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Case Report

Axillary Skin Biopsy as an Early Diagnostic Tool in Lafora Disease: A Case Report

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ABSTRACT

Lafora disease is a rare autosomal recessive form of progressive myoclonic epilepsy that usually begins during adolescence. Early diagnosis is often difficult because neuroimaging may be normal, and clinical features can overlap with other causes of refractory seizures. We report the case of a 16-year-old male who presented with recurrent generalized seizures, myoclonus, and a significant family history of similar illnesses. Routine radiological investigations were unremarkable. Histopathological examination of an axillary skin punch biopsy revealed numerous PAS-positive intracytoplasmic inclusions within apocrine gland cells, consistent with Lafora disease. This case highlights the diagnostic value of an axillary skin biopsy as a simple, minimally invasive method for demonstrating characteristic Lafora bodies, particularly in the early phase when clinical suspicion is high, and imaging findings are nonspecific.

Key words: apocrine glands, epilepsy, myoclonic epilepsy, intracytoplasmic inclusions, Lafora disease, PAS staining, skin biopsy

INTRODUCTION

Lafora disease, also known as Lafora progressive myoclonic epilepsy (MELF), is a rare form of progressive myoclonic epilepsy with an estimated prevalence of fewer than four cases per million individuals worldwide. [1] It typically begins during adolescence and gradually leads to severe neurological decline. [2] Affected individuals often present with recurrent generalized seizures, myoclonus, and progressive cognitive impairment. [3]

The disorder is inherited in an autosomal recessive pattern and results from mutations in the *EPM2A* or *EPM2B* (also known as *NHLRC1*) gene. [4] These mutations disrupt normal glycogen metabolism, causing abnormal accumulation of insoluble, carbohydrate-rich inclusions known as Lafora bodies. [5] These inclusions are found in various tissues, most consistently within neurons and duct cells of sweat glands. [6] Neuroimaging studies may appear normal in the early phase of the illness, making early diagnosis difficult. Therefore, a tissue biopsy showing characteristic PAS-positive inclusions plays an important role in confirming the diagnosis. [2]

Skin biopsy, particularly from areas such as the axilla, has emerged as a practical and reliable method for confirming the diagnosis. [6] Early recognition is crucial because the condition is progressive and associated with significant morbidity and early mortality. [2]

CASE REPORT

A 16-year-old male, known to have a seizure disorder, presented to the pediatric outpatient department of Raipur Institute of Medical Sciences, a tertiary care hospital, Raipur, India, with recurrent convulsions for the past year. He experienced four episodes in the last month, each characterized by frothing from the mouth, loss of consciousness lasting approximately 10 minutes, and tonic extension of the limbs. The patient also complained of pain in both ankle joints. The patient had a poor appetite for the past year. He had been hospitalized 2 years earlier for bilateral foot pain. The family history was significant, with two siblings reported to have died with similar symptoms. On examination, the patient was conscious between episodes, with normal vital parameters. There were no focal neurological deficits. Cognitive slowing was noted on clinical assessment.

Radiological studies

Ultrasound of the whole abdomen showed no significant abnormalities. Non-contrast computed tomography of the head revealed no intracranial pathology. Electroencephalogram (EEG) and magnetic resonance imaging of the brain were unremarkable.

In view of adolescent-onset progressive seizures, positive family history of similar illness, and unremarkable neuroimaging and EEG, a progressive myoclonic epilepsy was suspected, with Lafora disease as a differential consideration. As an axillary skin biopsy is a minimally invasive investigation with a high diagnostic yield for Lafora bodies in apocrine glands, a decision was made to perform bilateral axillary punch biopsies to achieve histopathological confirmation.

Histopathology

Skin punch biopsies were obtained from both axillae and submitted for histopathological examination.

Gross findings

Two containers labelled right and left axilla, each containing a single skin punch biopsy measuring approximately 0.5 cm.

Microscopic findings

The epidermis and adnexal structures were examined in detail. The apocrine glands showed numerous well-defined, homogenous, amphophilic, round to ovoid bodies within the cytoplasm of the acinar cells. These inclusions were predominantly located in the basal portion of the cells, often adjacent to the nucleus, and were surrounded by a distinct, clear halo (**Figure 1A, B**). These intracytoplasmic inclusions were strongly PAS-positive (**Figure 2A, B**). The overall features were consistent with apocrine gland involvement in Lafora disease, correlating with clinical suspicion.

