Imaging and EEG Findings of Rare Heidenhain Variant of Creutzfeldt-Jakob Disease

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Background: Creutzfeldt-Jakob disease (CJD) is a rare neurodegenerative spongiform encephalopathy. Findings are usually consistent with basal ganglia and frontal lobe destruction. However in certain variants, the clinical and diagnostic findings can differ. This case illustrates the occipital findings of the rare Heidenhain variant of CJD.

Methods: We describe the clinical course and radiologic findings of a 65-year-old with the Heidenhain variant of Creutzfeldt-Jakob disease. Diagnostic studies included lumbar puncture, EEG and MRI scans of the brain.

Results: This case illustrates the findings of the rare Heidenhain variant of CJD, including prominent changes in MRI and EEG in the occipital region. This was further supported by the positive enolase and 14-3-3 in cerebral spinal fluid.

Conclusions: In patients presenting with clinical symptoms of visual disorders of unclear origin presenting with or shortly after psychosis or dementia, this variant of CJD must be considered in the differential diagnosis.

Keywords: Creutzfeldt-Jakob; Periodic sharp wave complexes; Myoclonus; Optical hallucinations; Heidenhain

Introduction

Creutzfeldt-Jakob disease (CJD) is a uniformly fatal and rapidly progressive transmissible spongiform encephalopathy. Typically 85% of cases are considered to be sporadic with no known cause. A small number of cases have followed known exposure and rare familial mutation as vectors of transmission [1]. Mutations of the prion protein gene (PRNP) are the cause of familial CJD, which supports the explanatory model of prions as the disease vector [2]. The Heidenhain variant is a rare (< 20%) variant of sporadic Creutzfeldt-Jakob disease (sCJD) in which visual disturbances are the primary presenting symptoms and has more rapid progression [3]. Seventy seven percent of patients with this variant initially present to ophthalmology clinics secondary to these visual symptoms, but have no intraocular findings [4]. The visual symptoms can manifest in different ways including disturbed perception of colors or structures, optical hallucinations, or even cortical blindness. Sadly, the prognosis is grim. Life expectancy for sCJD is 8–12 months and 6–8 months for the Heidenhain variant [5]. These deficits match the pronounced neuropathological changes found in the occipital lobe.

Case Description

Our patient was a 65-year-old male who stated that he began developing vision problems three months prior to seeking medical attention. When he was driving, he felt that his depth perception was lost and vision would come and go intermittently. One month prior to admission, his vision progressed to the point where he reportedly could not see in his left visual field, his vision loss further progressed over the next weeks to complete blindness bilaterally. At the time of presentation to our center, he had also developed physical signs of left-sided weakness, slight jerking of the left hand and speech changes. His wife was beginning to notice some mild personality changes.

On physical exam, pertinent findings included elevated blood pressure of 190/100 but otherwise normal vital signs. The exam was notable for a bizarre indifferent affect, slight weakness in left upper limb, and decreased visual acuity of 20/125 in the right eye and 20/400 in the left eye; myoclonic jerks were also appreciated on exam the next day.

Work up included an initial magnetic resonance imaging (MRI) which was limited secondary to motion, but given strong suspicion for sCJD, we obtained MRI under sedation. There was increased fluid-attenuated inversion recovery (FLAIR) signal in the cortical ribbon and deep gray matter. Diffusion-weighted imaging (DWI) and Apparent Diffusion Coefficient (ADC) showed cortical restricted diffusion in the occipital lobes illustrating cortical ribboning, without definite involvement of the basal ganglia structures (Figure 1 A,B,C). Electroencephalograph (EEG) featuring parieto-occipital predominant periodic sharp wave complexes (PSWC) with a frequency of 1 HZ with background slowing were also noted (Figure 2).

Cerebrospinal fluid (CSF) analysis showed 36 nucleated cells (75% monocytes), a glucose of 80 and elevated proteins of 393. Lyme antibodies, fungal and viral CSF analysis were negative. Neuron specific enolase was elevated at 49 and 14-3-3 was positive. Additional lab work including a serum heavy metal screen, HIV and drug screen, estimated sedimentation rate, C reactive protein, complete metabolic panel, complete blood count, lactate, creatinine phosphokinase and paraneoplastic antibodies were unremarkable.

In the week he was hospitalized, he developed hallucinations which required atypical antipsychotics to help control his symptoms. Given his deterioration and poor prognosis, he was discharged to hospice. The patient died 5 months after symptom onset.

Discussion

The patient’s clinical presentation along with characteristic EEG, MRI, and CSF findings of enolase and 14-3-3 protein is consistent with the Heidenhain variant of CJD. Definitive diagnosis is based on brain biopsy; however the diagnosis of probable CJD requires a rapidly progressive dementia with at least two out of four clinical signs of myoclonus (startle), visual or cerebellar signs, pyramidal/ extrapyramidal signs, seizures, and ultimately akinetic mutism as well as positive EEG, MRI or 14-3-3 CSF protein [6]. Our patient presented with several of these findings including myoclonus, rapid dementia, visual changes, and extrapyramidal signs.

In sporadic CJD, EEGs typically show background slowing often...
beginning with frontal intermittent rhythmic delta wave activity (FIRDA) with further changes depending on the stage of the disease [7]. While these are nonspecific findings, repeat EEGs are warranted if there is progression of symptoms. In middle and late stages, two thirds of patients’ EEGs typically progress to the characteristic periodic sharp wave complexes (PSWC) of 0.5–2 Hz frequency [8]. These can be lateralized or generalized. Lateralized PSWC may initially resemble periodic lateralized epileptiform discharges and may reflect just an earlier finding before further spread and in serial EEGs, these will often progress to PSWCs [9]. In typical sCJD, these findings are expected in the frontotemporal area, but as this is the Heidenhain variant, this patient’s EEG had maximal potentials over the occiput matching his primary symptoms and other imaging findings (Figure 1). The progression ends with readings of coma in preterminal EEG recordings [10].

Imaging should be the first test in considering CJD, given its sensitivity, specificity and ability to rule out other dementias based on findings, and will often show abnormal signals even before myoclonus or PSWCs are present [11]. MRI findings in sCJD vary based on the subtype of the disease and region affected. sCJD typically show increased signal intensity in putamen, caudate nucleus and cortical involvement on FLAIR and DWI MRI sequences [12]. The cortical involvement characteristically involves high DWI intensity in most of the following areas: insula, cingulate, superior frontal gyri, occipital gyri, and in the cortical areas near the midline [13]. New USCF proposed guidelines for sCJD require an increase in DWI more than FLAIR and ADC cortical ribboning, sparing of central gyrus, asymmetric involvement of midline neocortex for cortical involvement or ADC subcortical hypointensity with striatum anterior-posterior gradient [14]. Further genetic sampling combined with MRI imaging has allowed for proposed characterization of MRI lesion patterns for each molecular subtype, with MM1 being more consistent with the cortical ribboning [15]. Patients with vCJD have the unique increased bilateral pulvinar signal that produces the classic hockey stick sign [16]. Our patient had the classic cortical ribboning, however his MRI findings had the strongest signal changes in the occipital region (consistent with the Heidenhain variant), with notable absence of any basal ganglia changes. Other case reports on imaging in the Heidenhain variant support the increase occipital enhancement on DWI as well as hypometabolism on positron emission testing [3,17,18].

Conclusions

In patients presenting with clinical symptoms of visual disorders of unclear origin presenting with or shortly after psychosis or dementia, the Heidenhain variant of CJD must be considered in
the differential diagnosis. After a thorough history and physical, an MRI followed by EEG and spinal fluid analysis will help support this diagnosis.

References


