University Journal of Medicine and Medical Sciences

ISSN 2455-2852 Volume 2 Issue 4 2016

A CASE OF LAFORA BODY DISEASE

KANNAN BALAKRISHNAN

Department of Neurology,

MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract :

Lafora body disease is a rare autosomal recessive disease which is characterized bymyoclonus, seizures, progressive cognitive impairment and demonstration of Lafora bodies. It is also one of the differential diagnosis for progressive myoclonic epilepsy. Herein we are presenting 16 years old male who presented with refractory seizures and new onset myoclonic seizure with progressive cognitive decline. Investigations showed a normal MRI brain, normal CSF lactate, and pyruvate. CSF Anti measles antibody was negative. He had mild elevation of serum ammonia. EEG showed polyspike and wave discharge and Somatosensory evoked potential showed a Giant cortical potential. Axillary skin biopsy revealed Lafora Bodies and patient was dia nosed as Lafora body disease. This case highlights the importance of recognizing the syndromic approach in childhood seizures and for its rarity.

Keyword :

Lafora Body Disease, Myoclonus, Progressive Myoclonic epilepsy, Somatosensory evoked potential

INTRODUCTION:

Lafora body disease is a rare inherited autosomal recessive disease characterized by myoclonus, seizures, dementia and the presence of Periodic Acid Schiff (PAS) positive Lafora bodies in neurons, liver, skeletal muscles, heart, and sweat gland duct cells. It is more common in male. Onset is between 10 to 30 years of age with median age of 14 years.[1,2] Myoclonus with generalized seizure with progressive cognitive decline is usually present in all cases. Occipital seizures with visual phenomenon are present in one third of cases.[2] Some patients have behavioral changes. In EEG 95% have generalized background slowing, 85% have epileptiform discharge and some have focal discharge.[1,2] In SSEP giant cortical potential is seen in 25% of Lafora body disase.[1] MRI brain may reveal diffuse cortical atrophy. It is one of the causes for progressive myoclonic

epilepsy.[1] In Progressive Myoclonic Epilepsy (PME), Lafora Body disease constitutes 37%, Neuronal Ceroid lipofuscinosis 44%, MERRF 7%, Taysachs disease 7%. [1] We herein present an interesting case of myoclonic seizures which turned out to be a case of Lafora body disease.

CASE REPORT:

16 years old male was admitted in our institute, with chief complaints of recurrent seizures for past 12 years, inability to walk and tremulousness of entire body for past 4 months, reduced alertness and impaired consciousness for past two weeks. He was born of non-consanguinous parentage with preterm normal vaginal delivery with history of birth asphyxia in the form of not cried immediately after delivery and he was admitted in neonatal ICU for 3 weeks. All motor and language milestones were delayed. He walked with partial bending of knees. He also had delayed speech onset with speech disturbances in the form of dysarthria, siallorhoea. He was immunized fully. He was able to do his daily activities, took care of self and went to school on his own. Scholastic performance was reasonably good. At the age of 4 years there was history suggestive of measles. At 5 years of age(2001) he had frequent episode of generalized tonic clonic seizures which recurred every 6 months and he was started on anti epileptics, sodium valproate 200mg 1bd and phenobarbitone 30mg 1BD. At 7 years of age (2003) seizure frequency increased to once a month, in spite of good compliance. At the age of 14years (2010) he was stopped from school due to recurrent seizures and valproate was stopped and he was started on oxcarbazepine and levetiracetam. 1 year later his seizure frequency increased further and he was again put on sodium valproate controlled release 500mg 1bd, oxcarbazepine 300mg 1 bd , levetiracetam 500mg 1 bd , clobazam 20mg 1Hs. , Despite the multiple antiepileptics, seizure persisted and he developed new onset of symptoms in the form of tremulousness and jerkiness of all four limbs and trunk and could not walk, and fell down after few steps. Tremulousness was present in all four limbs in the form of gross jerky movements of proximal and distal joints, increased on standing and walking precipitated by seizure. His general daily activities slowly declined, became dependent on parents for all daily activities. Conscious level deteriorated over the last 2-3weeks and he was admitted with decreased level of consciousness. He also had history suggestive of cognitive decline, with decreased memory without any disturbance in cranial nerves, motor or sensory symptoms. He had occasional bed wetting. After adjusting the anti epileptics, his conscious level improved and he was following simple commands and answering questions. He was also able to tell the visual phenomenon in the form of colored circles appearing in one hemi field, preceding the seizure.

On Examination-Initially patient was drowsy. After adjusting anti epileptics his consciousness level improved. He was well built and well nourished, not cyanosed, not anemic, no clubbing**,** no neurocutaneous marker. He was a right handed individual and studied upto IX th standard. He was poorly cooperative for detailed examination. His limited higher mental function testing showed that he had poor attention, impaired language function in the form of decreased fluency, comprehension, repetition, naming and also difficulty in reading, writing and copying. His immediate, recent, remote memory were impaired. He was not attempting higher cognitive function examination.

