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Cerebellar Ataxia and Hearing Impairment

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A 51-year-old man presented with progressive difficulty walking that developed over 1 month shortly after he ran a marathon. He frequently fell and had difficulty climbing the stairs. He stated he had hearing problems, but with further questioning, it was discovered he actually had difficulty deciphering speech. He did not have dizziness on standing nor bowel or bladder incontinence. He did not take medications, and he drank socially. He had no family history of imbalance problems. He still worked full-time as a lawyer.

His neurological examination showed mild cerebellar ataxia without myoclonus or parkinsonism. His Montreal Cognitive Assessment score was 28 of 30 points (2 points deducted from “delayed recall”). Pure tone audiometry showed no conductive or sensorineural hearing loss. Brain magnetic resonance imaging (MRI) revealed no abnormal signal, including from the pons and cerebellum. A computed tomography scan of the chest, abdomen, and pelvis showed no malignancy. Results from cerebrospinal fluid (CSF) testing were normal without oligoclonal bands and a normal level of protein 14-3-3. He had no paraneoplastic antibodies in his serum or CSF. Results from electroencephalogram (EEG) were normal.

One month later, his condition progressed; he required a wheelchair, declined cognitively, and developed personality changes. Neurological examination showed slurred speech, worsened cerebellar ataxia, and impaired postural reflex without myoclonus/asterixis. He developed seizures and was admitted to a hospital. His mental status continued to progressively decline, and he became completely mute; he could only open his eyes and follow commands to protrude his tongue but was unable to move his eyes or any limbs. Electroencephalogram showed diffuse slowing. Repeated MRI was unremarkable (Figure 1).

Diagnosis

D. Creutzfeldt-Jakob disease.

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Discussion

The clinical presentation of this patient was rapidly progressive cerebellar ataxia with problems deciphering speech, which provides diagnostic clues. Of note, the difficulty in deciphering speech might be interpreted by patients as hearing impairment. Peripheral hearing loss refers to the hearing loss caused by ear structures, and it includes conductive and sensorineural hearing loss. Pure tone audiometry and brainstem auditory evoked responses could be used to differentiate the localization of the cause of hearing impairment. In the setting of subacute cerebellar ataxias combined with peripheral hearing impairment, paraneoplastic syndrome could be associated with sensorineural hearing loss when ganglia of Corti and/or the cochlear nuclei in the brainstem are involved.

Adult-onset cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss (CAPOS) syndrome caused by *ATP1A3* mutation should also be considered, even though CAPOS syndrome is often characterized by childhood onset and relapsing and remitting cerebellar ataxia followed by fever.¹ However, the patient did not have peripheral hearing impairment, and myoclonus and seizures are uncommon in patients with paraneoplastic cerebellar ataxia and CAPOS syndrome. In central hearing impairment with subacute ataxias, vascular events and infectious and inflammatory diseases (ie, meningitis and cerebellitis) should also be investigated.

Subacute ataxia can be a manifestation of thiamine and vitamin E deficiency; vestibular dysfunction without hearing loss is a common finding in Wernicke encephalopathy. This patient had normal serum vitamin B₁ and E levels. His MRI had no typical Wernicke encephalopathy findings. We empirically gave intravenous thiamine replacement to this patient, but he did not improve clinically.

Steroid-responsive encephalopathy was considered, but results from an anti-thyroperoxidase antibody test were normal. Because the sensitivity and specificity of anti-thyroperoxidase is still unclear, pulse therapy with methylprednisolone was given, which was not effective.

Hearing problems, such as bilateral hypoacusis² and hyperacusis,³ usually without tinnitus and vertigo, have been reported as initial presentations of sporadic Creutzfeldt-Jakob disease (CJD). Auditory agnosia and cortical deafness due to damage of bilateral temporal cortices were the causes of cortical hearing deficit. Creutzfeldt-Jakob disease usually presents with rapidly progressive ataxic dementia. In this patient, the diagnosis of CJD was originally not prioritized—the dementia was initially not obvious and the hearing problem was a confounder. While results from CSF testing and EEG could be normal, normal MRI is rare. Despite the fact that laboratory and imaging tools for CJD diagnosis have moderate to high sensitivity and specificity (92% and 80% for CSF 14-3-3 protein, respectively; 67% and 86% for periodic sharp waves complexes on EEG; and 83%–92% and 87%–95% for diffusion-weighted imaging sequence of MRI),^{4–6} the absence of laboratory, imaging, and EEG findings can occur in patients with sporadic CJD, particularly in patients with an initial presentation of isolated cerebellar ataxia. The MRI and EEG of this patient did not show typical findings, even when the disease progressed to akinetic mutism, highlighting that CJD should still be considered even in “triple-negative” patients.

The patient's autopsy showed classic spongiform features in the thalamus, hippocampus, and cerebellar dentate nucleus (Figure 2). Western blot analyses confirmed the presence of the abnormal, protease-resistant prion protein (PrP). Gene sequencing revealed no pathogenic mutation in the coding region of the PrP gene that would otherwise indicate familial prion disease. The extensive involvement of the thalamus, cerebellum, and inferior olivary nucleus in this patient could be pathologically consistent with thalamic CJD/sporadic familial insomnia, a rare form of CJD with sleep disturbance and autonomic dysfunction; however, the patient did not have these symptoms.^{7,8}

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WHAT IS YOUR DIAGNOSIS?

- A.** Paraneoplastic cerebellar ataxia
- B.** Adult-onset cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss syndrome
- C.** Wernicke encephalopathy
- D.** Creutzfeldt-Jakob disease

Figure 1.

Magnetic resonance imaging of the brain demonstrates (A) no pontine or cerebellar atrophy and no cortical ribbon sign, ie, high signal intensity of the cerebral cortex, on (B) fluid-attenuated inversion recovery, or (C) diffusion-weighted imaging sequence.

Figure 2.
The brain autopsy showed spongiform changes with neuronal dropouts, including in the cerebellar dentate nucleus.