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**Case Report**

# Lafora disease in a teenage girl with epilepsy

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**ABSTRACT**

Lafora disease is rare group of progressive myoclonic epilepsies, worldwide. It is more common in children and adolescents and is genetic, glycogen metabolism disorder. It has Autosomal recessive (AR) inheritance. Lafora bodies are inclusion bodies within cytoplasm of cells in heart, liver, muscle, and skin. Disease clinically has triad of seizures, myoclonus, and dementia. Lafora disease is a neurodegenerative disorder. In the absence of laforin function long glucose chains in specific glycogen molecules extrude water form double helices and drive precipitation of molecules which accumulate into Lafora bodies. That leads to impairment in development of cerebral cortical neurons. Clinical on set of disease is range in between 8-19 years of age and peaks around 15 years of age. In our case, 16-year-old girl presented to emergency of tertiary care hospital with complain of episode of convulsions 40 minutes before admission. She is known case of generalized tonic-clonic seizures for past two years. Axillary skin biopsy on H&E staining showed pilosebaceous glandular unit with peri-adnexal and perivascular infiltrate. PAS-D stain showed round, globular, tiny PAS positive material noted within sweat glands. MRI brain was suggestive of right vertebral artery partial occlusion

**Keywords:** Epilepsy, convulsions, Lafora disease, PAS-D.

## INTRODUCTION

Lafora disease is the principal form of adolescence-onset progressive myoclonus epilepsy. Lafora disease is an autosomal recessive first described in 1911.[1] It is particularly frequent in Mediterranean countries (Spain, Italy, France), Northern Africa, the Middle East. Most patients are completely normal in childhood, Earliest symptoms are headaches, decline in school performance, spontaneous and induced myoclonus, and convulsive seizures.[2] Neuropsychiatric symptoms, such as behavioural changes, depression and apathy, are also often present. Initial symptoms are followed by rapidly progressing dementia, refractory status epilepticus, psychosis, cerebellar ataxia, dysarthria, mutism, and respiratory failure.[3] All these symptoms worsen over time and within 5 years become intractable which lead to death within about a decade. Convulsive seizures need not be frequent but are never fully controlled.[4] Pathologically, Lafora disease is characterized by increased glycogen content in tissues and presence of malformed glycogen molecules called polyglucosans. The latter accumulate over time into masses called Lafora bodies. Mutations found in LD is the EPM2A or EPM2B (NHLRC1) genes, yet very incompletely understood pathway regulating glycogen metabolism.[5]

## CASE REPORT

A 16-year-old girl presented to emergency of tertiary care hospital with complain of episode of convulsions, 40 minutes before admission (Figure 1). She is known case of generalized tonic- clonic seizures (GTCS) since past two years. She is on treatment of sodium

valproate, levetiracetam and clobazam for GTCS for two years.

**Figure 1- Clinical photo**

She became bedridden, became totally dependent in activities of daily living, and lost the ability to speak since past one year. Her MRI brain was suggestive of right vertebral artery partial occlusion.

Her routine blood test blood tests were unremarkable. Serum B12, copper and folate were within normal range. The other serological tests for SLE, HIV, hepatitis B and hepatitis C were negative. The results of blood work for lysosomal enzymes (Hexosaminidase, Alpha-galactosidase, Arylsulfatase A, gluco- cerebrosides were normal.

On electroencephalogram (EEG), there were continuous generalized spikes and background showed diffuse slowing in the range of theta and delta waves discharges over both hemispheres.

Received axillary skin tissue bit measuring 0.4x0.2x0.2 cm in size. Histopathology: H& E-stained skin section showed epidermis, dermis and separated fragment subcutis. Epidermis is unremarkable. Dermis showed increased density of pilosebaceous glandular unit with peri-adnexal and peri-vascular infiltrate. Rest of dermis was fibro collagenous. Vasculitis was not seen. Subcutaneous is unremarkable (Figure 2). In PAS-Diastase stain: Round, globular, tiny PAS-D positive material was noted within sweat glands (Figure 3).

**Figure 2- Microphotograph of skin biopsy showing pilosebaceous glandular unit with peri-adnexal and perivascular infiltrate (H&E, X100)**