Lobar function testing showed frontal lobe signs in the form of perseveration, not able to do rhythmic tapping and alternate sequencing, glabellar tap was non accommodative.Palmomental reflex was bilaterally present. Testing of parietal lobe showed difficulty in sensory localization and also difficulty in construction and dressing. Testing temporal lobe showed impairment of verbal and visual memory. Occipital lobe impairment in the form of color anomia and visual memory impairment was noted. Cranial nerves examination revealed difficulty in following objects. Pupil were equal reacting to light, Menace reflex was present. Other cranial nerves were normal including fundus. Testing spino motor examination showed normal bulk, tone, power. All deep tendon jerk were brisk with bilateral plantar extensor. Sensory examination could not be tested. Extra pyramidal system showed spontaneous and stimulus sensitive generalized synchronous predominantly negative myoclonus involving proximal joints of both UL and LL. Predominant action myoclonus evident on standing and walking was also noted which increased on walking few steps and he fell down. Investigations revealed normal blood Hb, complete blood count, differential counts, renal, liver parameters. Serum ammonia was mildly elevated. CSF pyruvate, lactate was normal and anti measles antibody titre was negative. MRI brain was normal. EEG showed a non periodic polyspike and wave discharges and SSEP showed a Giant Cortical potential. Axillary skin biopsy revealed Lafora bodies.

DISCUSSION:

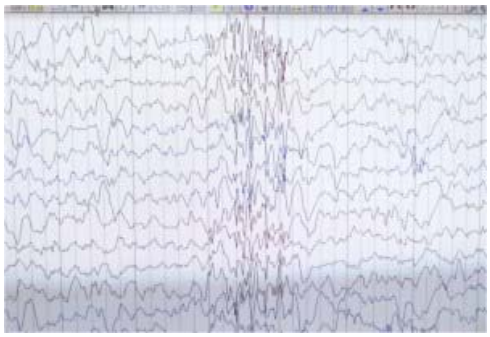
Our patient was initially diagnosed to have mental retardation with generalized seizures and was on polypharmacy with poor seizure control. Subsequent development of generalized stimulus sensitive myoclonus, occipital lobe seizures, and fresh cognitive decline suggested the possibility of Progressive Myoclonic Epilepsy.

The presence of Lafora Bodies in the axillary skin biopsy clinched the diagnosis of Lafora Body Disease. Lafora body disase is one of the differential diagnosis for Progressive Myoclonic Epilepsies which are characterised by myoclonic seizures, generalised tonic clonic seizures, progressive cognitive decline, ataxia and lastly dementia. Myoclonus in PME is typically fragmentary and multifocal which is precipitated by posture, action, or external stimuli such as sound, light, or touch.

LAFORA BODY DISEASE:

It was first described by Lafora and Gluelkin in 1911 which is characterised by GTCS, myoclonus, dementia, and Lafora bodies (periodic-acid–Schiff-positive intracellular polyglucosan inclusion bodies) found in neurons, skeletal muscle, heart, liver and sweat gland duct cells.[3] It is an autosomal recessive disorder and the mutation is in the EPM2A gene on chromosome 6q at locus 24.[4]The gene encodes laforin which cause glycogen synthase hyper function, contributing to the endoplasmic reticulum associated polyglucosan depositions. Most common age of onset is between 5 to 15 years.[1,2,3]Clinical course starts as generalized seizures and develops into different seizure types like myoclonus, occipital seizures with transient blindness and visual hallucinations, atonic, atypical absences and complex partial seizures. As the disease progresses, seizures become more intractable and status epileptics of any seizure type may occur. Progressive cognitive decline, ataxia and dysarthria may appear early. Usually ataxia is not demonstrated due to severe Myoclonus.

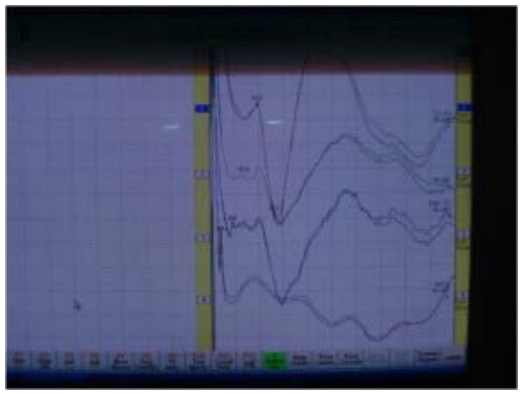
Later patients are disabled with continuous myoclonus. Most patients die within 10 years of onset. The presence of Lafora Bodies in the axillary skin biopsy clinches the diagnosis of Lafora Body Disease. Treatment for Lafora's disease is mainly palliative. Antiepileptic drugs, especially sodium valproate is preferred for the treatment of both myoclonic and generalized seizures. In future Stem-cell therapies may allow replacement of the defective protein. Laforin replacement therapy using Neutral Pegylated Immunoliposomes is under investigation.



EEG showing Polyspikes

CONCLUSION:

This case is presented to highlight the importance of recognizing the syndromic presentation of seizures in any patient with intractable seizures since childhood and also for its rarity.



GIANT SSEP

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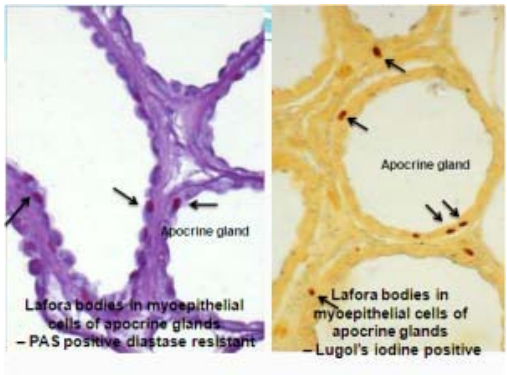

Lafora body in Axillary Skin Biopsy