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Case Report

A type of progressive myoclonic epilepsy, Lafora disease: A case report

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Abstract. Lafora disease is a rare group of progressive myoclonic epilepsies characterized with progressive neurological dysfunction, myoclonus, focal and generalized seizures. Generally, a generalized tonic clonic seizure is the first symptom of the disease. An 11-year-old male patient had been followed-up at another center for epilepsy for 8 years. The patient had a history of myoclonic seizures for nearly every day for the last 2 years and cognitive detoriation for the last 8 months. He admitted to our hospital with the desire of his family. Eccrine sweat gland biopsy was performed. The biopsy of the sweat gland was positive for PAS and contained diastase resistant polyglican content (Lafora bodies), and thus, a diagnosis of Lafora disease was established. The patient presented here constitutes a rare case of pediatric epilepsy, which caused neurodegeneration in late-childhood and onset with typical epilepsy symptoms. This report also aimed to show that biopsy obtained from proper area is important for diagnosis Our patient developed cognitive dysfunction a short period of eight months. To our knowledge, this is the shortest period in literature.

Key words: Lafora Disease, progressive myoclonic epilepsy, neurodegeneration

1. Introduction

Progressive myoclonic epilepsy is a rare group of diseases characterized with progressive neurological dysfunction, myoclonus, focal and generalized seizures. Lafora is an autosomal recessive disease belonging to this group of diseases. Its onset is usually in the form of typical generalized epilepsy that responds well to antiepileptics. After a few years, myoclonic seizures occur, followed by a rapid and progressive dementia. Patients suffer from apraxia, aphasia, visual loss, vegetative state, and die (1-3). In this report, a typical case of Lafora has been presented.

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2. Case report

An 11-year-old male patient had been followed-up for epilepsy for 8 years. He had a history epilepsy with generalized clonic seizures between the ages of 3 and 8 years that were well-controlled with valporic acid. According to the history, the patient also had myoclonic, generalized tonic clonic seizures almost daily for the last 2 years with poor response to various antiepileptic drugs, and suffered from severe cognitive regression and visual loss for the last 8 months. In another center, the patient was suspected to have a neurodegenerative disease. The MRI of brain showed mild cerebral and cerebellar atrophy and non-specific signal changes in the posterior periventricular area. Laboratory investigations including Tandem-MS, ammonia, toxic screening, ceruloplasmin, urine copper content, viral markers (EBV, CMV, Rubella, Toxoplasmosis, HSV, varicella, mumps, measles), and urine organic acid levels were normal. The results of blood work for lysosomal enzymes (Hexosaminidase, Alpha-galactosidase, Arylsulfatase A, gluco- cerebrosidase) and CSF

evaluation of measles IgM and IgG for SSPE were normal as well. The autoimmune and paraneoplastic investigations including alpha-fetoprotein, LDH, VMA, thyroid function tests /thyroid antibodies, beta hcg, 5 HIAA were normal. , The abdominal USg was unremarkable. During the clinical observation, the frequency of seizures was increased. The scalp electroencephalography (EEG) showed increased background activity, which was attributed to risperidone used at that period that subsequently was discontinued. However, the patient made more eye-contact and were more energetic when he was on risperidone. Therefore, the drug was restarted. The muscle biopsy for mitochondrial diseases was normal. The family of the patient did not consent for brain biopsy procedure. The patient was discharged with family's desire and was seizure-free with clonazepam, levetiracetam, and vitamin B complex.

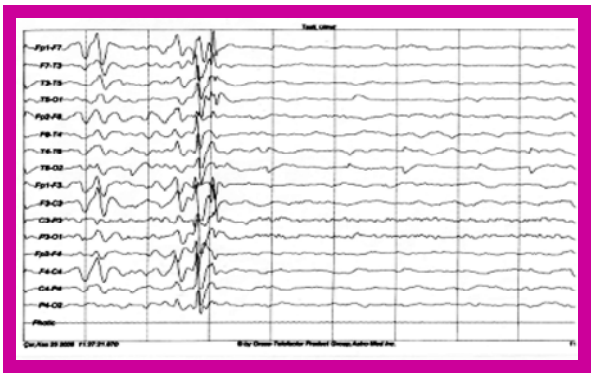

Fig. 1. Generalized spikes and sharp slow wave activity on encephalopathic (delta activity) background as seen on the EEG of the patient.