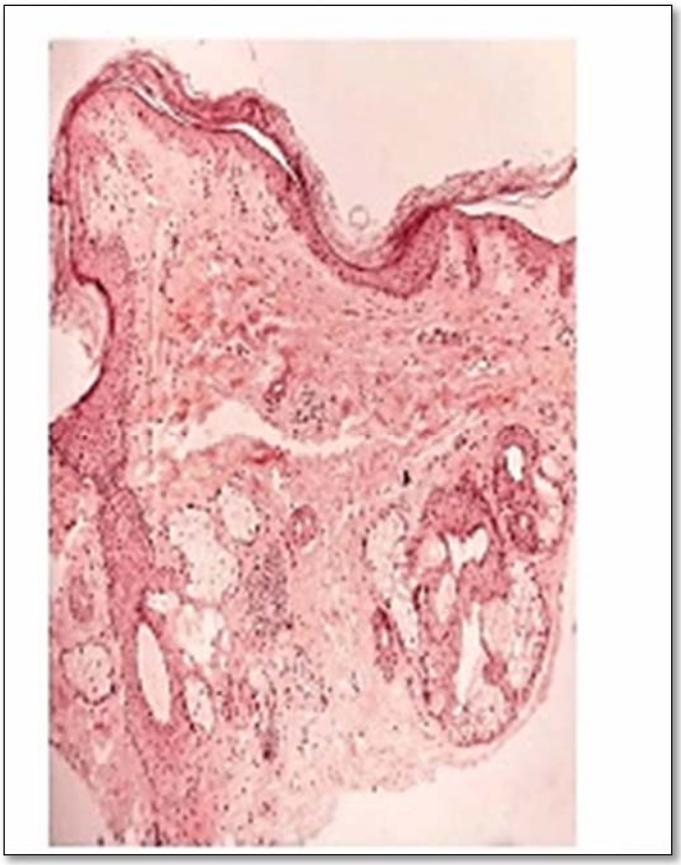
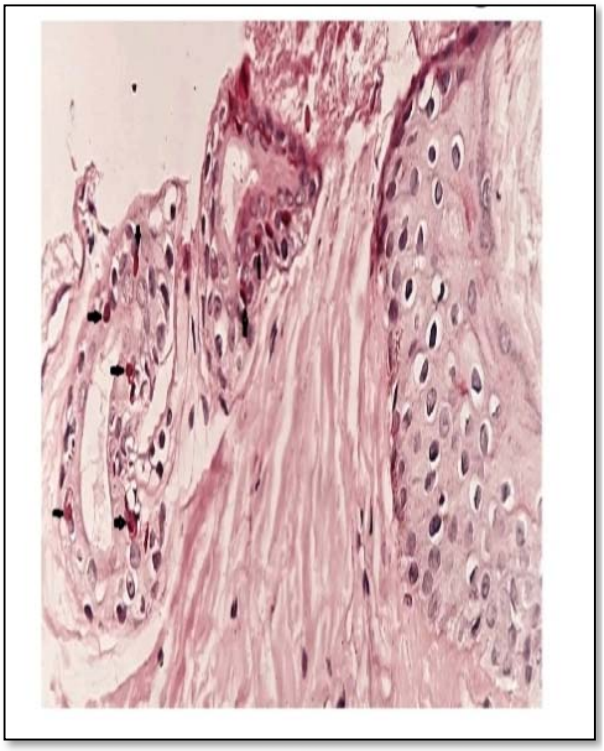


**Figure 3- Microphotograph of skin biopsy, arrows showing round, globular, tiny PAS-D positive inclusions within sweat glands (PAS-D, X400)**



History of epilepsy, increased pilosebaceous glandular unit, dermal mononuclear infiltrate, PAS-D positive material noted in the sweat gland was confirmatory of Lafora disease. Such PAS-D positive inclusions are associated with poor prognosis in such epileptic adolescents

## DISCUSSION

In Lafora disease, symptoms start in early adolescent age & symptoms progress as time passes. In few cases at age of five years symptoms present as a learing disorder. In previously healthy adolescents lafora disease can be appear in future. After onset of symptoms death can commonly occur within ten years. [6]

Due to the frequency of seizures in lafora disease behaviour changes symptoms are commonly associated. Lafora disease have brain changes that cause confusion, impaired judgement, depression, speech difficulties, decline in intellectual function and impaired memory. If areas of the cerebellum are affected by seizures, it is common to see problems with speech, coordination, and balance in Lafora patients.[7]

Condition mostly begins with epileptic seizures with incestuous relationships. The disease is named after Spanish neuropathologist, “Gonzalo Rodriguez Lafora (1886-1971)”. Due to mutations in either EPM2A Gene or NHLRC1 (EPM2B) gene, these proteins ubiquitinate the protein targeting to glycogen and glycogen synthase for proteasomal degradation. These lead to characteristic accumulation of polyglucans .[8]

Lafora bodies seen in light microscopy of skin biopsy when studied in accordance with appropriate clinical data are diagnostic for Lafora disease. A characteristic Lafora body is periodic acid-Schiff (PAS) positive & diastase-resistant. Lafora bodies are free-lying & located mainly perikaryon and large pyramidal cells of the third and fifth layers of the cerebral cortex. Lafora bodies also present in eccrine and apocrine sweat duct cells and the myoepithelial cells of the secretory acini of the apocrine sweat glands, like in our case.Skin biopsy from the axilla is preferable and diagnostic because PAS-positive inclusion bodies can be more easily detected.[9]

The presence of Lafora bodies alone, independent is not diagnostic. Lafora bodies may be seen in diseases such as: ALS, type 4 glycogen depot disease, double athetosis and adult polyglycosan body disease whereas similar polyglycosan bodies can also be seen in the normal brain aging process as corpora amylacea.

Antiepileptic drugs such as sodium valproate help in both generalized seizures and myoclonic seizures. Social and psychological management is of equal importance. Death occurs within 4–10 years after onset. The majority of cases die after six years of the onset of symptoms .[10]

Non sense mutations in lafora PME is identifies by genotyping so genotyping is more important in lafora disease. Report suggest drug such as gentamycin can be use in correction of nonsense mutation in mices with lafora disease. Compared to costlier Genotyping, affordable axillary skin biopsy seems to be the most reliable and least aggressive method for demonstrating

the presence of Lafora disease.Electro-microscopic observation shows that the PAS positive materials were made of numerous glycogen granules. [8-10]

## CONCLUSIONS

History of epilepsy, increased pilosebaceous glandular unit, dermal mononuclear infiltrate, PAS-D positive inclusion material noted in the sweat gland was confirmatory of Lafora disease. Such PAS-D positive inclusions are associated with poor prognosis in such epileptic adolescents. Despite advances in the genetics of Lafora disease, skin biopsy always a primary diagnostic modality. Axillary skin is advised for biopsy due to more density of sweat glands.

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