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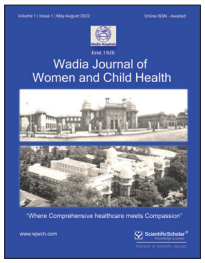
Wadia Journal of Women and Child Health



Case Report

Progressive myoclonus and neuroregression – a dreadful combination

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Received : 21 August 2022
Accepted : 04 November 2022
Published : 14 May 2023

DOI
10.25259/WJWCH_18_2022

ABSTRACT

Progressive myoclonic epilepsy (PME) is a gradually progressive neurological disorder characterized by the development of progressive myoclonus, ataxia, and cognitive impairment with other neurodeficits. There are a wide variety of PMEs, such as Lafora body disease (LBD), neuronal ceroid lipofuscinoses, Unverricht-Lundborg disease, myoclonic epilepsy with ragged-red fiber syndrome, sialidoses, dentato-rubro-pallidal atrophy, storage diseases, and some of the inborn errors of metabolism, among others. Although the modern genetic tests are helpful in discerning underlying etiology, the clinical differentiation is often possible with historical background and clinical examination. We report a case of PME, where we suspected LBD on basis of clinical history and examination, which was confirmed with skin biopsy and next-generation sequencing.

Keywords: Progressive myoclonic epilepsy, Lafora body disease, Stimulus sensitive myoclonus

INTRODUCTION

Progressive myoclonic epilepsy (PME)[1] is a heterogeneous group of neurological disorder presenting with progressive myoclonus along with neurological deterioration in the form of dementia, ataxia, movement disorders, and other systemic manifestations.[2] Various diseases have been grouped under PME, such as Unverricht-Lundborg disease (ULD), myoclonic epilepsy with ragged-red fiber, sialodosis, dentato-rubro-pallidal atrophy, neuronal ceroid lipofuscinosis (NCL), and Gaucher disease. Each of these individual disease entities have their distinct ages of onset, presentation, etiopathogenesis, and modes of progression. Thus, it is of utmost importance to recognize this syndrome and delve into the clinical history and examination findings so as to reach a possible etiological diagnosis. Further investigations would largely depend on this exercise. We present here a case of one of such PME, called Lafora body disease (LBD) and discuss clinical differentiation between various common types of PME.

CASE REPORT

Our patient was a 16-year-old boy, born out of third degree consanguineous marriage, third by birth order with normal pre-morbid status. He presented at 9 years of age with first episode

How to cite this article: Kaudinya S, Gawali V, Kulkarni S, Shah P. Progressive myoclonus and neuroregression – a dreadful combination. Wadia J Women Child Health 2023;2(1):38-40.

of a fever-triggered seizure in the form of right hemiclonic seizure with impaired awareness.

The child was apparently well for next 5 years with no such episodes thereafter. Later at 14 years of age, he developed generalized onset tonic–clonic seizure preceded by elemental visual auras, which progressively worsened over time.

Over the next few months, he also developed stimulus sensitive focal and generalized clonic seizures along with myoclonic jerks. During this period, the child progressively became emotionally labile, fearful, and socially withdrawn. He became non-ambulant after development of myoclonic drop attacks, which occurred multiple times in a day making him bed-bound eventually. Slowly, he also lost the ability to express himself in sentences and his communications reduced to sentences with few words. He also started showing difficulty in comprehending complex command and concepts. Memory remained unaffected.

There was no specific finding on examination which would point towards a diagnosis. In view of myoclonic epilepsy along with deterioration of intellectual and motor function, possibility of a PME was considered.

As the child presented in his adolescence and had, visual aura with seizures, and severe myoclonic epilepsy along with rapid neurological deterioration, LBD was suspected. MRI brain was normal. EEG was suggestive of generalized epileptiform discharges with occipital predominance. The child was treated with, phenytoin (6 mg/kg/day), brivaracetam (200 mg/day), perampanel (6 mg/day), clobazam (20 mg/day), lacosamide (8 mg/kg/day), and topiramate (4 mg/kg/day).

Skin biopsy revealed periodic acid Schiff positive polyglucosan bodies in eccrine glands consistent with diagnosis of LBD. Genetic analysis confirmed a homozygous mutation in exon 1 of NHLRC1 gene suggestive of myoclonic epilepsy of Lafora.

DISCUSSION

In any child presenting with severe myoclonic epilepsy with progressive deterioration, PME should be considered apart from other genetic syndromes. Age of onset may range from neonatal to adulthood. Juvenile-onset NCL has earlier age of onset at around 4–7 years while adult-onset NCL has later age of onset at around 40 years.[3] ULD occurs in late childhood, peaking at around 12–13 years, range is 8–15 years.[4] Myoclonic epilepsy with ragged red fiber (MERRF) and Gaucher disease have age of onset ranging from 10 to 40 years.[5] Age of onset in Lafora disease is 8–19 years, peak age of onset is 14–16 years.[6]

One should be having high degree of suspicion to correctly diagnose as every PME presents with different set of symptoms with peculiar electrophysiological and pathological findings.

At present, there are four most common PMEs, namely LBD, NCL, ULC, and Tay Sach's disease (TSD). Among them, LBD presents as early dementia with predominantly occipital lobe involvement as visual failure and occipital seizure, with giant stimulated sensory evoked potential (SSEP) and shows photosensitivity at high frequency. NCL usually presents in 1st decade of life with severe dementia, retinal degeneration, and optic atrophy, there are giant SSEP with hardly any seizure at low frequency photosensitivity. Patients with ULD have ataxia and myoclonus but preserved cognition and usually presents in 1st/2nd decade of life. It has giant SSEP with no seizure per se. TSD usually manifests in first 2 years of life and presents as startle myoclonus with cherry red spot as clinical pointer towards it. They have absent visual evoked potential. Clinical differentiation of these entities is necessary for appropriate diagnosis and evaluation. Genetic study is required to accurately diagnose the PME.

LBD is an autosomal recessive PME, with mutation in EPM2A (laforin) and EPM2B (malin) genes.[6] It is characterized by formation of abnormal glycogen, polyglucosans, which gets accumulated in brain, periportal hepatocytes, skeletal and cardiac myocytes, and in the eccrine as well as apocrine myoepithelial cells of sweat glands. Focal visual seizures are early manifestations – may present initially only as transient blindness or complex visual hallucination. EEG abnormalities often precede clinical symptoms and initially consist of almost normal or slowed background. They usually have action-sensitive and stimulus sensitive myoclonus, refractory seizure, psychosis, ataxia, and dysarthria. Subsequently, a rapidly progressive dementia with apraxia and visual loss sets in.

CONCLUSION

Progressive myoclonic epilepsy is a dreadful condition that presents with ataxia, movement disorder and epilepsy. Diagnosis is largely based on clinical suspicion along with characteristic EEG and MRI findings. Outcomes are disappointing even with treatment but newer advances and anti-oxidants are proving their much needed role in preventing the advancement of disease.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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