JAMA Ophthalmology Clinical Challenge

Homonymous Hemianopia With Normal Magnetic Resonance Imaging

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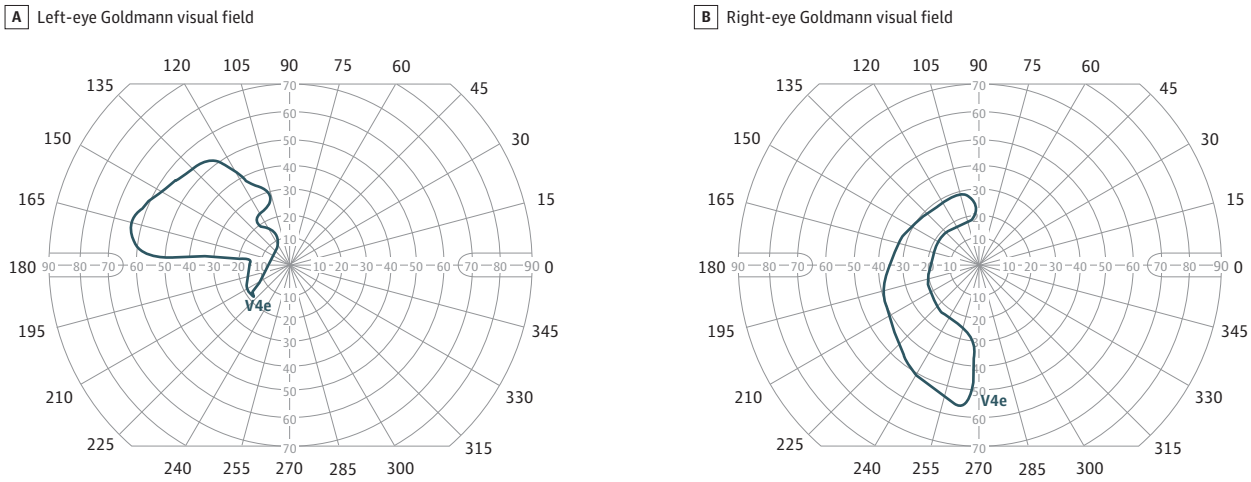

Figure 1. Goldmann perimetry (V4e stimulus) of left (A) and right (B) eyes shows right homonymous hemianopia, left inferotemporal visual field loss, and right nasal paracentral visual field loss.

A man in his 80s presented with 3 months of painless progressive vision loss, followed by gait changes, memory loss, and 10-lb unintentional weight loss. Medical history was notable for coronary artery disease, hypothyroidism, and prostate cancer in remission.

On ophthalmic examination, visual acuity was hand motion OU (baseline from 9 months prior was 20/50 OD and 20/30 OS), with briskly reactive left pupil and trace right relative afferent pupillary defect. He could detect 2/4 gross colors in the right eye and 1/4 gross colors in the left eye. Confrontation visual fields revealed dense right homonymous hemianopia with additional asymmetric deficits on Goldmann perimetry (**Figure 1**). Extraocular movements were full with gaze-evoked nystagmus. Horizontal vestibulo-ocular reflex, assessed by head impulse testing, was normal. Slitlamp and dilated fundus examination revealed pseudophakia and mild epiretinal membrane in the right eye and mild nuclear sclerosis in the left eye.

Neurologic examination showed full motor strength, decreased vibration sense and proprioception in the feet, positive Romberg sign, and inability to tandem walk. Mini-Mental State Examination score was 6 of 30.

Magnetic resonance imaging brain and orbits with and without contrast and magnetic resonance angiography head and neck were unremarkable. An electroencephalogram showed no localizing signs. Syphilis screen was negative. Serum thiamine, vitamin B_{12}, and thyrotropin levels were normal. Cerebrospinal fluid composition, infectious studies, cytology, flow cytometry, and paraneoplastic panel showed only mildly elevated protein.

WHAT WOULD YOU DO NEXT?

- **A.** Pars plana vitrectomy with vitreous biopsy
- **B.** Prescribe aspirin for secondary stroke prevention
- **C.** Order cerebrospinal fluid prion disease panel
- **D.** Refer to psychiatry for functional vision loss

Diagnosis

Creutzfeldt-Jakob Disease (CJD), Heidenhain variant

What to Do Next

C. Order cerebrospinal fluid prion disease panel

Discussion

The combination of rapidly declining visual acuity, homonymous hemianopia, nystagmus, and neurologic and cognitive deficits merits high suspicion and appropriate diagnostic workup for rapidly progressive neurodegenerative disease, such as prion disease (choice C). Pars plana vitrectomy with vitreous biopsy (choice A) is inappropriate without clinical evidence of intraocular infection or malignancy. Secondary stroke prevention (choice B) is not indicated with normal neuroimaging. The examination findings strongly suggest organic rather than functional disease (choice D).

