CASE REPORT
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Creutzfeldt-Jakob Disease Presenting with Isolated Visual Complaints: Heidenhain's Variant

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Heidenhain variant of Creutzfeldt-Jakob disease (CJD) may include visual field defects, visual hallucinations, visual agnosia, cortical blindness, and abnormal color or visuospatial perception. We report a 47-year-old man presenting with visual symptoms, prosopagnosia, simultagnosia. Myoclonus was synchronous with generalized periodic epileptiform discharges on electroencephalography. Diffusion-weighted magnetic resonance brain images showed increased signal intensity in the bilateral caudate and putamen, both occipital cortices, and left frontal and temporal cortices. 14-3-3 protein was positive in the cerebrospinal fluid. The Heidenhain variant of CJD should be considered in patients with isolated visual complaints and either.

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Key Words Creutzfeldt-Jakob disease, Heidenhain's variant.

Introduction

Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare and uniformly fatal prion disease that classically presents as a rapidly progressive dementia resulting in death usually within 6 months.[1,2] sCJD occasionally presents with isolated visual symptoms which may persist in the absence of cognitive decline for some weeks.[3] This type of sCJD was termed the 'Heidenhain variant' after the works by Heidenhain in 1928.[4] He described three cases of spongiform encephalopathy and two of them had prominent, early visual symptoms. We report a patient with Heidenhain's variant of CJD whose clinical findings are consist of visual symptoms, prosopagnosia, simultagnosia.

Case Report

A 47-year-old man reported visual blurring and sudden visual loss in 2 months ago. However, a thorough ophthalmological assessment revealed no visual defect. One month later, he was reviewed at a psychiatric clinic for anxiety, and was noticed to have slurred speech. Initial investigations, including computed tomographic scan and magnetic resonance imaging (MRI) of the brain, were normal (Fig. 1). However, his mental state deteriorated rapidly as he became increasingly agitated, incoherent and paranoid over the two weeks that followed. He felt that his vision was 'fogging up' and complained of tunnel vision. Attempts to control his psychiatric symptoms with benzodiazepines, anti-psychotic and anti-depressive agents were unsuccessful. On admission to the hospital, examination revealed a profoundly demented patient. He scored 4/30 on his mini mental status examination. There were no depressive symptoms. Neurologic examination was prosopagnosia, simutagnosia, optic ataxia, ocular apraxia, color agnosia and mild cortical blindness. Mild bilateral pronator drift, bilateral finger-to-nose dysmetria, and extensor plantar responses were noted. There was no past history of diabetes, hypertension, renal failure, exposure to toxic chemicals, radiation, or drugs. There was no family history. he was a non-smoker and drank little alcohol. A neuro-ophthalmologic examination, performed within days after the episodes of word-finding difficulty, revealed visual acuities of 20/25 OU (Fig. 2). The pupils and fundi were normal. Routine blood exam, metabolic and endocrine work up, thyroid function, serum B12 and red cell folate, VDRL, RA factor, ANA, p-ANCA, chest X-ray, ECG, EEG were normal. Diffusion-weighted magnetic resonance brain images showed increased signal intensity in the bilateral caudate and putamen, both occipital cortices, and left frontal and temporal cortices (Fig. 3). MR spectroscopy showed mild decreased of the peak of NAA. At map of lactate area, lactate was no increased (Fig. 4). Results from a carotid ultrasound and echocardiogram were normal. Frontal intermittent rhythmic delta activity was also seen. Cerebrospinal fluid (CSF) examination was unremarkable

except for mildly elevated protein (60 mg/dL) and positive 14-3-3 protein. Prion protein gene codon was methionine homozygote. Toxicology screen was unremarkable.

