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Navigating Complexity: A Case of Progressive Myoclonic Epilepsy - Lafora Body Disease

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Abstract: ***Introduction: Progressive myoclonic epilepsy (PME) is a rare and complex group of inherited disorders characterized by epileptic seizures, myoclonus, and progressive neurological degeneration. Among these, Lafora body disease stands as an exceptionally severe form. This case report explores the diagnostic journey of a 17-year-old male with PME-Lafora body disease, emphasizing the critical role of early recognition and multidisciplinary care in managing this rare neurological condition. Aim: This article aims to shed light on the intricate clinical course of PME-Lafora body disease and the diagnostic challenges it presents. It underscores the importance of timely diagnosis and a multidisciplinary approach to improve the patient's quality of life and potentially slow symptom progression. Case History: The 17-year-old male patient's history encompasses a spectrum of symptoms, beginning with jerky hand movements and progressing to cognitive decline and seizures. Diagnostic assessments included neuroimaging, cerebrospinal fluid examination, ceruloplasmin level evaluation, Skin biopsy histopathology examination and electroencephalography. A clinical diagnosis of Progressive Myoclonic Epilepsy - Lafora Body Disease was established. Conclusion: The complexity of PME-Lafora body disease necessitates a meticulous diagnostic journey that includes clinical assessments, neuroimaging, and specialized laboratory tests. Despite the absence of a cure, early recognition and comprehensive care involving antiepileptic drugs and supportive measures play a crucial role in managing this debilitating condition. This case highlights the challenges in diagnosing and managing rare neurological diseases and emphasizes the need for continued research to enhance our understanding and treatment options for PME.***

Keywords: Progressive Myoclonic Epilepsy**,** Lafora Body Disease**,** Neurological Degeneration**,** Rare Neurological Condition, seizures

1. Introduction

Progressive myoclonic epilepsy (PME) is a rare group of inherited disorders characterized by epileptic seizures, myoclonus (involuntary muscle jerks), and progressive neurological degeneration.[1,2]Progressive myoclonic epilepsy is an umbrella term encompassing a spectrum of disorders that share common features, including progressive neurological decline, myoclonus, and epilepsy.[3] These conditions are typically inherited, and while they vary in their genetic underpinnings, they often lead to debilitating and, in some cases, life-threatening outcomes. The hallmark of PME is the presence of myoclonus, which refers to sudden, brief muscle jerks that can affect various body parts. These myoclonic jerks are often one of the earliest signs of the disease.[1]

Among the various types of PME, one particularly rare and severe form is Lafora body disease, named after the presence of abnormal intracellular inclusion bodies called Lafora bodies.[4]It is an autosomal recessive disorder, meaning that both parents must carry a mutation in the same gene for their child to develop the disease. Lafora body disease typically becomes clinically evident during adolescence, as was the case with our patient.[5]

Lafora bodies are abnormal aggregates of glycogen, a complex sugar normally used for energy storage. These aggregates are toxic and lead to cellular dysfunction and, ultimately, neurodegeneration. This relentless process results in the characteristic clinical features of PME, including myoclonus, epilepsy, cognitive decline, and behavioural changes.[6]

Diagnosing Lafora body disease can be exceptionally challenging due to its rarity and the overlap of symptoms with other neurodegenerative disorders.[7] Furthermore, the diagnostic process typically involves a series of clinical assessments, neuroimaging, and specialized laboratory tests.

The management of Lafora body disease remains a significant clinical challenge, as there is currently no cure for this devastating condition. Treatment primarily focuses on symptom management and supportive care, including antiepileptic drugs to control seizures and strategies to alleviate myoclonus.[8]

We present here a case of Lafora disease that presented with PME and investigated at our center. He was diagnosed to have Lafora disease with positive for the pathogenic mutation on genetic testingand typical histological findings on skin biopsy.

2. Case History

The case in question, a 17-year-old male, experienced a sudden onset of generalized convulsions, with each episode lasting approximately 5 minutes.

