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Case Report

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Lafora Disease: A Case Report of Progressive Myoclonic Epilepsy

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ABSTRACT

Lafora disease is a rare genetic disease caused by the accumulation of malformed glycogen products in the tissues. The disease usually manifests with idiopathic generalized tonic colonic seizures with poor response to antiepileptic drugs (AEDs). We report the case of a 19-year-old girl with the chief complaint of generalized refractory seizures, jerky movement, and cognitive deterioration with a positive history of epilepsy in her younger brother. The disease onset was at the age of 16 with jerky movement and blurred vision. She was admitted to our ward to have a long-term video EEG monitoring for further evaluation. Clinical presentation accompanied with abnormal EEG characteristics for Lafora disease, and the positive familial history were highly suggestive of Lafora disease. The disease was confirmed with genetic testing by which the mutation of EPM2A was detected.

Introduction

Lafora disease is autosomal recessive myoclonus epilepsy usually seen in children of consanguineous marriages. This disease is a form of glycogen storage disease due to mutation in the EPM2A or EPM2B (NHLRC1), the genes responsible for encoding Lafora and maline proteins [1]. Although the role of these proteins is yet not completely understood, the accumulation of inclusion bodies in the neural system, especially in the cell bodies and dendrites, leads to neurologic manifestations [2]. While most of these signs involving seizure, transient blindness, dysarthria, confusion and drop in school performance begin between the age of 9 and 18, there are some reported cases of later manifestation of the disease [3]. These symptoms later progress to refractory seizures and dementia, and death usually occurs ten years after the disease onset, primarily due to

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respiratory failure [4]. EEG has some characteristics which help determine the diagnosis since patients experience a broad spectrum of different types of seizures, including tonic colonic, absent, myoclonic, occipital and atonic [5]. The EEG's abnormalities mostly precede the clinical symptoms, and practically an occipital discharge arising from slowed posterior rhythm on EEG in the presence of clinical symptoms is highly suggestive of Lafora disease [4]. Although the diagnosis is always confirmed with genetic testing and finding the homozygous mutation of the genes, skin biopsy from axilla and seeing the pathological hallmark of polyglucans accumulation called Lafora bodies can be another beneficial diagnostic tool [6].

Case report

A 19-year-old female patient was admitted in December 2020 to our neurology ward with the chief complaint of frequents myoclonic jerk and daily myoclonic tonic colonic seizure accompanied by progressive cognitive impairment and ataxia. The early manifestations of the disease started at the age of 16, prior to which the patient did not have any clinical problem. The first sign was noted as frequent myoclonus and jerky movement in upper extremities following by visual aura and blurred vision. Then the myoclonic tonic colonic seizure occurred, which was refractory to AEDs. Other neurological manifestations such as visual disturbances, progressive cognitive impairment, ataxia, dysarthria and personality changes (tantrums) accompanied the seizure in this state. Her school performance was average prior to the onset of the seizures, however, after that, her school performance dropped significantly, and she was not capable of graduating from high school. The patient is the first child of consanguineous marriage, and she was a product of normal vaginal delivery with meconium-stained amniotic fluid without any serious complication. She has a younger brother with a grand mal seizure that started at the age of fifteen. All the early laboratory tests, including CBC, serum calcium, phosphor, magnesium, sodium, and liver and thyroid function tests, were within normal limits. The neurological exams did not show any cranial nerves function abnormalities; however, mild ataxia and dysarthria accompanied with a jerky movement of upper extremities were present at the time of admission.

Furthermore, the patient was under treatment with valproate from sixteen to seventeen, which was discontinued due to the patient complaint about weight gain and insufficient control of the seizures. Currently, the patient is taking 3000 mg of levetiracetam and 300 mg of lamotrigine daily. During her stay in the hospital, she went under a long-term electroencephalographic monitoring to determine a diagnosis. The video EEG monitoring scheduled for two days period, which was then reviewed in bipolar, monopolar and referential montages. The abnormal interictal finding was as listed below: sleep organization was abnormal due to extreme sleep spindle, generalized frontal dominant spike-wave complex three or more than 3 Hz, generalized paroxysmal frontal dominant fast activity and paroxysmal generalized fast spike-wave complex during sleep. We captured multiple clinical seizures during the two days of monitoring. The ictal activity started with generalized background attenuation activity followed by generalized frontal dominant fast activity (18-20 Hz), which lasted less than 10 seconds. The neurodegenerative symptoms of the patient accompanied with the characteristic findings of the EEG, positive history of epilepsy in her brother and the fact that she was a product of first-degree marriage raise a high clinical susception for Lafora disease. In order to determine the diagnosis, she underwent a whole-exome sequencing genetic test in which a homozygous NM-005670.3 mutation in EPM2A was detected. Briefly, DNA from the blood was taken and analyzed for EPM2A and EPM2B by polymerase chain reaction.

Discussion

Lafora disease is a rare neurodegenerative disease that is caused by the accumulation of insoluble glycogen in all body tissues, especially in the nervous system [6]. Lafora is considered one of the diagnoses if the patient presents with progressive myoclonic epilepsies (PMEs). PMEs are rare genetic disorders characterized by progressive myoclonic seizures and cognitive impairment [7]. Lafora disease, Unverricht-Lundborg disease, the neuronal ceroid lipofuscinoses, type I sialidosis, action myoclonus-renal failure syndrome, Dentatorubral-pallidoluysian atrophy (DRPLA), and Type III Gaucher disease are all part of PMEs. All of the mentioned diseases are lysosomal storage diseases except Lafora [8]. The diagnosis of Lafora requires both genetic testing and excluding other PMEs [7]. Although there are not many treatments available, the ketogenic diet has been proven to be beneficial in controlling epilepsies through maintaining a low level of blood glucose and producing less malformed glycogen and eventually resulting in lower LB accumulation [9]. Some other experimental drugs, such as antibody-enzyme fusion and sodium selenite, are still under investigation to become approved [10].

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors have no conflict of interest to declare.

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