Treatment plan and outcome

The patient was managed with optimization of antiepileptic therapy, including levetiracetam and valproate, along with clonazepam for myoclonus. Genetic counselling was provided to the family, including discussion of autosomal recessive inheritance and the role of molecular testing for EPM2A and EPM2B mutations. The patient continues on symptomatic therapy with regular follow-up, but the disease course remains progressive.

DISCUSSION

Confirmation of Lafora disease depends on the identification of typical intracytoplasmic polyglucosan inclusions known as Lafora bodies. These inclusions may be found in the liver, skeletal muscles, or brain. [7] However, skin biopsy has become the preferred method because it is simple, minimally invasive, and reliably demonstrates inclusions within sweat gland structures. [8]

Recent studies by Zeka et al. in 2022, [9] Kimiloğlu et al. in 2021, [4] and Kaur et al. in 2020, [3] support this approach

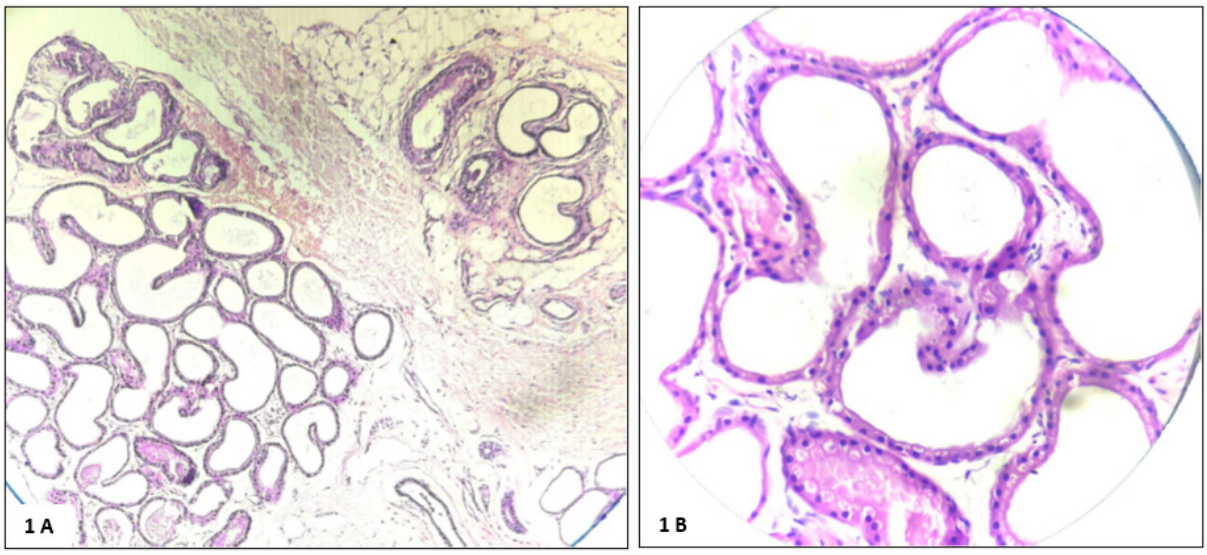

Figure 1: (A) 10× view and (B) 40× view showing multiple apocrine gland acini with abundant intracytoplasmic, round to ovoid, amphophilic inclusions predominantly located in the basal cytoplasm of secretory cells.

