Case Report

MRI findings in neuronal ceroid lipofuscinosis✩,✩✩

Anna M. Craina, Deanna L. Kitchen, MD, MPHb, Nikhil Godiyalb, Cory M. Pfeifer, MD, MPHb,∗

aUniversity of Texas at Dallas, 800 W Campbell Rd, Richardson, TX 75080
bDepartment of Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390

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ABSTRACT

Neuronal ceroid lipofuscinosis is a rare cause for developmental delay and seizures that results in neurodegeneration. Presented here is a case of a 5-year-old male who presented for MRI following a delay in achieving developmental milestones and epilepsy. MRI was performed demonstrating a thinned corpus callosum and generalized low parenchymal volume with periventricular gliosis. Magnetic resonance spectroscopy showed glutamate/glutamine accumulation and diminished N-acetylaspartate. The diagnosis of neuronal ceroid lipofuscinosis was revealed following genetic testing. This case is useful in showing findings of this rare disorder.

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Introduction

Neuronal ceroid lipofuscinoses (NCLs) are a group of inherited lysosomal storage disorders characterized by the accumulation of ceroid lipofuscin, an autofluorescent pigment, in neuronal and extraneuronal cells. Dr. Otto Christian Stengel published the first clinical description of NCL in 1826, but it was largely overlooked by the scientific community until the 1950s [1]. Fourteen human NCLs have been described, with age of onset ranging from congenital to late adult [1]. The diseases are classified as ceroid lipofuscinosis-neuronal (CLN) followed by a number (e.g., CLN1, CLN2, etc.). The various CLN diseases are caused by distinct mutations in diverse locations on different chromosomes. These disorders are also classified by the age of onset, though some forms of CLN may exhibit subtypes that have different onsets. CLN1, for instance, may have an infantile or juvenile onset. NCLs often show an autosomal recessive mode of inheritance, though at least 1 adult-onset form shows autosomal dominant inheritance [2]. Patients typically present with progressive vision loss followed by a decline in cognitive and motor skills, epileptic seizures, and eventually premature death [3]. Hyperventilation episodes, Rett-like onset, and speech delay have also been described [4].

Presented here is a case of neuronal ceroid lipofuscinosis in which MRI and MR spectroscopy was performed.

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∗ Corresponding author. (C.M. Pfeifer)
E-mail address: cory.pfeifer@utsouthwestern.edu (C.M. Pfeifer).
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Case report

The patient was originally diagnosed with seizures at age 3. The seizures consisted of bilateral leg jerking and were well controlled on valproic acid. By age 4, he had lost bladder function. He was developmentally delayed and spoke few words. He could not walk or crawl. Past medical history included a spontaneous vaginal delivery with no complications. There was no family history of a neurodegenerative disorder.

MRI performed at age 5 showed a thinned corpus callosum and mildly attenuated caliber of the brainstem (Fig. 1). T2-weighted images showed periventricular increased signal intensity (Fig. 2). Overall brain volume was less than expected for age. Magnetic spectroscopy was performed at an echo time of 30 ms with a voxel placed in the right frontal white matter. The dominant peak was at 2.2–2.4 ppm, likely indicative of glutamate or glutamine accumulation, and there was a peak at 3.5 ppm, likely reflecting myo-inositol. The n-acetyl-aspartate peak at 2.0 ppm was diminished.

Genetic testing confirmed a mutation in the MFSD8 gene.

Discussion

Mutations in the MFSD8 gene underlie a variant form of late infantile onset NCL [3,5]. The coded protein has 12 transmembrane domains and belongs to the major facilitator superfamily (MFS) of proteins [6]. MFS transporters use chemiosmotic gradients to move small solutes across the membrane [5]. This protein localizes to lysosomes and late endosomes in neurons more than glia [7]. Mutations lead to accumulation of glycolipids and lipoproteins in lysosomes, which causes cell degeneration and gliosis [8]. Death is common in the teenage years.

Autopsies have revealed significant neuron loss in the Purkinje and granule cell layers of the cerebellum, cortical layer V, the CA2 region of the hippocampus, and the ganglionic layer of the retina [7]. Affected brain areas showed high levels of ceroid storage, but some areas show storage without large-scale neuron loss [7]. MRIs show progressive cortical and cerebellar atrophy [9]. Additional clinical clues to CLN in other studies have included EEG findings, such as occipital spikes [3,5]. Our patient had significant white matter volume loss with global cerebral atrophy, which is consistent with other studies that have shown cortical and cerebellar atrophy on MRI [9]. Additionally, accumulation of glutamate/glutamine and myo-inositol with diminished N-acetyl-aspartate on magnetic resonance spectroscopy has been described with neuronal ceroid lipofuscinosis [10], as was evident in the patient presented here.

The findings presented in this case provide additional insight into the possible prospective diagnosis of this disorder. Though the white matter and structural findings demonstrated here are relatively nonspecific, magnetic resonance spectroscopy may provide insight in suggesting genetic testing.

Consent statement

Informed consent was obtained for publication of the findings related to this patient’s diagnosis.
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Fig. 3 – Magnetic resonance spectroscopy with a voxel placed in the frontal white matter shows a major peak at 2.2 to 2.4 ppm (black arrow with white outline). The NAA peak at 2.0 ppm is diminished (white arrow). There is an additional peak at 3.5 ppm (striped arrow).