Discussion

Although dementia, myoclonus, and ataxia are the most com-

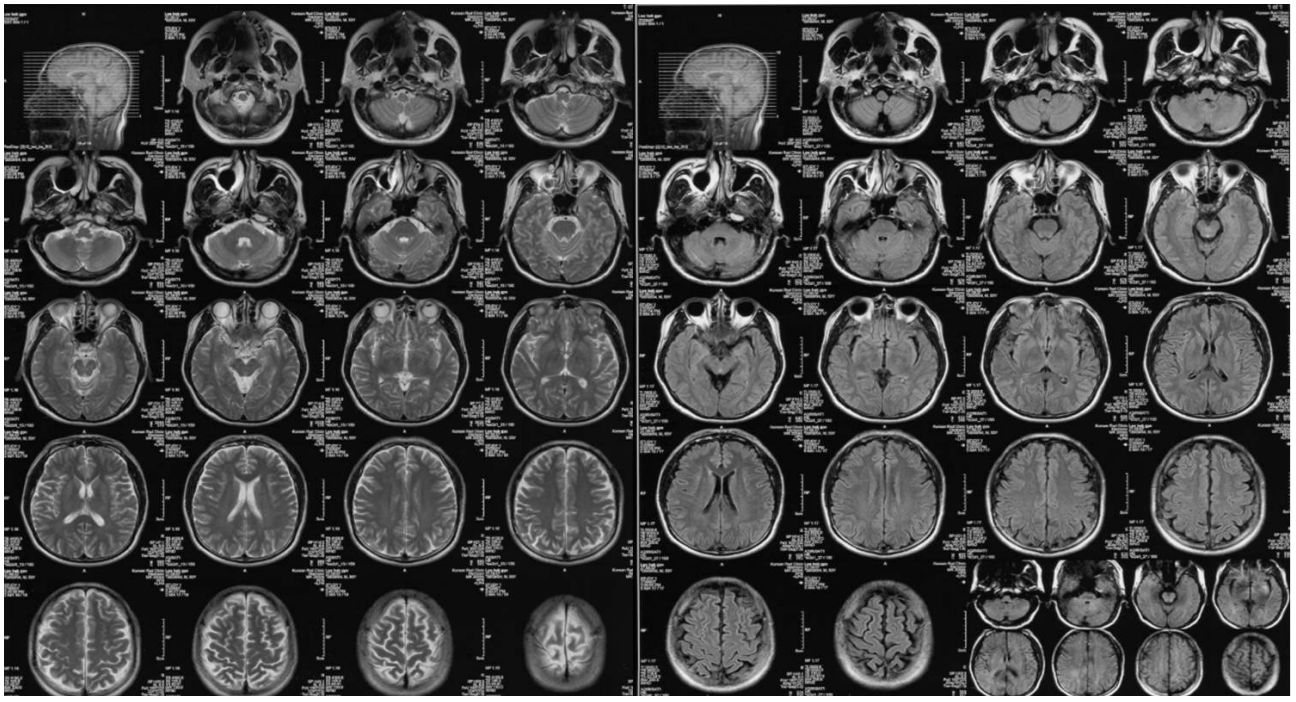

Figure 1. Magnetic resonance imaging of the brain showed normal.

