

A Man Who Changed Six Spectacles: a Case of Heidenhain Variant of the Creutzfeldt–Jakob Disease

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Abstract

Creutzfeldt–Jakob Disease (CJD) is a rare and rapidly progressive condition. A 54-year-old professor initially presented with insidious, progressive visual symptoms. Imaging suggested post-infectious encephalitis, but symptoms progressed to ataxia, coordination difficulties, and cognitive decline. Repeat MRI revealed findings consistent with CJD, supported by clinical and electrophysiological evidence. Though 14-3-3 protein in CSF was inconclusive, Heidenhain variant CJD was strongly suspected. Isolated visual symptoms progressing rapidly alongside ataxia and dementia prompt suspicion of this variant. Clinical examination, neuroimaging, and EEG play crucial roles in the diagnosis.

Keywords: Creutzfeldt–Jacob disease; Heidenhain variant

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Человек, который шесть раз менял очки. Описание клинического случая пациента с болезнью Крейтцфельдта–Якоба (вариант Хайденхайна)

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Аннотация

Болезнь Крейтцфельдта–Якоба (БКЯ) представляет собой редкое и быстро прогрессирующее заболевание. Пациент 54 лет, профессор, впервые обратился за медицинской помощью по поводу постепенно прогрессирующего ухудшения зрения. Данные визуализации позволили предположить наличие постинфекционного энцефалита, однако симптомы усиливались, появились нарушения координации, атаксия и снижение когнитивных функций. При повторной МРТ были выявлены признаки БКЯ, что также подтверждали данные клинического и электрофизиологического обследований. Несмотря на то что определение уровня белков 14-3-3 в спинномозговой жидкости не позволило прийти к однозначным выводам, возникло серьёзное подозрение на наличие у пациента БКЯ, вариант Хайденхайна. Быстро прогрессирующие изолированные зрительные симптомы, атаксия и деменция подкрепляют это предположение. В установлении такого диагноза важнейшую роль играют результаты клинического обследования, нейровизуализации и электроэнцефалографии.

Ключевые слова: болезнь Крейтцфельдта–Якоба; вариант Хайденхайна

Этическое утверждение. Исследование проводилось при наличии информированного согласия законных представителей пациента.

Источник финансирования. Авторы заявляют об отсутствии внешних источников финансирования при проведении исследования.

Конфликт интересов. Авторы заявляют об отсутствии явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Introduction

Creutzfeldt–Jakob disease (CJD) is a fatal neurodegenerative disorder typically characterized by rapidly progressive dementia associated with other neurological or ophthalmologic symptoms [1]. The Heidenhain variant defines a peculiar clinical presentation of sporadic CJD, characterized by isolated visual disturbances at disease onset and reflecting the early damage to the occipital cortex by prions. These isolated visual symptoms can progress for weeks challenging the diagnosis [1]. We report a 54-year male who presented with progressive visual symptoms, followed by neurological symptoms, and after the evaluation was diagnosed with Heidenhain variant of CJD (HVCJD).

Clinical case

A 54-year-old male professor developed insidious onset visual disturbances 4 months prior to presentation. The visual symptoms were noted when he complained of difficulty setting and correcting question papers. They included a blurring of the entire visual field, with no field restriction, blank spots, flashes of light, headache or ocular pain or difficulty recognizing shapes and objects. He had no diplopia, visual hallucinations, visual distortion, altered depth perception, or perception of movement/persistence of images. He had an initial ophthalmological consultation and was prescribed glasses. However, the visual symptoms had been persistent and mildly progressive over the next two months for which his glasses were changed repeatedly at least 6 times. Subsequently, a month prior to presentation, following dengue infection, his symptoms had worsened. One week prior to the presentation, the patient developed a slowing of his gait with unsteadiness when using his right hand. No history of fever at that point, seizures, vomiting, nuchal rigidity, sensory, or autonomic symptoms had been reported.

