Visual symptoms and rapid cognitive decline: Heidenhain variant of Creutzfeldt-Jacob Disease

Karim M Mahawish, Christopher Kabban, Holly Wilson

Creutzfeldt-Jacob Disease (CJD) is a rare, progressive and usually fatal prion disease and one of a number of causes of rapidly progressive dementia. Subtypes include familial CJD (inherited gene defect), iatrogenic CJD (transmission during neurosurgical procedures) and variant CJD (transmission of prions from bovine spongiform encephalopathy). Sporadic CJD is the most common form and is thought to arise spontaneously. The main presenting features of CJD are cognitive decline, ataxia and myoclonus. Visual complaints are common and may be the initial presenting symptom in a subset of patients. When these occur in patients who subsequently develop other characteristic features of CJD and specific MRI changes, this is termed the Heidenhain variant of CJD.¹

Case report

A 72-year-old woman presented with a two-month history of altered vision and reduced mobility. The visual disturbance was initially described as spots ‘like flies’ affecting her entire visual field. Subsequently she experienced a loss of spatial awareness with inability to judge distances resulting in falls and difficulty reaching for and picking up items. An initial review by an optometrist identified no abnormality. In the weeks leading up to her admission, cognitive decline was becoming apparent, with difficulty remembering appointments, names and repetitive conversations, though she was still capable of managing her own financial affairs. During her admission, she was noted to have difficulty positioning limbs, co-ordination and difficulty with transfers. Two weeks following her admission, her vision deteriorated further, with reduced visual acuity and stationary objects appearing to move.

Her past medical history included diabetes and hypertension. There was no family history of note and she had not undergone neurosurgical interventions previously. Admission medication included metformin 850mg BD and amlodipine 5mg OD. Clinical examination revealed a bitemporal hemianopia and binocular reduced visual acuity. Admission electrocardiogram demonstrated atrial fibrillation. An MRI brain showed bilateral abnormal high signal in the subcortical regions of the occipital and parietal lobes on diffusion weighted imaging suggestive of acute ischaemia (Figure 1).

Figure 1: MR DWI demonstrating cortical ribboning in the occipito-parietal lobes bilaterally.

The patient was treated for ischaemic strokes secondary to atrial fibrillation and commenced on dabigatran 150mg BD. At the time of discharge, she was mobile with a frame and the assistance of one and was relocated to rest home-level care.

She was referred to hospital four months later for rapidly deteriorating cognition and behaviour and jerking limb movements. She had become aggressive towards family,
paranoid and experiencing distressing visual hallucinations which included reptiles, animals and children. Cognitive and visual impairment and distress limited physical examination, however, she was noted to have increased tone and multifocal myoclonic jerks (Video 1) and vision limited to perception of hand movement.

An electroencephalogram demonstrated theta and delta slowing with a paucity of alpha frequency activity consistent with a moderate diffuse encephalopathy. A lumbar puncture was performed, which showed a normal white cell count but an elevated protein (0.77g/L). Cerebrospinal fluid was positive for protein 14-3-3 and coupled with the previous MRI findings were highly suggestive of Heidenhain variant of CJD. The patient was commenced on quetiapine and her agitation resolved once the dose was increased to 50mg BD. The patient was deemed to be in the palliative stage of her illness and was discharged to a nursing home, passing away two weeks later.

Discussion

Visual symptoms are the presenting feature of the Heidenhain variant of CJD and was first described in 1929. Patients often initially present to an optometrist, with early preservation of cognition. Current sCJD classification recognises six major variants, each with distinctive clinic-pathological features with genotypic determination at the polymorphic codon 129 in the prion protein. Heidenhain variant has been linked to the MM1 or MM1 + 2C type. Though there is a broad overlap of symptoms, there are clinico-pathological differences within the subtypes of CJD, summarised in Table 1. Protein 14-3-3 describes a migratory pattern of CSF proteins seen on electrophoresis and is 93% sensitive for CJD. MRI findings of restricted diffusion in the occipital lobes are a common finding in this form of CJD but may be easily mistaken for other pathologies such as stroke. Final confirmation of the diagnosis requires autopsy, which was declined by the family.
Table 1: Differences in subtypes of CJD.

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<th>sCJD</th>
<th>HvCJD</th>
<th>vCJD</th>
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<tbody>
<tr>
<td>Early features</td>
<td>Great diversity in presenting features</td>
<td>Visual defects, hemi-anopia, hallucinations, agnosia, abnormal colour/spatial perception</td>
<td>Psychiatric symptoms including anxiety and depression</td>
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<td>Predominant features</td>
<td>Dementia, myoclonus, Ataxia</td>
<td>Visual hallucinations, myoclonus, dementia</td>
<td>Mood and behavioural abnormalities, paraesthesias, dementia</td>
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<td>Mean age of onset</td>
<td>65 years</td>
<td>65 years</td>
<td>26 years</td>
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<tr>
<td>Mean duration of illness before death</td>
<td>4.5 months</td>
<td>5.7</td>
<td>14 months</td>
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<td>Neuropathological findings</td>
<td>Diverse pathological changes more marked within limbic system and basal ganglia^4</td>
<td>Gliosis and neuronal loss and spongiform vacuolation in occipital lobe gray matter^5</td>
<td>Florid plaques of kuru and spongiform change most severe in the thalamus, but also prominent in the cerebral cortex and cerebellum^6</td>
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Competing interests:
Nil.

Acknowledgements:
We would like to thank Dr Andrew Chancellor, Consultant Neurologist for providing clinical advice.

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