Summary of Previous Admissions and Diagnoses:
Before this current presentation, the case had a complex medical history.The patient was admitted for myoclonic epilepsy. He had been experiencing myoclonic jerks for approximately one year at this point. No specific diagnosis beyond myoclonic epilepsy is mentioned in the provided information.

Disease progression

Thirteen months prior to admission the patient's medical history begins with the sudden onset of jerky movements in his hands. These movements were disruptive enough to cause him to drop items he was holding, including food. These episodes were most pronounced just before meals.

Over the subsequent 9 months, the patient's condition worsened as he began to experience a decline in cognitive abilities. He started to struggle with tasks such as reading slides and making notes, particularly during online classes. This cognitive decline led to difficulty understanding the material taught during these classes.

While preparing to go for an examination, the patient suddenly lost postural control and fell to the ground. This episode was not associated with limb shaking, frothing from the mouth, bowel or bladder incontinence, or loss of consciousness. He sustained a knee injury as a result.

In same monththe patient experienced a similar episode, leading to injury to his head and required stitches. These episodes, characterized by a loss of postural control, increased in frequency over time.

He subsequently experienced multiple seizures characterised by similar symptoms.The frequency of episodes escalated, with the patient experiencing them once a week initially and eventually multiple times per hour.

Approximately 5 months prior to admission, patient experienced his first documented seizure. This seizure began with a right-sided head version followed by tonic posturing of both upper and lower limbs. It was accompanied by a loss of consciousness. This seizure then progressed to involve movements of both the upper and lower limbs.

The medical history provided by the patient's guardian revealed that the patient had encountered three such convulsive episodes within the past 1.5 months of admission.

By the course of disease progression we made a provisional diagnosis of Progressive Myoclonic Epilepsy.

Family history: Cognitive impairment of paternal uncle and cousin sister of patient’s father in the form of executive dysfunction is present. No consanguineous marriage in family.

Current findings:

Upon admission to our institute, the case'sGeneral, Respiratory, Cardiovascular, and Abdominal examination was normal with all Vitals normal. Neurologically, the case was conscious but confused, with an unresponsive demeanour. Bilateral Pupil size was 2mm and equally reactive to light.

Cognitive Decline and Behavioral Changes:

- The patient's cognitive decline beganduring online classes.
- He had difficulty reading slides, making notes, and understanding the material taught during online classes.
- He also began forgetting the locations of items placed in front of him.
- Despite these memory issues, he retained the ability to remember details about his meals.
- The patient displayed increased irritability and anger, particularly regarding food and when denied certain items.
- He experienced confusion when trying to perform simple tasks, such as opening doors or deciding which direction to go.
- The patient required assistance with dressing.

3. Examination Findings

- A thorough General, Respiratory, Cardiovascular, and Abdominal examination with no significant abnormalities noted.
- Neurological examination showed specific deficits related to the patient's seizures and cognitive decline:
- Higher Mental Functions: Normal, Mini-Mental State Examination: 20/30, Attention: 3/5, Recall: 0/5, Language: 0/9
- Language: Spontaneous Speech, fluency decreased, Impaired Verbal fluency and FAS Test
- Impaired: Repetition of large sentences, naming parts of objects, reading comprehension, writing words and sentences.
- Frontal lobe function examination: Trail making A Impaired, Trail making B Impaired, motor luria and graphic luria, verbal similarities and verbal fluency tests are impaired, Proverb interpretation impaired.
- Temporal lobe function examination: New learning ability significantly impaired, Visual memory impaired.
- Parietal lobe function examination: Construction ability, Calculation, Cortical sensations Impaired.
- Occipital lobe function examination: Normal, Cranial Nerve examination: Normal
- Abnormal Movements: Non Rhythmic jerky movements present in both hands.
- Superficial Reflexes Present and Sensory Examination Normal.
- This detailed case history highlights the progression of the patient's symptoms, from the onset of jerky movements in the hands to the development of cognitive decline and seizures. It provides a chronological account of the patient's medical journey towards progressive myoclonic epilepsy, setting the stage for further diagnostic evaluation and treatment.

