A Rare Diagnosis Presenting as a Posterior Circulation Stroke: A case report and learning points

Dr Fiona Macdonald, Dr Luke Attwell, Dr Oliver Pearce, Dr Kamy Thavanesan

INTRODUCTION

Sporadic Creutzfeldt-Jakob disease (CJD) is a rare neurodegenerative disorder caused by the accumulation of prion proteins in the brain. Diagnosis is made on clinical history and examination as well as supportive investigations such as EEG, MRI and CSF analysis. Definitive diagnosis can only be achieved through post mortem examination. Currently there is no treatment for CJD, and care remains symptom based.

CASE REPORT

We present the case of an 81 year old man with a history of unsteadiness, falls and hallucinations. He had a background of type 2 diabetes mellitus on insulin, hypertension, asthma & previous pulmonary tuberculosis. 6 weeks prior to admission the patient started to complain of diplopia and dizziness on standing. He also experienced visual hallucinations, an example of this being seeing a fox running across the car windscreen whilst driving. He presented to his GP with these symptoms, who investigated for postural hypotension and worsening diabetic eye disease. He subsequently attended eye casualty where no intra-ocular cause was identified. As he deteriorated further his GP became concerned about an acute intracranial pathology. At the point of admission he was significantly confused and needed to be guided around the house by family members due to deteriorating vision.

On initial examination he was found to have diplopia on rightward gaze, left sided visual neglect and ataxia in the form of past pointing and a broad based gait. He was referred to the stroke team as a possible posterior circulation stroke. He was promptly reviewed by our team who found the progressive nature of his symptoms went against an acute vascular event such as a stroke, and therefore intravenous acetylsalicylic acid was commenced to cover for viral encephalitis. Blood investigations excluded a metabolic cause for his presentation. After his initial unremarkable CT, MRI imaging was performed to further aid diagnosis. This was initially reported as normal. However, on closer review by a neuroradiologist, cortical ribboning was noted in the frontal, parietal, temporal and occipital lobes bilaterally, more pronounced on the right, felt to be in keeping with sporadic Creutzfeldt-Jakob disease (CJD). A lumbar puncture revealed an elevated protein at 0.71g/L (0.4).

The CSF sample sent to the laboratory at The National CJD Research and Surveillance Unit (NCJDRSU) in Edinburgh was weakly positive for the 14-3-3 protein and RT-QuIC positive. The team at the National CJD Research and Surveillance Unit reviewed imaging, CSF findings and clinically assessed the patient, confirming the diagnosis of sporadic CJD. They assisted in suggesting symptomatic management options included clonazepam, levetiracetam and risperidone as well as family counselling.

The patient continued to progress and deteriorate following diagnosis. Initially his personality became exaggerated, followed by becoming more withdrawn. He developed cortical blindness within a week of admission as well as significant spontaneous and stimulus sensitive myoclonus in all four limbs. He became comatose, and at the end of a four week admission died peacefully on the ward.

DISCUSSION

Prion diseases also known as transmissible spongiform encephalopathies (TSE’s) can occur in humans and animals. First described in humans by German neurologist Hans Gerhard Creutzfeldt in 1920 and shortly after by Alfons Maria Jakob, the disease became known as Creutzfeldt-Jakob disease (CJD).

There are four major categories of CJD:

• Sporadic – accounts for 90% of cases of CJD and is thought to be caused by abnormal folding of prion proteins.
• Variant – likely to be caused by consuming meat infected with bovine spongiform encephalopathy. New accounts for <1% of cases due to changes in farming regulations.
• Iatrogenic – caused by medical or surgical treatment. For example, human growth hormone or neurosurgical procedures.
• Inherited – an autosomal dominant condition.

Sporadic CJD affects 1-2 per million of the population worldwide, with no sex or geographical variation. It typically affects people between the ages of 45 and 75. The onset is insidious, followed by a rapid decline in neurological function. Early signs include dizziness, headaches, fatigue, sleep disturbance and behavioural change. This is followed by a rapidly progressive dementia and myoclonus. The disease process from onset to death is usually less than a year, but can be as short as 6 weeks.

Isolated visual symptoms at onset is typical of the Heidenhain variant, with prion deposition in the occipital cortex, as seen in this gentleman.

The NCJDRSU laboratory is a centre of excellence recognised by The World Health Organisation in analysing CSF for brain specific proteins. The most recent technique introduced is called real-time quaking induced conversion (RT-QuIC) and is used for investigating patients with suspected sporadic CJD. The sensitivity is approaching 95% with a specificity of 100%.

Our patient was reviewed by the national CJD research and surveillance unit based at the University of Edinburgh, who had access to his CSF results & imaging and were able to confirm the diagnosis and counsel family members regarding genetic testing and options for post mortem examination of the brain for diagnostic confirmation.

Table 1: Cases of suspected CJD by year and category in the UK. Taken from the National CJD Research and Surveillance Unit.

<table>
<thead>
<tr>
<th>Year</th>
<th>Referrals of suspected CJD</th>
<th>Sporadic</th>
<th>Variant</th>
<th>Iatrogenic</th>
<th>Genetic</th>
<th>vCJD</th>
<th>Total deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>178</td>
<td>182</td>
<td>1</td>
<td>1</td>
<td>93</td>
<td>0</td>
<td>190</td>
</tr>
<tr>
<td>2012</td>
<td>180</td>
<td>195</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>199</td>
</tr>
<tr>
<td>2016</td>
<td>188</td>
<td>193</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>126</td>
</tr>
<tr>
<td>2017</td>
<td>154</td>
<td>179</td>
<td>0</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>131</td>
</tr>
<tr>
<td>2018</td>
<td>75</td>
<td>91</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>57</td>
</tr>
</tbody>
</table>

LEARNING POINTS

• In this case the initial normal MRI report did not fit the clinical picture of diplopia, ataxia and visual neglect. Therefore re-reviewing the imaging was key in obtaining a diagnosis. Without this crucial intervention, the diagnosis would not have been made.
• The timeline of symptom progression is important, particularly when considering the aetiology of a neurological condition. A disease of vascular origin such as stroke would usually have an onset of seconds to minutes.
• Management options remain symptom based for this progressive neurodegenerative condition along with family counselling and support.

REFERENCES

https://www.cjd.ed.ac.uk/  
https://www.prion.ed.ac.uk/ncjdrsu/services/information/sporadic-prion-disease/  
https://bioinformatics.pasteur.fr/attwell-prion-stuff/  

Figure 1: Magnetic resonance imaging (MRI) showing cortical ribboning in the occipital, temporal and frontal lobes.