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Epileptological aspects of juvenile neuronal ceroid lipofuscinosis (CLN3 disease) through the lifespan

Vibeke Arntsen [a], John Strandheim [b, c], Ingrid B. Helland [d], Trond Sand [a, b], Eylert Brodtkorb [a, b]

[a] Department of Neurology and Clinical Neurophysiology, St. Olav's University Hospital, Trondheim, Norway
[b] Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
[c] Hemne Health Centre, Kyrksæterøra, Norway
[d] Department of Clinical Neurosciences for Children, Rikshospitalet, Oslo University Hospital, Norway

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Highlights

- In CLN3 disease, tonic–clonic seizures are common at onset; focal seizures increase with age.
- Epileptiform discharges may evolve from focal to multifocal and bilateral with age.
- Combined generalized and focal epilepsies are characteristic of advanced CLN3 disease.
- Cardiac conduction abnormalities may mimic seizures.
- Paroxysmal sympathetic hyperactivity may be misdiagnosed as epileptic symptoms.

Abstract

Purpose

Juvenile neuronal ceroid lipofuscinosis (CLN3 disease) is the most common neurodegenerative disorder in childhood with survival until young adult age. Visual loss is followed by epilepsy, cognitive, neuropsychiatric, and motor symptoms. We have studied the evolution of electroencephalographic (EEG) and seizure characteristics.

Methods

Twenty-four patients were recruited via the Norwegian CLN3 disease parent association. Parents were interviewed. Medical records and EEG reports/recordings were collected. Electroencephalographic elements were classified according to Standardized computer-based organized reporting of EEG (SCORE). The evolution of EEG features along with

seizure types was assessed by testing the difference in proportions with standardized normal deviate comparing findings below and above 15 years of age.

Results

Mean age at study or death (n = 12) was 21.2 (10–39) years. Twenty-two patients had experienced seizures; the first was usually bilateral tonic–clonic (TC). Later, focal motor seizures frequently occurred, often with increasing multifocal and polymorphic features. Paroxysmal nonepileptic motor and autonomous symptoms were also suspected in several patients. Distinct myoclonic seizures were uncommon. In four patients, we identified episodes of bradycardia/sinus arrest. Electroencephalography showed progressive slowing of the background activity ($p = 0.029$). Focal epileptiform discharges were rare and mainly seen at age < 10. Combined multifocal and bilateral epileptiform discharges increased in adolescence ($p = 0.002$).

Conclusion

Seizure and EEG characteristics change with time in CLN3 disease. Tonic–clonic seizures are common at onset, and multifocal motor seizures increase with age. In contrast, focal epileptiform abnormalities are more common in childhood, compared to later multifocal and bilateral discharges. This seizure disorder belongs to the combined generalized and *focal epilepsies*. Paucity of myoclonic seizures does not warrant classification as a classic *progressive myoclonic epilepsy*. When attacks with only behavior arrest occur, cardiac conduction abnormalities should be considered.