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Case Report

Neuronal Ceroid Lipofuscinosis (NCL) Unveiled: A Case Study of a 6-Year-Old Boy

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Abstract

This case study delves into the intricacies of Neuronal Ceroid Lipofuscinosis (NCL) through the lens of a 6-year-old boy's journey. Initially born without complications, the patient's developmental trajectory was abruptly interrupted by the onset of epilepsy at the age of 4.5 years. Subsequent neurological regression manifested as loss of motor skills and speech, alongside debilitating seizures. Diagnostic investigations revealed a homozygous mutation in the MFSD8 gene, confirming NCL diagnosis. Despite multidisciplinary therapeutic interventions, the patient's condition exhibited minimal improvement, underscoring the challenges of managing this progressive neurodegenerative disorder. This case underscores the importance of accurate diagnosis, comprehensive care, and ongoing research efforts in addressing the complex spectrum of NCL.

Case Presentation

The patient is a 6-year-old male, born at term without complications and achieving developmental milestones appropriately until experiencing regression in motor skills. Epilepsy onset occurred at the age of 4 years, presenting initially with tonic seizures. Subsequently, the patient experienced neurological regression, losing the ability to walk and talk, with limited verbal communication consisting of "baba." Notable seizures include tonic seizures lasting approximately 3 minutes, occurring once nightly, alongside multiple episodes of absence seizures daily. The patient is currently receiving treatment under the care of a neurologist in Jordan.

Medical History:

The patient's medical history is significant for uneventful perinatal circumstances, followed by a regression in motor skills and the onset of epilepsy at 4.5 years old. Genetic testing revealed a homozygous mutation in MFSD8 gene (c.1393C >T, p. Arg465Trp), confirming the diagnosis of Neuronal Ceroid Lipofuscinosis (NCL). Additional investigations included MRI brain imaging, which showed abnormal hyperintense signals in the cerebral periventricular white matter and insular cortices, suggestive of white matter demyelination. The patient also presented with speech difficulties, lack of coordination, and weakness.

Medications: Valproic acid, Levetiracetam, Topiramate

Investigations:

- EEG demonstrating generalized 3Hz spike-wave activity correlated with absence seizures
- MRI brain revealing abnormal hyperintense signals in the periventricular white matter and insular cortices.
- Genetic testing confirming homozygosity for MFSD8 mutation associated with NCL.

Despite the earnest efforts put forth in occupational therapy, physiotherapy, and feeding therapy, the patient's condition has regrettably shown no discernible improvement.

Discussion

Neuronal ceroid lipofuscinoses are lysosomal storage disorders characterized by abnormal accumulation of autofluorescent material in lysosomes of the cells (6), leading to a progressive and debilitating neurodegenerative course. NCLs represent the most common degenerative brain diseases in childhood (4), manifesting with a triad of symptoms including dementia, epilepsy, and motor decline. Additionally, visual impairment is often a prominent feature, particularly in childhood forms of the disease. With age, the symptoms can vary and the onset of the disease can range from birth to young adulthood. In a school child, first symptoms are usually visual loss and behavior change, followed by dementia (3).

CLN7 disease, also called the “Turkish” variant but has been shown to occur worldwide (2). The age at onset ranges from 2 to 7 years. The initial symptoms are mainly seizures followed by other symptoms including myoclonus, progressive motor decline, cognitive changes, and vision loss. The diagnosis is through gene analysis.

The pathophysiology of NCLs stems from mutations in various genes associated with lysosomal function and neuronal health. The genetic heterogeneity of NCLs poses a diagnostic challenge, with numerous identified NCL genes contributing to a wide phenotypic variability.

In almost all NCL forms the patients are initially healthy and have a normal developmental profile (2). The main alerting symptoms are the combination of two or more of dementia, visual loss, epilepsy, and motor deterioration.

Therapeutic options for NCLs are limited, focusing primarily on symptomatic management and palliative care. Treatment is difficult as most patients have severe visual impairment and may not be able to communicate verbally with caregivers (4). Antiepileptic medications, including valproic acid and levetiracetam, are commonly employed to manage seizures associated with NCLs. Additionally, interdisciplinary collaboration

involving specialized teams experienced in NCL management is essential for optimizing palliative therapies and addressing the multidimensional needs of patients and families affected by the disease. Recognition and management of pain in NCL patients requires particular skills (1)

The presented case of a 6-year-old male pinpoints the complexity of the disease. The age of the patient precisely aligns with the typical onset range of NCL type 7 as outlined in the literature. As he was born without any complication, the patient's developmental stages were interrupted at the age of 4.5 by the onset of epilepsy. As mentioned in research studies: "Before onset of symptoms, patients show a largely normal psychomotor development" (5). Initially presenting with tonic seizures, the disease then progressed and caused neurological deficits, resulting in regression of motor skills and speech. Notable features, including frequent absence seizures confirmed by the EEG and nightly tonic clonic seizures highlights the neurological disturbances associated with NCLs. Genetic testing confirmed a homozygous mutation in the MFSD8 gene which was a hallmark finding consistent with NCL diagnosis and reflecting on the genetic heterogeneity described in the literature. This case highlights the importance of accurate identification of NCL subtypes based on clinical presentation and genetic testing. Additionally, the management plan outlined for this patient, including continued monitoring of VPA levels, referral to occupational therapy and speech therapy, and ophthalmologist follow-up, reflects the comprehensive multidisciplinary approach advocated in the literature for optimal patient care in NCL.

References

1- Hauer J. Identifying and managing sources of pain and distress in children with neurological impairment. Pediatr Ann. 2010;39:198–20

2- Cooper, J. D., Tarczyluk, M. A., & Nelvagal, H. R. (2015). Towards a new understanding of NCL pathogenesis. Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, 1852(10), 2256–2261.

3- Mole SE, Williams R, Goebel HH. Contemporary Neurology Series. Oxford University Press; Oxford: 2011. The neuronal ceroid lipofuscinoses

4- Schulz, A., Kohlschütter, A., Mink, J., Simonati, A., & Williams, R. (2013). NCL diseases — clinical perspectives. Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, 1832(11), 1801–1806.

5- Nickel, M., & Schulz, A. (2022). Natural History Studies in NCL and Their Expanding Role in Drug Development: Experiences From CLN2 Disease and Relevance for Clinical Trials. Frontiers in Neurology, 13.

6- Radke A, Stenzel W, Goebel HH. Human NCL neuropathology. Biochim Biophys Acta. (2015) 1852:2262–6. 10.1016/j.bbadis.2015.05.007.