The patient had 30 seizures a week and fever for the last 2-3 days after being discharged from the other center. He admitted to our hospital with the desire of his family. The neurological examination of the patient revealed that he was not responding to verbal stimuli, able to locate pain stimulation (GCS=9), and his eyes were spontaneously open. In addition, the patient had abnormality of upper motor neuron functions as well as coarse breath sounds. The acute phase reactant level was high and the postero-anterior pulmonary graph showed infiltration in the left lobe of the lungs. The patient was started on cephoperazone/sulbactam and continuous oxygen support for the diagnosis of pneumonia. Visual evoked potentials (VEP) and electro-retinogram (ERG) latencies were observed delay in response. Furthermore, the patient's showed delayed bilateral 1st wave response on brainstem auditory evoked potentials (BAEP). The blood lactate and pyruvate levels were normal. Deterioration of the general condition along with prolonged ERG response were suggestive of neuronal ceroid lipofuscinosis. The gene analysis was negative. The fundus examination was normal. The EEG revealed generalized spike-wave, and sharp slow-wave activity with encephalopathic background (Figure 1). The clinical condition of the patient, EEG findings, and evoked potentials of the patient suggested Lafora disease. Lafora bodies were not detected in the previous muscle biopsy of the patient. Nonetheless, eccrine sweat gland biopsy was performed considering the high specificity to determine Lafora bodies. The results of the biopsy study showed PAS (+), diastase resistant polyglican inclusions (Lafora bodies) (Figures 2, 3). The patient received midazolam infusion for five days, and also was put on topiramate. The number of seizures markedly decreased (weeks 1-2). The family refused feeding via a gastrostomy catheter and genetic analysis. The patient was discharged with decreased seizures, without any oxygen supply.

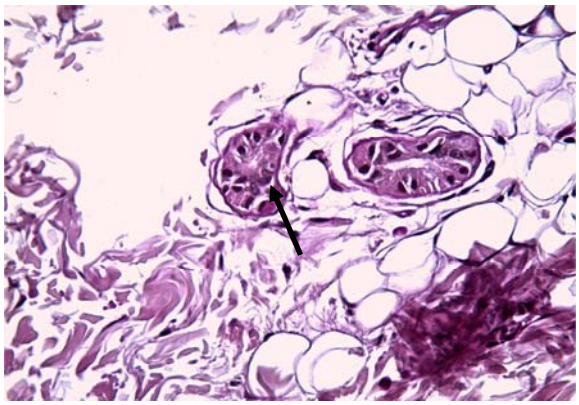

Fig. 2. D-PAS positive infranuclear globule, in the cytoplasm of ecrine ductus epithelium. H&Ex40.

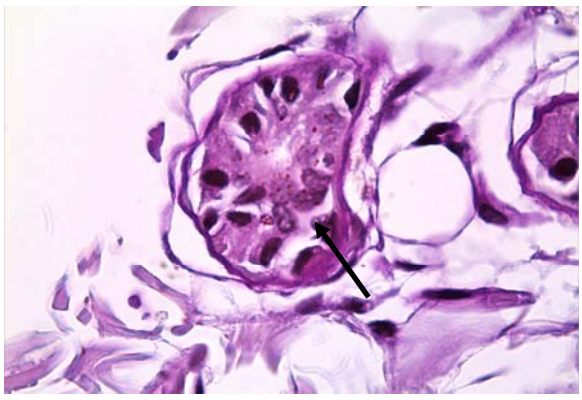

Fig. 3. D-PAS positive infranuclear globule, in the cytoplasm of ecrine ductus epithelium. H&Ex100.

3. Discussion

The onset of Lafora disease is usually in the second decade, nearly at the mean age of 14 years (9.5-18), It generally presents with tonic clonic seizures, followed by non-synchronized, rapid, and massive myoclonic jerks in the extremity and mouth. Rapid progressive dementia and global cognitive dysfunction develop 2-6 years after the disease onset. It initially responds well to antiepileptics. Visual deterioration with normal fundus is common. Death occurs at a mean of 2-10 years after the diagnosis (1,4). Our patient developed cognitive dysfunction a short period of eight months. To our knowledge, this is the shortest period in literature. The diagnosis is based on detection of Lafora bodies in the apocrine and eccrine sweat gland biopsies. This test is positive in 80-100% of the patients. In the liver biopsy, this rate is 40% (4-6). Due to delayed central conduction time, VEP and BAEP latencies may be prolonged. Cranial images may be normal, but with the progression of the disease, diffuse atrophy may be seen (1,4,7). The background is normal on the EEG at the beginning. However, with the progression of the disease, progressive teta and delta activities can be observed. Epileptic discharges may be in the form of spike-wave, multi spike-wave, and sharp slow-wave discharges (7-9). In 75-85% of the families affected, EPMA2A mutation was detected in the 6q23-25th chromosome (10,11).

Our case is a typical Lafora disease with onset of generalized epilepsy and good response to antiepileptics at the beginning of the disease. With this case, we wanted to emphasize that proper biopsy from correct area is very important for the diagnosis and with proper diagnosis many unnecessary laboratory investigations can be avoided.

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