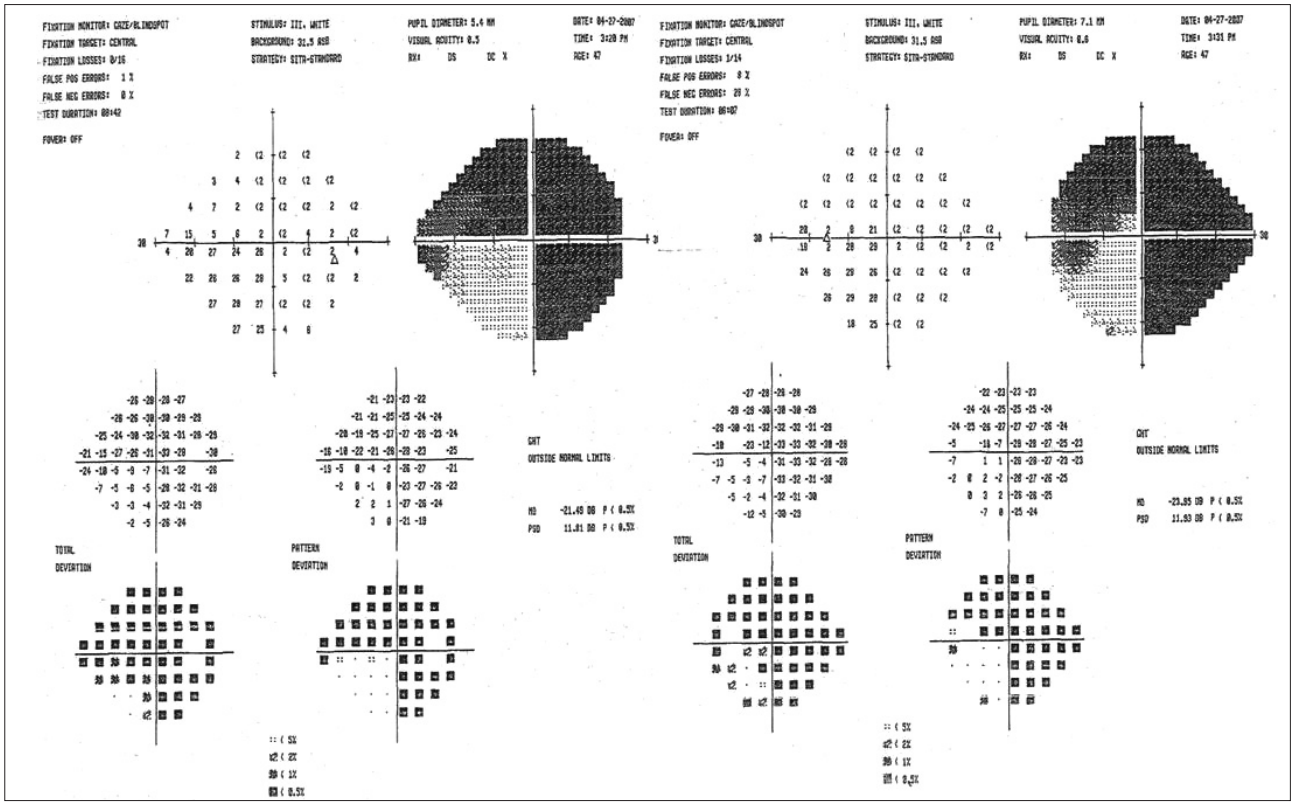

Figure 2. Humphrey visual field test shows right homonymous hemianopia and left homonymous superior quadrantanopia.

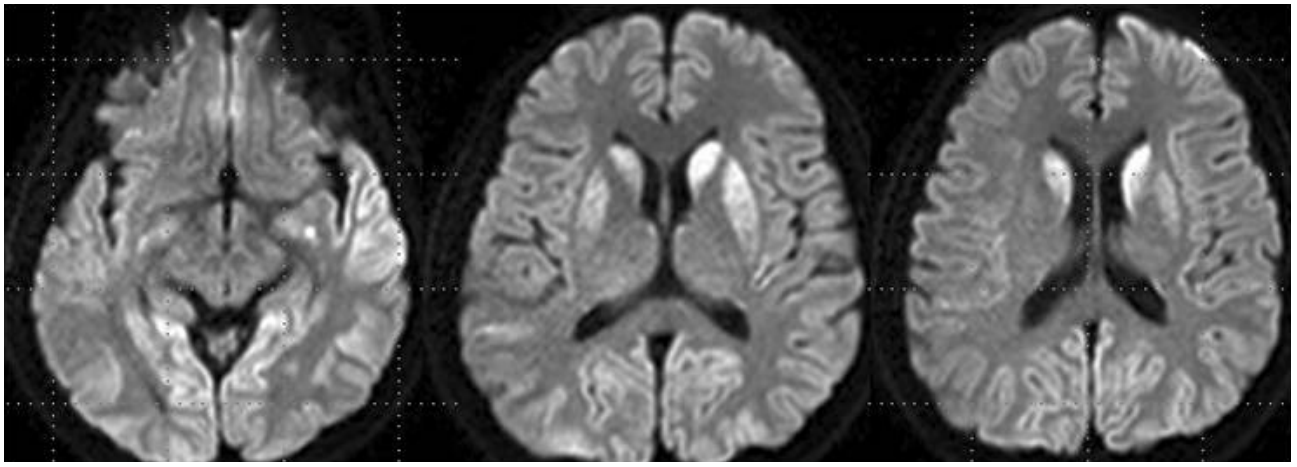

Figure 3. Diffusion-weighted magnetic resonance brain images showed increased signal intensity in the bilateral caudate/putamen and bilateral occipital cortex, Lt frontal and Lt temporal cortex.