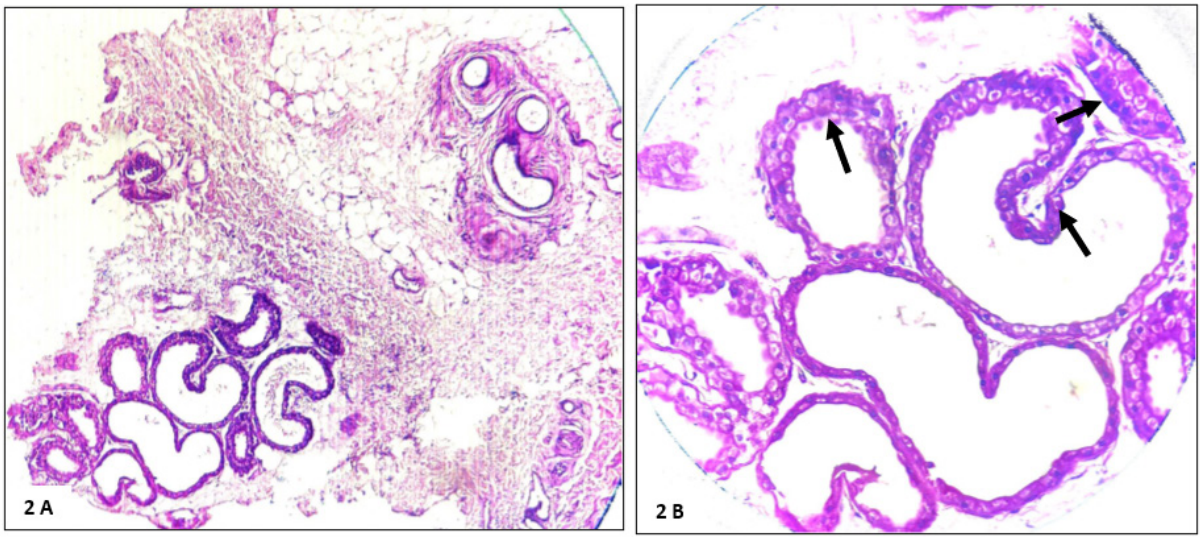

Figure 2: (A) 10× view and (B) 40× view highlighting well-defined PAS-positive intracytoplasmic inclusions (arrows) surrounded by a distinct perinuclear halo within apocrine acinar cells, characteristic of apocrine gland involvement in Lafora disease.

and show that the axillary skin provides the best diagnostic yield. Axillary skin contains both eccrine and apocrine glands, which often show PAS-positive diastase-resistant inclusions in affected individuals. [10–12]

The study done by Pondrelli et al. in 2021 [10] described the polyglucosan nature of Lafora bodies. [2] Their specificity is supported by the fact that similar changes are generally not observed in other forms of myoclonic epilepsy. However, careful interpretation is required because polyglucosan deposits may occasionally appear in other metabolic or degenerative conditions such as adult polyglucosan body disease, Andersen disease (glycogen storage disease type IV), and age-related neurodegeneration. [9] Histopathologically, Lafora bodies in skin biopsy are typically PAS-positive, diastase-resistant inclusions located within the cytoplasm of apocrine gland cells, particularly in the basal portion adjacent to the nucleus. In contrast, adult polyglucosan body disease predominantly shows central and peripheral nervous system involvement without characteristic apocrine gland inclusions on skin biopsy.

Correlation with clinical presentation of adolescent-onset progressive myoclonic epilepsy and identification of EPM2A or EPM2B mutations aid in distinguishing Lafora disease from other polyglucosan storage disorders. [9]

Lafora disease is associated with rapid progression and poor prognosis. Accurate differentiation has important clinical implications. Although curative therapy is not yet available, diagnosis enables rational antiepileptic selection, anticipatory guidance regarding disease progression, and genetic counselling for at-risk relatives. The present case report reaffirms the practical value of axillary skin biopsy in establishing an early diagnosis and guiding further clinical decisions.

CONCLUSIONS

Axillary skin biopsy is a practical and reliable method for demonstrating PAS-positive inclusions that define Lafora disease. Because imaging studies may appear normal in the early phase, this straightforward procedure allows confirmation of the diagnosis without the need for more invasive tissue sampling. Prompt recognition of the disease is important for clinical management, family counselling, and follow-up of young patients presenting with worsening seizures and myoclonus.

PATIENT CONSENT

Written informed consent was obtained from the patient for publication of this case report.

AUTHORS' CONTRIBUTION

All authors have significantly contributed to the work, whether by following the case at the bedside, conducting literature searches, drafting, revising, or critically reviewing the article. They have given their final approval of the version to be published, have agreed with the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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CONFLICT OF INTEREST

None.

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