On examination, he appeared as an attentive, well-groomed, mildly anxious man, with a normal Montreal Cognitive Assessment score (MoCA) score of 29 points. Visual examination revealed a best-corrected visual acuity of 20/60 bilaterally, with inconsistent right hemianopia. His eye movements, pupil and fundus were normal. During the examination, macropsia was also observed. Spino-motor examination revealed asymmetrical (right > left) cerebellar signs, mild bradykinesia, and impaired tandem walk, with normal muscle power. The other neurological and systemic examination was unremarkable.

The patient's routine lab evaluation including CBC, renal, hepatic, thyroid tests, glycemia and electrolytes was normal. Gadolinium-enhanced magnetic resonance imaging (MRI) of the brain revealed T2/FLAIR gyriform hyperintensities with corresponding restricted diffusion in the left parafalcine parieto-occipital cortex with no evidence of abnormal contrast enhancement with MR angiogram was unremarkable (Fig. 1, A–C). The gyriform lesion pattern along with insidious symptoms were suggestive of encephalitis and CSF analysis showed an acellular tap with normal protein levels. Infections and immune work-ups in both CSF and serum were normal. Considering the recent dengue infection, possible post-infectious encephalitis was considered and the patient was pulsed with high-dose steroids.

The patient continued to progress, with the development of new visual symptoms of macropsia and agnosia with worsening discoordination. He had developed memory loss to the extent that he couldn't recall his wife's name or his education. A neurological examination revealed a MoCA score of 8/30 with a significant increase in his cerebellar signs and bradykinesia. The duration between the two MoCA assessments were less than 3 weeks. A repeat gadolinium-enhanced MRI brain showed an increase in the gyriform diffusion restriction with corresponding T2 FLAIR hyperintensities noted in bilateral temporal and

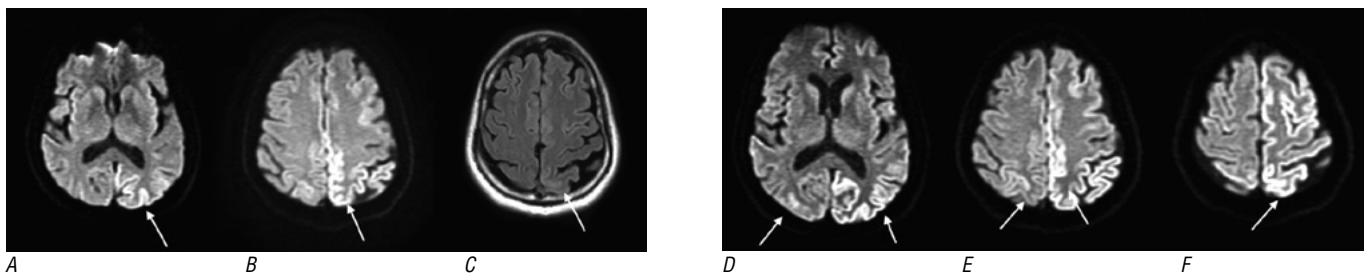


Fig. 1. Brain MRI (axial section, diffusion-weighted images; *A, B*) performed during the initial admission shows left occipito-parietal and parafalcine gyri form diffusion restriction (arrows). *C* – T2 FLAIR hyperintensity in the corresponding areas; *D–F* – subsequent brain MRI (diffusion-weighted sequences, axial section) done during the next admission show an increase of the gyriform diffusion restriction to involve the contralateral hemisphere and high frontoparietal region, sparing the perirolandic cortex.

left parieto-occipital lobes with sparing of the perirolandic region with no contrast enhancement (Fig. 1, *D–F*). Considering the rapidly progressive cognitive decline, onset with visual symptoms, and cerebellar signs, with imaging features, the Heidenhain variant of CJD (HVCJD) was suspected. Electroencephalography showed repeated cycles of short interval periodic discharges of triphasic morphology with background slowing (Fig. 2). For confirmation of CJD, RT-QuIC and 14-3-3 protein were available. The results of 14-3-3 protein test were in high normal range which was attributed to very early measurement in the course of disease. Moreover, 14-3-3 protein is relatively nonspecific and its levels can be high in a variety of neurological diseases. RT-QuIC test was not done due to logistical reasons. Pa-

tient attendees were counselled regarding the disease, and the supportive care was initiated. The patient was later followed up via telephone communication, a month after discharge. By that time, he had become completely bed bound and mute.

