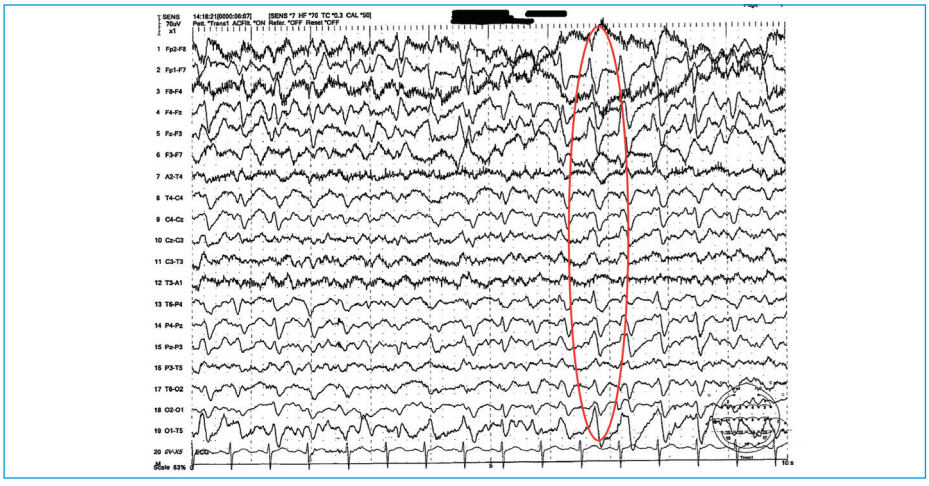


Figure 2. Magnetic resonance image of his brain showed increased signal restricted diffusion within the caudate nuclei bilaterally.

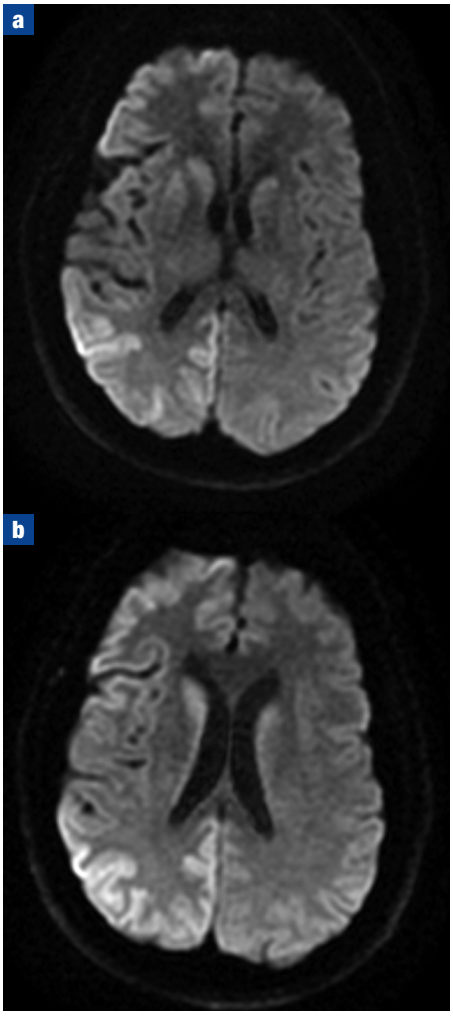
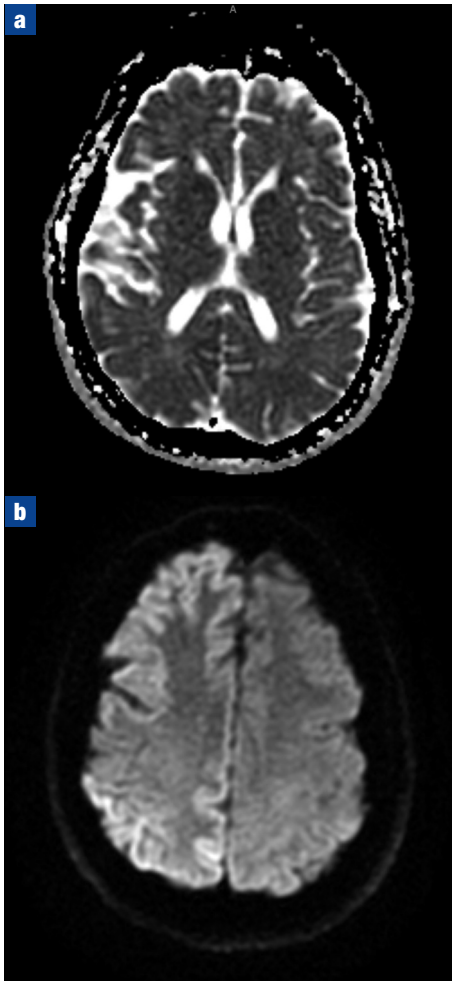


Figure 3. Magnetic resonance image of his brain showed restricted diffusion of the cortex in the frontal, parietal and occipital lobes on the right.



LEARNING POINTS

- Acute confusional state and visual hallucinations can be an acute presentation of the Heidenhain variant of Creutzfeldt–Jakob disease.
- Clinicians should have a high index of suspicion for the very rare aggressive Heidenhain variant of Creutzfeldt–Jakob disease in patients presenting with rapidly progressive confusion dementia with myoclonus, visual hallucinations, aphasia, cerebellar ataxia, cortical blindness and spasticity.
- Heidenhain variant Creutzfeldt–Jakob disease has a rapid and poor prognosis.
- Effective palliation of myoclonus and distressing agitation can be achieved with a continuous subcutaneous infusion of phenobarbital in the terminal stage.

A less well-known aggressive variant of Creutzfeldt–Jakob disease known as Heidenhain (occipitoparietal) was first described by Heidenhain (1929) and is distinct from other variants in that the visual disturbances are seen initially before the onset of the more established symptoms. Literature on the Heidenhain variant of Creutzfeldt–Jakob disease is scarce, but Jacobs et al (2001) described two cases where patients presented first with visual disturbances followed by myoclonus, ataxia and dementia. BJHM

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