CASE REPORT

Creutzfeldt-Jakob disease presenting with visual symptoms: a case of the 'Heidenhain variant'

Rajesh Verma, Vivek Junewar, Ritesh Sahu

Department of Neurology, King George Medical University, Lucknow, Uttar Pradesh, India

Correspondence to
Professor Rajesh Verma,
drrajeshverma32@yahoo.com

SUMMARY

Creutzfeldt-Jakob disease (CJD) belongs to a group of prion diseases that may be caused by the abnormal folding of proteins called prion proteins. The 'Heidenhain variant' is a subclass of patients with CJD, who present with isolated visual symptoms at the onset without any cognitive decline. Here we report such a case of an elderly man presenting with progressive diminution of vision, forgetfulness, abnormal behaviour, myoclonic jerks and akinetic mutism since the last 5 months. On clinical examination, lead pipe rigidity was present in all four limbs, and plantars were bilateral extensors. In view of rapidly progressive dementia associated with myoclonus, a possibility of CJD was entertained. As visual symptoms preceded dementia, hence the Heidenhain variant was strongly suspected. MRI of the brain revealed cortical ribboning, and EEG showed periodic triphasic waveforms with background slowing. The patient succumbed to the illness within 1 month of hospitalisation.

BACKGROUND

Creutzfeldt-Jakob disease (CJD) belongs to a group of prion diseases, classified into sporadic, familial or acquired form.¹ Eighty to 90% of the cases are sporadic CJD (sCJD).² Patients usually belong to the age group between 50 and 75 years.³ The most common clinical manifestations of CJD are rapidly progressive dementia, myoclonus and ataxia.⁴ Visual symptoms are mentioned in at least 20% of patients with sCJD. However, a subclass of patients with sCJD present with isolated visual symptoms which persist even without any cognitive decline for a few weeks, known as the 'Heidenhain variant' of sCJD. We present one such case of the Heidenhain variant of sCJD. This case highlights the importance of suspicion of the Heidenhain variant of CJD in all patients who present with isolated visual complaints at onset, and these patients should be followed for the development of dementia, ataxia or myoclonus.

CASE PRESENTATION

This 60-year-old man presented to us with a history of progressive painless bilateral diminution of vision since the last 5 months. He had developed difficulty in reading and consulted many ophthalmologists for the same. He was repeatedly given correction for refractive error, but there was no improvement in the patient's vision. Relatives of the patient also mentioned that the patient had difficulty in seeing objects on the right-hand side. The patient used to neglect objects on the right half of his visual field.

He used to collide with objects on the right-hand side while walking. There was no history of diplopia. Since the last 4 months, he had developed forgetfulness. Relatives noticed abnormal behaviour in the form of irritability and agitation since the last 3 months. There was a history of insomnia. There was no history of delusion or auditory or visual hallucinations. Over the last 2 months, the patient had also developed sudden shock-like jerky movements of all four extremities. During the course of illness, the patient developed a monotonous speech which gradually progressed to akinetic mutism and severe bradykinesia. He has become bedbound since the last 2 months. There was no recent history of any surgical procedure or vaccination. There was no history of hypertension, diabetes mellitus or any other major medical or surgical illness.

On examination, vitals were found to be stable. The patient was conscious but disoriented. His attention span was decreased, and hence the other higher mental functions could not be tested. The patient was not cooperative for visual acuity and colour vision testing. He was found to have right-sided hemianopia with the help of menace reflex. Fundus examination was normal. His pupils were normal sized, reacting to light. There was no obvious oculomotor abnormality. There was no localised wasting. Lead pipe rigidity was present in all four limbs. Multifocal myoclonic jerks were present with a frequency of 6 to 8 per minute. Deep tendon reflexes were normal. Plantars were bilateral extensors. In view of rapidly progressive dementia associated with myoclonus, a possibility of CJD was entertained. Visual symptoms preceded dementia, and hence the Heidenhain variant was strongly suspected (figures 1–3).

INVESTIGATIONS

Biochemical blood investigations in the form of haemogram, random blood sugar, renal and liver function tests, thyroid profile and serum vitamin B₁₂ levels were normal. Cerebrospinal fluid (CSF) examination was unremarkable. CSF viral titres were normal. CSF 14–3–3 protein examination was not done due to non-affordability. CT of the brain was normal. MRI of the brain revealed cortical ribboning and hyperintensities at the occipital region on diffusion-weighted images (DWI). His EEG showed diffuse background slowing and periodic triphasic waveforms.

TREATMENT

The patient was put on supportive care.

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Figure 1 T2 fluid-attenuated inversion recovery image showing subtle hyperintensity in the left caudate nucleus and parietal cortex.

OUTCOME AND FOLLOW-UP

The condition of the patient deteriorated rapidly, and he succumbed to the illness within 1 month of hospitalisation. The relatives did not give consent for brain biopsy or necropsy.