Discussion

CJD is a rare prion (proteinaceous infectious particles)-associated neurodegenerative disorder resulting in a spongiform encephalopathy with an estimated incidence of 1 case per 1 million people annually [1]. The HVCJD is a form of sporadic CJD associated with visual signs and symptoms at onset. The majority of reports detailing

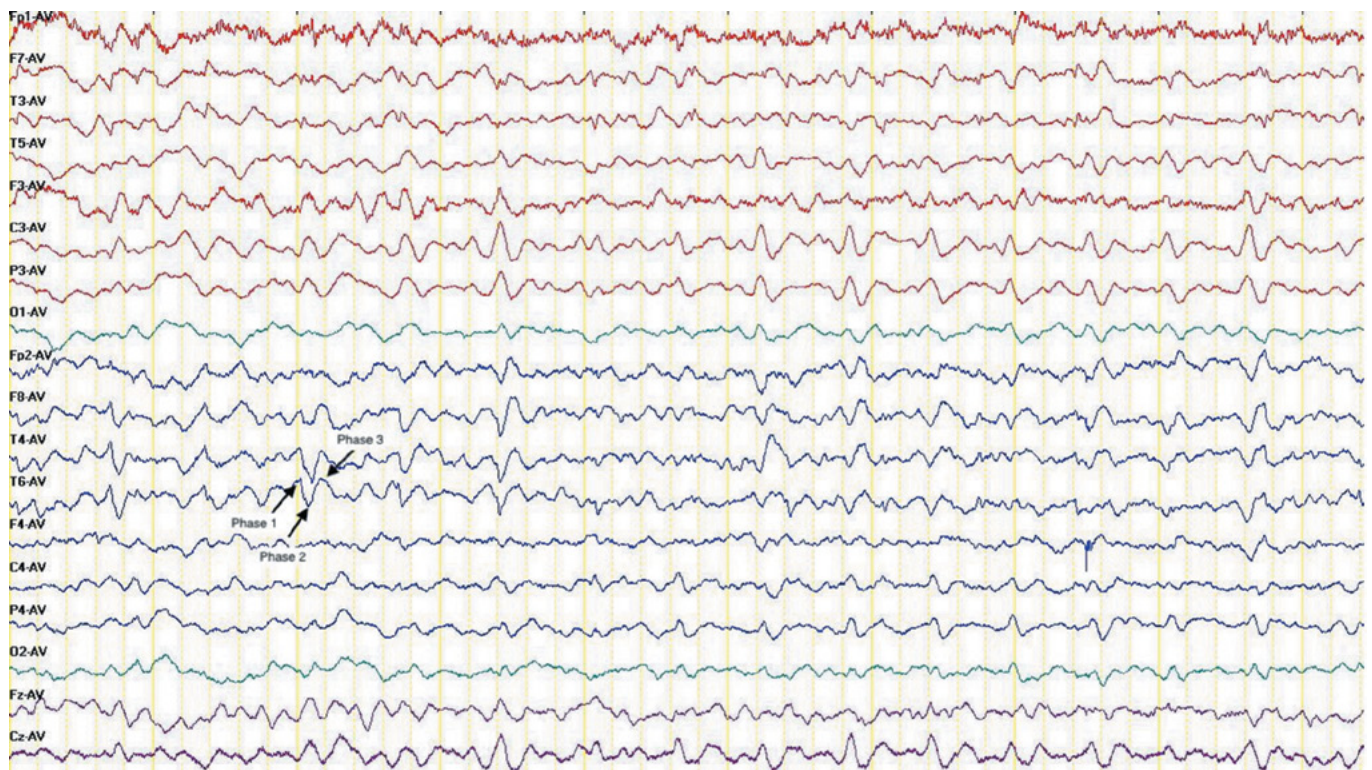


Fig. 2. Electroencephalogram recording of the patient in the average montage shows intermittent runs of short interval periodic triphasic discharges (arrows).