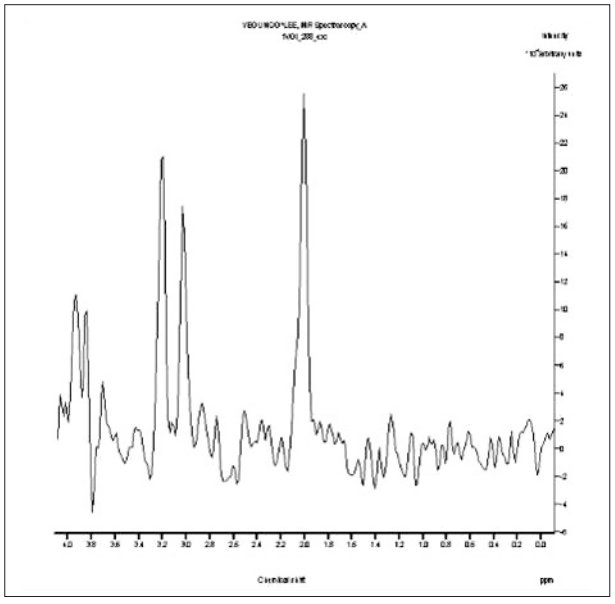

Figure 4. MR spectroscopy showed mild decreased of the peak of NAA. At map of lactate area, lactate was no increased. NAA: N-acetyl-aspartate.

mon clinical manifestations of CJD, our patients presented initially with isolated visual symptoms, consistent with the Heidenhain variant.[5,6] Presenting signs and symptoms in patients with the Heidenhain variant of CJD may include visual field defects, visual hallucinations, visual agnosia, cortical blindness, and abnormal color or visuospatial perception.[5,6] Isolated eye movement disturbances may also occur.[7] Patients may initially complain of vague visual disturbances and may give up reading or watching television.

Purvin et al.[8] described a patient who presented with palinopsia as a presenting manifestation of CJD. Ophthalmologic examinations early in the course of CJD are often unrevealing, and patients may try new eyeglasses without resolution of symptoms.[6] Despite isolated early visual symptoms, a rapid progression to dementia and death follows. Histopathologic changes characteristic of CJD, including spongioform degeneration, neuronal loss, and astrocytic gliosis, are most pronounced in the occipital lobes of patients with the Heidenhain variant.[9] The characteristic triad of dementia, myoclonus, and abnormal EEG may be lacking in as many as 25% of patients with the Heidenhain variant of CJD. The classic EEG finding of 1 cycle/second triphasic waves may not be present until late in the disease. Short of brain biopsy, testing to confirm the diagnosis of CJD with certainty before death is lacking. The spinal fluid assay for the 14-3-3 protein may be a useful marker for the disease[10] but may be negative in some patients with pathologically confirmed CJD. The 14-3-3 assay also lacks specificity for CJD and may be positive in patients with other conditions causing neuronal death, such as stroke, hypoxic- ischemic injury, and herpes encephalitis.[10] Our patient emphasizes the need for suspicion of CJD (Heidenhain variant) in patients with apparently isolated visual symptoms or field defects and normal MRI image. A recent study has shown that diffusion-weighted MRI is indeed helpful for confirming CJD based on demonstration of cortical lesions.[11] Although conventional MRI may show cortical and basal ganglia abnormalities on T2- and proton density-weighted images, such scans may be normal upto 21% of patients during the early course of CJD.[12] Gadolinium enhancement is unusual.[12] Diffusion-weighted imaging may be abnormal secondary to cell lysis and membrane disruption.[13] Diffusion-weighted imaging and fluid attenuated inversion recovery (FLAIR) sequences should therefore be included in MRI protocols for patients with unexplained visual loss and normal T1- and T2-weighted images. Recent reports have suggested that the ERG may also provide a useful adjunct in cases of suspected CJD.[13] Patients with CJD have been demonstrated to have a decrease in the b-wave amplitude of the ERG.[13] This abnormality most likely relates to degenerative changes in the outer plexiform layer and Mueller cells.[13] Whereas a decrease in the b-

wave amplitude is not specific for CJD, the magnitude of this finding may correlate with disease progression.[13] Richard et al.[14] reported progressive reduction in the b-wave amplitude in two patients with CJD during the course of their disease.[14] ERG abnormalities may appear before the emergence of characteristic EEG findings in CJD,[14] particularly among patients with visual symptoms. The Heidenhain variant of CJD must be considered in all patients who present with isolated visual complaints and either normal conventional brain neuroimaging or findings that do not completely correlate with signs and symptoms. In such patients, diffusion-weighted and FLAIR MRI may reveal early cortical changes. CSF assay for the 14-3-3 protein, if positive, may also aid in the diagnosis for patients in whom the degree of suspicion for CJD is high.

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