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Case Report

When can a skin biopsy reveal Lafora disease

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ABSTRACT

Lafora disease (LD) is a rare and particularly severe form of progressive myoclonic epilepsy (PME). It is an autosomal recessive hereditary disorder, with the responsible gene recently localized to chromosome 6q23-27. It is characterized by the onset, between the ages of 6 and 19, of generalized seizures followed by myoclonus. A major intellectual decline develops rapidly and progressively, eventually leading to dementia. Histological examination is essential for confirming the diagnosis of LD. The most practical procedure is a skin biopsy performed in the axillary region, allowing visualization of PAS positive inclusions within the excretory duct cells of the sweat glands-findings that are consistent with Lafora bodies. We report a clinical case of LD in a 16 years old adolescent girl and discuss the diagnostic challenges associated with this condition.

Keywords: Progressive myoclonic epilepsy, Axillary skin biopsy, Lafora bodies, Periodic acid-Schiff

INTRODUCTION

Lafora disease (LD) is a rare autosomal recessive genetic disorder caused by a defect in glycoprotein metabolism.[1] It manifests as PME, which should be suspected in adolescents presenting with an early combination of myoclonus, occipital partial seizures, and severe progressive cognitive decline. Electroencephalogram (EEG) findings are characteristic, and the diagnosis is confirmed through histological examination, which reveals Lafora bodies within the sweat glands of the axillary region.[2]

CASE REPORT

A 16 years old girl, born to healthy parents with a history of first degree consanguinity, had been followed in the Neurology department since the age of 12 for generalized tonic-clonic and myoclonic seizures resistant to antiepileptic medications, evolving in the context of progressive cognitive decline. Neurological examination revealed impaired comprehension and difficulty executing commands. The EEG was consistent with myoclonic epilepsy, showing a slowed background activity. Cerebrospinal fluid (CSF) analysis and other biological workup were normal. Brain MRI showed widening of cortical sulci as well as the ventricular enlargement.

The diagnosis of LD was strongly suspected based on the combination of typical clinical features, their progressive nature, and neurophysiological findings. A skin biopsy, performed by dermatologists in the axillary region, revealed intracytoplasmic granular inclusions within the epithelial cells of apocrine sweat glands. These inclusions stained positively with periodic acid-Schiff (PAS) and were consistent with Lafora bodies. This histological evidence confirmed the diagnosis of LD.

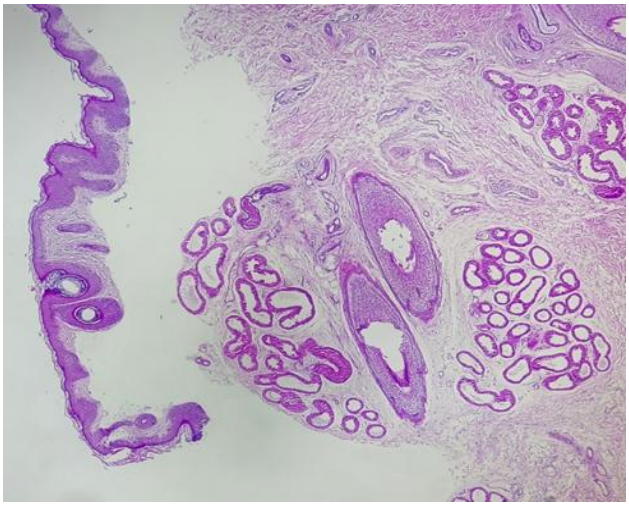

Figure 1: Histological section of skin tissue demonstrating apocrine sweat glands and hair follicles stained with HES.

