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Case Report

Lafora disease: A rare case report

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ABSTRACT

Lafora disease is an autosomal recessive disorder characterized by seizures, myoclonus, and progressive intellectual deterioration leading to dementia. The gene locus has been mapped to chromosome 6q23-27. Diagnosis often involves demonstrating Lafora bodies, typically confirmed through axillary skin biopsy showing PAS positive inclusion in the cells of the sweat ducts. It typically begins in adolescence and worsens over time, leading to significant disability and early death. It's indeed a challenging diagnosis, especially given its rarity and complex presentation. We present a case of Lafora disease diagnosed in a 15-year-old man.

1. Introduction

Lafora disease is a rare autosomal recessive disorder characterized by progressive myoclonic epilepsy, which involves myoclonus, focal-generalized seizures, and progressive dementia. Its rarity and severe manifestations make it a challenging condition to manage.[1–3] Lafora disease was initially described as a form of progressive myoclonic epilepsy by Lafora and Gluech in 1911.[4] The presence of Periodic Acid-Schiff (PAS) stain positive spherical inclusion bodies is considered diagnostic for Lafora disease.[1,3,5] This histological feature is crucial for confirming the diagnosis and distinguishing it from other forms of epilepsy and neurodegenerative disorders. In this article, we present a case of a 15 year-old male presented with generalised tonic clonic seizures, uprolling of eyes, jerky movements in all 4 limbs and cognitive dysfunction.

2. Case History

A 15 years old male was admitted due to complaints of tonic clonic movements of all 4 limbs with uprolling of eyes and frothing from mouth with difficulty in walking in form of imbalance and jerky movements in all 4 limbs. Past history of 1^{st} episode of seizure at the age of 3 years during febrile illness and 2^{nd} episode at the age of 10 years. He had history of multiple seizure types in the form of generalised tonic clonic seizures (GTCS), myoclonic jerks and occasional right focal seizure along with cognitive decline and ataxia. His EEG showed multiple spike and wave with background slowing. The absence of gross anatomical or pathological abnormalities on brain MRI and normal routine blood, urine, and biochemical tests can make diagnosing Lafora disease more challenging. However, the clinical presentation still warrants further investigation, including specialized tests such as genetic testing or skin biopsy to look for the characteristic inclusion bodies.

Left axillary skin biopsy done and tissue sent for histopathological examination.

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3. Result

3.1. Gross examination

Specimen consist of single skin covered whitish tissue portion measuring 0.5 cm.

Figure 1: Gross examination of left axillary skin biopsy

3.2. Microscopic examination

Serial section from left axillary skin biopsy shows unremarkable epidermis with sufficient eccrine and apocrine glands. Section stained with PAS and PAS Diastase resistant, show intracytoplasmic polyglucosan inclusion bodies.

Histological findings are suggestive of LAFORA BODIES.

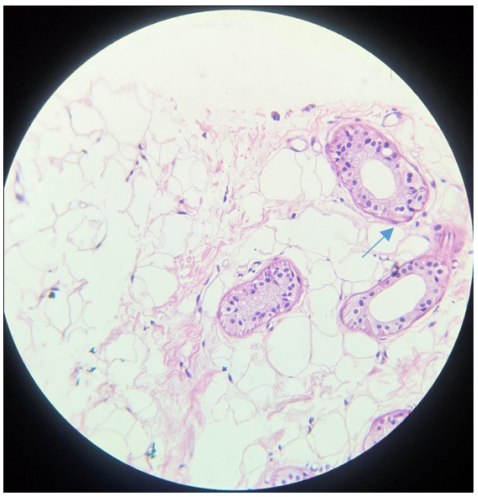

Figure 2: The figure shows intracytoplasmic spherical inclusions in the sweat gland duct (Hematoxyline and Eosin, 40X)

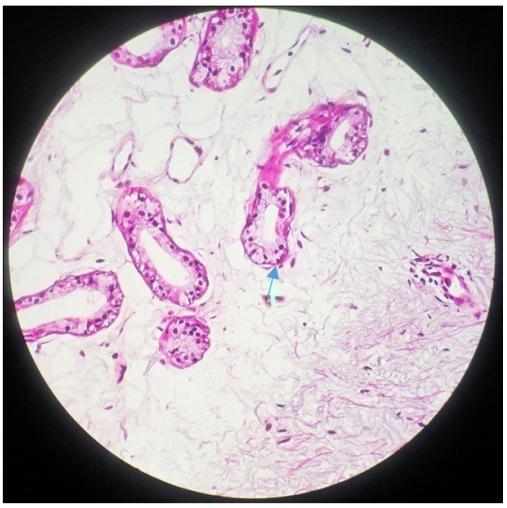

Figure 3: The figure shows Periodic Acid- Schiff stain highlight the inclusion. (PAS, 40X)