Creutzfeldt-Jakob Disease (CJD) is a rapidly progressive, fatal neurodegenerative disease caused by accumulation of pathologic misfolded prion protein in the brain. Eighty-five percent of cases

are sporadic, 10% to 15% are familial, and the remainder are iatrogenically transmitted through contamination of neurosurgical equipment, human pituitary hormones, or dura mater or corneal grafts.[1] The rare Heidenhain variant of sporadic CJD features early and initially isolated visual disturbances caused by occipital cortex degeneration, including cortical blindness, dyschromatopsia, visual distortions, visual field defects, and hallucinations.[2] Early isolated ophthalmologic involvement can lead to diagnostic confusion and delayed evaluation by a neurologist.[2]

Gold-standard diagnosis of CJD requires histopathologic confirmation from brain biopsy, but this is typically obtained post mortem.[3] Real-time quaking-induced conversion (RT-QuIC) has emerged as a novel, rapid premortem diagnostic assay for CJD that detects the presence of pathologic protease-resistant prion protein in a patient sample of cerebrospinal fluid (CSF) or nasal brushings by measuring the fluorescence released from binding of thioflavin T fluorescent dye to the amyloid fibrils that are created when patient pathologic prion protein is mixed with (and induces misfolding and aggregation of) recombinant normal prion protein.[4] The RT-QuIC analysis of CSF has been shown to have superior sensitivity (>85%) and specificity (98.5%-100%) to the previously identified CSF biomarkers for CJD, 14-3-3 protein, and tau.[5,6] All 3 CSF biomarkers are assayed in the National Prion Disease Pathology Surveillance Center prion disease panel (choice C). The RT-QuIC analysis of olfactory epithelial specimens has also shown promise as a less invasive, and perhaps even faster and more accurate, diagnostic assay than CSF analysis.[7,8] The updated 2018 US Centers for Disease Control and Prevention diagnostic criteria recognize a positive RT-QuIC result plus neuropsychiatric disorder as sufficient for probable CJD.[3] Although CJD is currently incurable, early diagnosis is important for patient and family counseling and supportive care, prevention of iatrogenic transmission,[9] and identification of patients who are candidates for clinical trials.

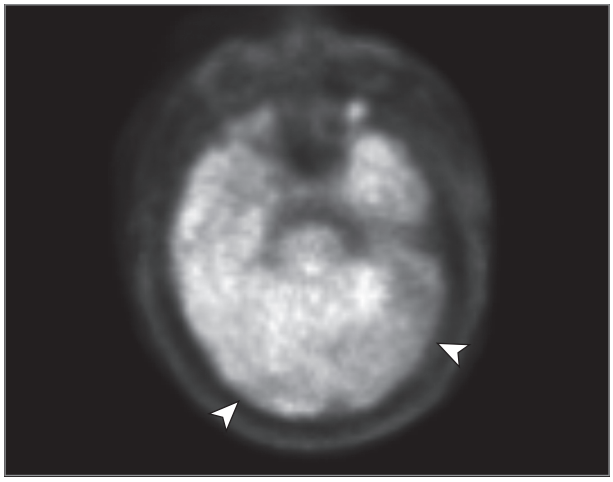

Figure 2. Representative nonfused axial positron emission tomography–computed tomography brain shows regional hypometabolism of bilateral occipital lobes, left more than right (arrowheads). This was confirmed with 3-dimensional statistical parametric map images (not shown). Additional scans (not shown) showed regional hypometabolism of the bilateral frontal lobes. This pattern, while nonspecific, can be consistent with Creutzfeldt-Jakob disease.

Patient Outcome

This patient's CSF prion disease panel returned positive for RT-QuIC and 14-3-3 protein and showed elevated total tau protein (more than 3 times the upper limit of normal), with greater than 98% estimated probability of prion disease. Brain positron emission tomography–computed tomography revealed decreased 18F-fluorodeoxyglucose uptake in the frontal and occipital lobes, a pattern consistent with CJD with visual symptoms (**Figure 2**).[10] The patient continued to deteriorate rapidly and died. No autopsy was performed.

ARTICLE INFORMATION

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