DISCUSSION

CJD belongs to a group of prion diseases also known as transmissible spongiform encephalopathies. It constitutes around 85% of all cases of prion diseases.¹ Prion diseases are caused by the abnormal folding of the proteins called prion proteins. Toxic aggregates are generated from this abnormally folded host-encoded prion protein (ie, PrPC), which is designated as the PrP^{Sc} protein. Progressive accumulation for many years results in spongiform degeneration of the brain.²

CJD may be sporadic, familial or acquired. Eighty to 90% of the cases are sCJD.² Patients usually belong to the age group between 50 and 75 years.³ The most common clinical manifestations of CJD are rapidly progressive dementia, myoclonus and ataxia.⁴ It is a uniformly fatal prion disease. Usually death occurs within 6 months of onset of symptoms. Visual symptoms are common in sCJD. They have been

mentioned in at least 20% of patients in the early stage. A subclass of patients of sCJD, however, present with isolated visual symptoms which persist even without any cognitive decline for a few weeks. This subgroup of cases is called the Heidenhain variant of sCJD. In 1929, Heidenhain described three cases of spongiform encephalopathy. Two of these cases had early and prominent visual symptoms, while the third one had sensory complaints and athetosis. In 1954, Meyer *et al* also reported the case of a 38-year-old gentleman presenting with dementia and visual impairment.⁵ Eighteen to 39% of patients with sCJD have prodromal psychiatric manifestations. These include mainly depression, personality changes and emotional lability.⁶

Our patient presented initially with isolated visual symptoms. This is consistent with the Heidenhain variant. Clinical features presenting in patients of the Heidenhain variant of CJD consist of visual field defects, abnormal colour or visuospatial perception, visual hallucinations, visual neglect, cortical blindness, visual agnosia and rarely isolated eye movement abnormalities.^{4–7} Patients may initially complain of difficulty in reading or watching television and subsequently give up such activities. They may present a history of repeated changing of eyeglasses without any improvement in visual complaints. Patients then develop rapidly progressing dementia, and death follows in a few months.⁴

Histopathologically, CJD is characterised by spongiform degeneration, neuronal loss and astrocytic gliosis. In patients with the Heidenhain variant, these features are most prominent in the occipital lobes.⁸

About 25% of patients with the Heidenhain variant of CJD may lack the characteristic triad of dementia, myoclonus and abnormal EEG. Characteristic changes in the EEG of patients with CJD are periodic sharp wave complexes which are noted in 70% of patients. Our case showed such periodic triphasic complexes in the EEG. A total of 15.10% patients showed only diffuse slowing.⁹ In terminal stages of the disease where myoclonus is absent, typical EEG findings cannot be elicited.¹⁰ The CSF assay for the 14–3–3 protein is a useful diagnostic marker for the disease. However, it may be negative in some patients with pathologically confirmed CJD. The 14–3–3 assay is also not specific for CJD. It may be positive in patients with stroke, hypoxic ischaemic injury and herpes encephalitis where there is neuronal death.⁴ The specificity of this finding may be as high as 95%, but the sensitivity range varies from 45–85%.²

Conventional MRI shows cortical and basal ganglia abnormalities on T2-weighted images and proton density-weighted images.¹¹ sCJD, however, may show increased signal intensity

Figure 2 Diffusion-weighted images showing hyperintense signal changes that characteristically involve the cortical ribbon of the frontal, parietal and occipital lobes on the left side, including the left caudate nucleus.

Figure 3 16-Channel EEG showing diffuse background slowing and periodic triphasic waveforms (arrow).

at the pulvinar thalami.³ However, in early stages of the disease, the scans may be normal in about 21% of cases. Gadolinium enhancement is most often not seen. However, DWI may be abnormal in the early course of the disease. This is probably due to cell lysis and membrane disruption.⁴ Therefore, when routine primary tests are negative, DWI is the neuroimaging sequence of choice in the diagnosis of CJD.³ MRI, in our case, showed hyperintensities in the occipital cortex on DWI.

According to the WHO criteria, the probable diagnoses of CJD require: (1) progressive dementia and two or more of the following four clinical features: myoclonus, visual or cerebellar dysfunction, pyramidal/extrapyramidal signs or akinetic mutism; (2) a typical EEG and/or a positive 14–3–3 CSF assay and a clinical duration of less than 2 years before death and (3) exclusion of alternative diagnoses with routine investigations. For definite diagnosis, in addition to the aforementioned criteria, one of the two following criteria should be established: characteristic pathological changes in the brain or a positive Western blot to confirm the presence of PrPSc.²

The disease is fatal within 1 year in 90% of cases. The mean duration of the disease was 6.6 (+6.11) months in 10 cases reported from North India.¹²

The Heidenhain variant of CJD must be considered in all patients who present with isolated visual complaints and should be followed for the development of dementia, ataxia or myoclonus.

Learning points

- ▶ Creutzfeldt-Jakob disease (CJD) must be considered as a differential diagnosis in cases which present with rapidly developing dementia, ataxia or myoclonus.
- ▶ The Heidenhain variant of CJD must be considered in all patients who present with isolated visual complaints which later on develop other classical features of CJD.
- ▶ MRI of the brain must be a necessary investigation in the evaluation of a suspected case of CJD. Diffusion-weighted imaging is the neuroimaging sequence of choice in the diagnosis of CJD.

Competing interests None.

Patient consent Obtained.

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