4. Diagnosis

The patient’s diagnostic journey was characterized by a combination of clinical presentation, prior medical history, series of investigations, each contributing a piece to the intricate puzzle of his condition. Here, we compile the findings of these investigations in his diagnostic report:

The examination of cerebrospinal fluid revealed the presence of specific antibodies against key receptors. Notably, antibodies targeting Glutamate receptor NMDA, Glutamate receptor AMPA, GABAg receptor, and VGKC receptors were detected in the CSF. These findings strongly

suggested an autoimmune component underlying his symptoms, potentially contributing to his neurological manifestations.

We sent patient's autoimmune profile to NIMHANS and it was found negative. The Measles IgG test was negative. While this results were unexpected, it added complexity to the diagnostic process.

Blood tests revealed that the patient had normal ceruloplasmin levels (33 mg/dL).

The CT scan revealed no significant CT evident neuro-parenchymal abnormality.

The EEG record was obtained with the 10-20 international electrode placement.. EEG showed frequent generalised spike and wave discharge with mild to moderate degree of generalised neurophysiological dysfunction favouring epileptic encephalopathy.

Psychological testing was done andIntelligenceQuotient was found 87 (Low average)

The MRI study of the brain was essentially normal.

Gene testing done detected variants of uncertain significance related to given phenotype (EPM2A and CBS Gene).

On getting the results of gene testing to confirm, we sent the patients Skin biopsy for special stain(PAS) andit revealed PAS-positive eosinophilic cytoplasmic inclusions in sweat glands suggestive of Lafora Bodies.

Treatment during Current Admission:
During the current admission, along with multiple diagnostic procedures patient received ICU Care, Anti convulsaants, Anti emetics, Antacids, Diuretics, and other symptomatic and supportive treatment with IV Fluids for normalising physiological functions.

Collectively, this multifaceted approach to treatment reflects the medical team's commitment to addressing the patient's needs comprehensively, aiming not only to manage the primary epilepsy condition but also to ensure their overall well-being and comfort during their admission.

Clinical Course and Discharge:
Throughout the course of his hospitalization, the patient maintained hemodynamic stability. Despite this, he continued to experience a state of altered consciousness, marked by disorientation and an inability to respond to verbal commands. Additionally, his oral intake remained reduced, requiring ongoing monitoring and support. Upon discharge, the patient was provided with essential advice and instructions, with a primary emphasis on rest. Furthermore, he was scheduled for a follow-up appointment after five days. This follow-up was crucial to monitor his progress and to potentially adjust his treatment plan.

5. Discussion

Lafora Body Disease, in particular, is characterized by the presence of abnormal intracellular inclusion bodies called Lafora bodies, which lead to cellular dysfunction and neurodegeneration. This case report emphasizes the critical role of early recognition and multidisciplinary care in managing this rare neurological condition.

The case history of a 17-year-old male patient is presented, showcasing the evolution of his symptoms over time. The journey begins with the onset of jerky hand movements, which gradually progressed to cognitive decline and seizures. The case history timeline demonstrates the complexity and severity of Lafora Body Disease, highlighting the need for prompt diagnosis and intervention.

Diagnosing Lafora Body Disease is challenging due to its rarity and symptom overlap with other neurodegenerative disorders. The diagnostic process involves a combination of clinical assessments, neuroimaging, and specialized laboratory tests. In this case, cerebrospinal fluid examination, EEG, ceruloplasmin level evaluation, genetic testing and Skin Biopsy played a crucial role in confirming the diagnosis.

6. Conclusion

In conclusion, this case report sheds light on the intricate clinical course of PME-Lafora Body Disease and the diagnostic challenges it presents. It underscores the importance of timely diagnosis and a multidisciplinary approach to improve the patient's quality of life and potentially slow symptom progression. Despite the absence of a cure, early recognition and comprehensive care involving antiepileptic drugs and supportive measures play a crucial role in managing this debilitating condition. This case highlights the challenges in diagnosing and managing rare neurological diseases and emphasizes the need for continued research to enhance our understanding and treatment options for Lafora Body PME.

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