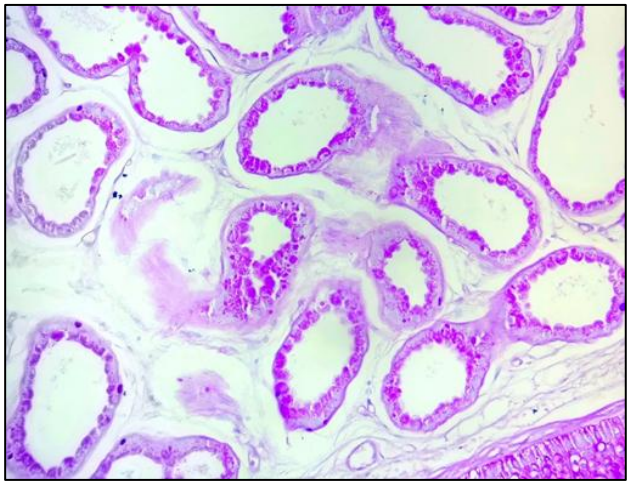

Figure 2 : Intracytoplasmic granular inclusions observed in the apocrine gland cells, positive for PAS staining.

DISCUSSION

LD is a particularly severe form of PME. Its distribution is worldwide, but it is more frequently observed around the Mediterranean basin. Its prevalence is estimated at less than 1 in 1,000,000 individuals.[1] It is an autosomal recessive hereditary disorder. Genetically, the disease is heterogeneous and, in approximately 80% of cases, involves a mutation in the EPM2A gene located on chromosome 6q23-27, which encodes the protein tyrosine phosphatase known as laforin. A second, less common familial variant accounts for 13-20% of cases and is associated with a mutation in the EPM2B locus (on 6q22), which encodes an ubiquitin ligase responsible for the degradation of laforin. Laforin is involved in regulating intracellular metabolism, and its dysfunction leads to the accumulation of polyglucosans, which have a neurotoxic effect.[3]

Clinically, the first symptoms usually appear between the ages of 6 and 19, presenting a typical PME picture, characterized by generalized tonic-clonic or clono-tonic-clonic seizures, severe myoclonus at rest and with movement, and occipital partial seizures accompanied by transient blindness. A rapidly progressive major cognitive decline then becomes the predominant feature and is often associated with severe depression.[4] This initial asymptomatic period is a key element in diagnosis, as observed in our patient.

EEG abnormalities are characteristic, typically showing a progressive slowing of the background rhythm, which worsens over time, and in about half of the cases, is associated with diffuse polyspike discharges, either isolated or in bursts.[1]

The diagnosis of LD is confirmed by identifying a glycoprotein storage in the form of Lafora bodies, which resemble normal corpora amylacea found in the brains of elderly individuals. These bodies are round, variable in size, and may appear isolated or grouped. The most typical ones exhibit a concentric structure with a basophilic central core and a radially striated, clearer periphery.[5] Lafora bodies can be found in multiple organs including the brain, heart, liver, skeletal muscle, and sweat glands.

The most commonly used diagnostic procedure is a skin biopsy performed in the axillary region, which allows identification of eosinophilic inclusions (PAS-positive and PAS-diastase-resistant) in the ductal cells of the sweat glands. These findings are consistent with Lafora bodies.[6]

Differential diagnoses depend on the disease stage. In early stages, juvenile myoclonic epilepsy or other idiopathic forms may be considered. In the established phase, the main differential diagnosis is Unverricht-Lundborg disease, while in the late phase, all causes of PME must be considered.[7]

Treatment of LD is purely symptomatic, mainly based on antiepileptic drugs targeting seizures and myoclonus. Psychological support is also critically important for both the patient and their family.[8]

In the absence of curative treatment, patients become bedridden due to the intensity of myoclonus and the frequency of seizures. Death usually occurs between 2 and 10 years after symptom onset, with a median survival of about 5 years, often due to status epilepticus and in a cachectic state.[1,9]

CONCLUSION

LD belongs to the group of progressive myoclonic epilepsies. However, it presents with distinct clinical and evolutionary features, notably resistance to antiepileptic drugs and progressive cognitive deterioration. As

highlighted in our case, axillary skin biopsy performed by the dermatologist to search for Lafora bodies is a key diagnostic tool that confirms this neurological disorder.

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