HVCJD are epidemiological studies, reviews, and case reports given the low incidence of the disease and lack of controlled clinical studies [2]. Ophthalmic manifestations of HVCJD may occur weeks or months before the onset of other symptoms, with a retrospective case series detailing that blurred vision and diplopia were the most common initial symptoms. The ophthalmologic manifestations of HVCJD include [2, 3]:

1. Eye signs:

- decreased visual acuity;
- sluggish pupils;
- absent optokinetic reflex;
- no response to visual threat;
- spasm of fixation;
- optic disc pallor;
- normal ophthalmoscopy and biomicroscopy;
- poor colour vision;
- visual field constriction;
- nystagmus;
- supranuclear palsy;
- ocular dipping;
- saccadic abnormalities;
- impaired convergence;
- eyelid abnormalities;
- homonymous hemianopia with and without macular involvement.

2. Eye symptoms:

- worsened visual acuity;
- cortical blindness;
- blurry vision;
- palinopsia;
- oscillopsia;
- diplopia;
- visual hallucinations;
- vision distortion;
- altered depth perception;

- simultagnosia;
- optic anosognosia;
- environmental agnosia;
- complete loss of vision;
- tunnel vision.

Diagnosis of HVCJD in its early stages can be difficult as it may not entirely satisfy the clinical criteria which required presence of dementia, and include cerebellar signs, and parkinsonism. But the visual symptoms actually denote occipital lobe involvement and represent the visuospatial domain. So, the diagnosis is usually made based on ancillary testing such as EEG and brain MRI. In a series of HVCJD, EEG was found to be the most sensitive, with periodic triphasic waves, which were spread both generally or with posterior predominance [4]. Other diagnostic modalities include the CSF 14-3-3 test or the RT-QuIC. Human 14-3-3 proteins are normal neuronal and nonneuronal proteins that participate in the modulation of signal transduction pathways and are released into the CSF when there is non-specific, rapid, and extensive destruction of brain tissue. The sensitivity of 14-3-3 protein gamma isoform has most commonly been reported as between 85% and 95% with a specificity anywhere from 40% to 100% for diagnosing CJD. In addition, the 14-3-3 protein test is not sensitive to other types of prion diseases [5]. The moderate sensitivity, but poor specificity is likely due to its elevation in a number of different neurologic diseases [5]. There are no effective treatment strategies at present for prion diseases.

Conclusion

This case report demonstrates the importance of considering this rare condition in patients with rapidly progressive visual disturbances. Prompt recognition of this condition prevents the patient and caregivers from additional evaluation and for early institution of end-of-life support services.

References / Список источников

1. Kropp S., Schulz-Schaeffer W.J., Finkenstaedt M. et al. The Heidenhain variant of Creutzfeldt–Jakob disease. *Arch. Neurol.* 1999;56(1):55–61. DOI: 10.1001/archneur.56.1.55.
2. Cooper S.A., Murray K.L., Heath C.A. et al. Isolated visual symptoms at onset in sporadic Creutzfeldt–Jakob disease: the clinical phenotype of the “Heidenhain variant”. *Br. J. Ophthalmol.* 2005;89(10):1341–1342. DOI: 10.1136/bjo.2005.074856
3. Cornelius J.R., Boes C.J., Ghearing G. et al. Visual symptoms in the Heidenhain variant of Creutzfeldt–Jakob disease. *J. Neuroimaging.* 2009;19(3):283–287. DOI: 10.1111/j.1552-6569.2008.00294.x
4. Keyrouz S.G., Labib B.T., Sethi R. MRI and EEG findings in Heidenhain variant of Creutzfeldt–Jakob disease. *Neurology.* 2006;67(2):333. DOI: 10.1212/01.wnl.0000208487.18608.41
5. Geschwind M.D., Martindale J., Miller D. et al. Challenging the clinical utility of the 14-3-3 protein for the diagnosis of sporadic Creutzfeldt–Jakob disease. *Arch. Neurol.* 2003;60(6):813–816. DOI: 10.1001/archneur.60.6.813

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