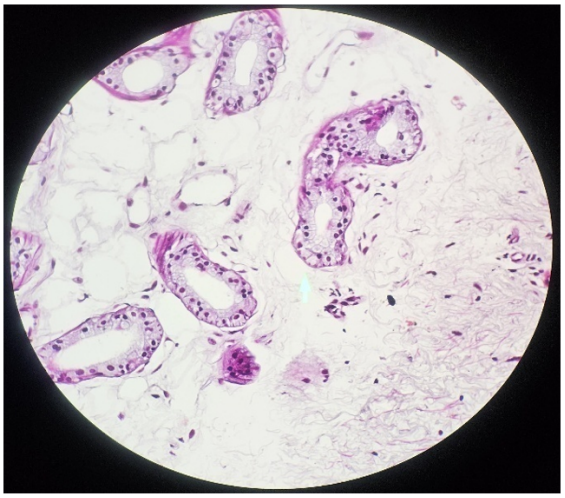

Figure 4: The figure shows inclusions are resistant to Periodic Acid-Schiff with diastase. (PAS-D,40X)

4. Discussion

Lafora bodies are a hallmark of Lafora disease when observed in skin biopsy samples, especially when correlated with clinical data. Their presence supports the diagnosis of Lafora disease, a rare, progressive form of epilepsy characterized by the accumulation of abnormal glycogen-like structures in cells. Performing a skin biopsy from the axillary region can be valuable in cases where Lafora disease is suspected as part of the clinical presentation. The presence of Lafora bodies in the biopsy, along with other clinical findings, can aid in confirming the diagnosis of Lafora disease. Electron microscopic evaluations have revealed that Lafora bodies are primarily composed of

complex glucose molecules, suggesting a high content of polyglycosan, which are glucose polysaccharides.[1] This composition further characterizes the unique nature of Lafora bodies and their association with Lafora disease. Mutations in the genes EPM2A (located on chromosome 6q24), EPM2B (located on chromosome 6q22.3), and PRDM8 have been implicated in causing the accumulation of polyglycosans, leading to the formation of Lafora bodies.[2] These genetic mutations are key factors in the pathogenesis of Lafora disease.

Despite advances in understanding the genetic basis of Lafora disease, its exact etiology remains unknown.[6] and most of these cases present with seizure and develop mental decline in the later course of disease.[7] In the present case also, the patient was presented with seizure and progressively developed the cognitive decline. The EEG showed multiple spike and wave with background slowing.

The identification of PAS-positive diastase-resistant polyglucosan cytoplasmic inclusion bodies in biopsy samples from various tissues, including the brain (axons and astrocytes), liver, skeletal muscle, and axillary skin, can confirm the clinical suspicion of Lafora disease. These inclusion bodies are characteristic histopathological features associated with the disease and provide definitive diagnostic evidence when observed in biopsy specimens from relevant tissues.[8]

A skin biopsy, particularly from the axillary region, is often preferred due to its less invasive nature compared to biopsies from other tissues like the brain or liver. Additionally, the axillary region is chosen because it contains a high density of sweat glands, which increases the likelihood of detecting Lafora bodies, aiding in the diagnosis of Lafora disease.[7] While the presence of PAS-positive diastase-resistant polyglucosan cytoplasmic inclusion bodies is strongly suggestive of Lafora disease, similar inclusions can be observed in other conditions as well. Therefore, a comprehensive clinical evaluation along with other diagnostic tests is essential to differentiate Lafora disease from other disorders that may exhibit similar histopathological findings.

These inclusions are not specific for Lafora disease, as similar inclusions can also be seen in other conditions like in normal aging, Type IV glycogen storage disorder, arylsulfatase A pseudodeficiency, amyotrophic lateral sclerosis and motor neuron disease.[4] One of the normal features of aging is corpora amylacea, which also resembles the Lafora bodies, but it is not found in neuronal structures.[9]

In the context of considering conditions related to Lafora bodies, the following should be considered in the differential diagnosis:

1. Subacute sclerosing panencephalitis (SSPE)
2. Progressive myoclonic ataxia (PMA)
3. Progressive encephalitis (including GM2 gangliosidosis, Niemann-Pick disease, and Gaucher disease)
4. Juvenile myoclonic epilepsy
5. Nonketotic hyperglycemia

Absolutely, the clinical history plays a crucial role in narrowing down the differentials. It provides valuable clues about the patient's symptoms, progression of the disease, family history, and any relevant exposures or comorbidities. This information helps guide further diagnostic investigations and ultimately leads to a more accurate diagnosis.

Antiepileptic drugs, particularly sodium valproate, are often preferred for the treatment of both myoclonic and generalized seizures due to their broad-spectrum efficacy. They can effectively control a variety of seizure types, including myoclonic seizures, absence seizures, and generalized tonic-clonic seizures. Henceforth, the diagnosis necessitates continuous, thorough genetic and psychological counseling and assistance.[10] A significant portion of instances result in mortality within six to ten years post symptom onset, frequently amidst status epilepticus, leading to aspiration pneumonia.[4,6,7,9,11]

5. Conclusion

Frequently, the skin biopsy may lack specific histomorphology. Nonetheless, an attentive pathologist should recognize these inclusions if present in a biopsy, essential for confirming the diagnosis. The prognosis for Lafora disease is grim, often resulting in patient mortality. However, early suspicion and axillary skin biopsy can facilitate promt diagnosis and intervention, potentially extending the lives of these young patients.

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7. Conflict of Interest

No competing interest.

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