

An Interesting Case of Progressive Myoclonic Epilepsy – Lafora Disease

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ABSTRACT

Lafora disease is a fatal autosomal recessive genetic disease characterized by recurrent seizures and a decline in intellectual function. The symptoms of the disease usually appear in late childhood or adolescence and worsen with time. It causes seizures, myoclonus, muscle spasms, difficulty in walking, dementia and eventually death. The disease is characterised by the presence of inclusion bodies known as Lafora bodies, within the cytoplasm of the cells of the heart, liver, muscle and skin. There is currently no therapy that has proven effective against disease progression. Most patients with this disease do not live past the age of twenty-five.

KEY WORDS : Lafora disease, Seizures, Myoclonus

Case Report

An 18 year old girl, born of non-consanguineous marriage, with normal developmental mile stones, presented with seizures since 3 years duration. Semiology of seizures was generalized. Her seizure frequency was 3 seizures per month for first 3 months. Antiepileptic medications levetiracetam at 1 gm/day was started at Cuddalore (TN) and there was no seizures for 6 months. EEG – epileptiform activity, C.T. Brain revealed a

normal study and basic lab investigations were normal.

6 months later at school, she developed one episode of visual obscuration for 3 minutes which was predominantly of negative origin (black discoloration), followed by unilateral headache of moderate intensity. Girl was brought to us and we converted levetiracetam to sodium valproate at 600 mg/day.

She developed rapid weight gain, tremulousness and seizures of generalized nature at a frequency of 1-2 per month. For seizures, clobasam at 20 mg/day was added. Due to weight gain, sodium valproate was tapered and stopped. Levetiracetam was restarted again at 1.5 gm/day.

Her seizure frequency of generalized nature increased to 2-3 attacks per month and levetiracetam dose was increased to 2gm/day and clobasam was made 30mg/day.

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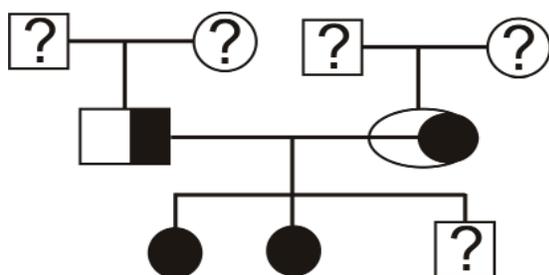
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MRI brain with volumetric analysis was done which revealed cerebellar atrophy.

EEG-diffuse slowing, polyspike and intermittent sharp and wave discharges, without lateralization. T₃, T₄ and TSH were normal.

Her younger sister also started developing similar complaints 1 year back. She has seizures, multifocal myoclonus sensitive to light and with cognitive disturbances. Neither their parents nor grand-parents had similar complaints.

Pedigree chart:



Her seizures did not abate, maintained a frequency of 2/month. Girl dropped out of school, failed her tenth board exams. Lost motivation, counseling sessions did not help. Stopped going outside and kept to herself. Neuropsychological evaluation was suggestive of bilateral frontal and temporal lobe dysfunction. Her cranial nerves, including fundus was normal. Spino motor system was normal.

Involuntary movement in the form of Multifocal myoclonus was present and the myoclonus was stimulus sensitive being sensitive to touch, light and sound. Later she developed difficulty in walking. At present she is confined to bed.

After the clinical examination the girl had following problems:-

- Seizures (generalized, medically refractory)

- Multifocal myoclonus (the myoclonus was stimulus sensitive to touch, light and sound)
- Cognitive disturbance
- One episode of visual obscuration
- Walking difficulty

As myoclonus and dementia were prominent a diagnosis of PME was made and the following differentials were considered:-

1. Unverricht Lundborg Disease (ULD).
2. Lafora disease (LD).
3. Mitochondrial disorder (MD).
4. Sialidosis (SD).
5. Neuronal ceroid lipofuscinosis (NCL).
6. Subacute Sclerosing Panencephalitis (SSPE)

Investigations

CBC and Chest X ray PA were normal. LFT, Serum ammonia, Renal profile, HIV, Serum VDRL, T₃, T₄, TSH, Anti thyroid antibodies were within normal limits. ANA, RA factor was found to be normal. Ultrasound abdomen showed a normal sonological report. EEG was repeated; it showed marked slowing with sharp wave discharges. Sharp wave discharges intensified on photic stimulation. No periodic complexes. VEP and SSEP was normal. CSF analysis was normal (protein -55, glucose - 60, chloride- 750, no cells) and measles antibody was negative. SKIN BIOPSY was positive for LAFORA BODIES. Muscle biopsy did not reveal any evidence of mitochondrial abnormality.

Discussion and Conclusion

Among the 6 differentials considered:

- ULD[1] is clinically not associated with dementia.

- Adult onset NCL[1] will have MRI changes in the basal ganglia and optic atrophy.
- Sialidosis is associated with younger age presentation and cherry red spots in eyes.
- Measles antibody was negative. So, SSPE was ruled out

Finally the differentials were mitochondrial disease and Laforas disease. Hence muscle biopsy and skin biopsy was ordered. The skin biopsy was positive for Lafora disease. Hence a diagnosis of Lafora disease was made.

Lafora disease [2],[3] is an inherited progressive myoclonic epilepsy[1],[4] which most commonly starts as epileptic seizures in adolescence. Most cases of Lafora disease are caused by mutations in one of two known genes: EMP2A and EMP2B. Both genes are located on chromosome 6 and are inherited in an autosomal recessive manner. A few cases of Lafora disease are caused by unidentified genes also.

A child with Lafora disease has a normal first decade of life and the symptoms of dementia, myoclonus, seizures and accumulation of Lafora bodies in nerve, skin, muscle and skin cells. Lafora bodies can be identified with PAS (periodic acid Schiff) staining histologically.

The prevalence of Lafora progressive myoclonic epilepsy is unknown. Although the condition occurs worldwide, it appears to be most common in Mediterranean countries including Spain, France, Italy, parts of Central Asia, India, Pakistan, North Africa and Middle East.

Lafora disease causes myoclonic seizures, muscle spasms, difficulty walking, dementia, and eventually death. There is currently no therapy that has proven effective against disease progression. Therapy is primarily palliative

and aimed at reducing seizures. However the symptoms worsen as the adults grow older and many individuals with the disease do not survive beyond the age of twenty-five.

Reasons For Presenting This Case:-

- Myoclonic seizures might present late in the course of illness
- Abnormal movements like myoclonus might give a clue for the diagnosis of epileptic encephalopathy.
- Importance of following up the case
- Rarity of the disease
- Discuss the practical approach to PME

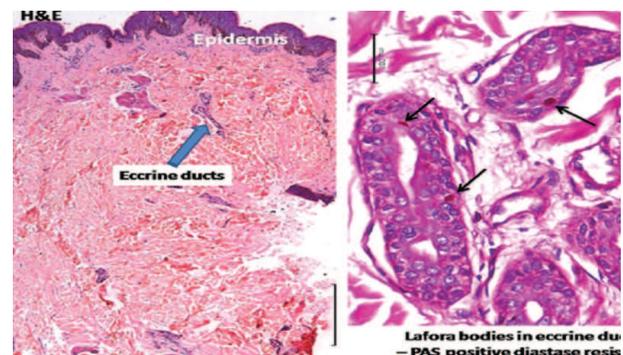


Fig. 1 & 2 Histological view of Lafora bodies

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