American Journal of Medical Case Reports, 2016, Vol. 4, No. 3, 80-82
Available online at http://pubs.sciepub.com/ajmcr/4/3/2

DOI:10.12691/ajmcr-4-3-2

Lafora Body Disease: A Rare Type of Progressive Myoclonic Epilepsy

Md Enayet Hussain*, Afjal Momin, Mahmudul Islam, S R Haque, Mohammad Akter Hossain, Rajib Nayan Chowdhury, Md Azharul Hoque

National Institute of Neurosciences (NINS), Agargaon, Dhaka, Bangladesh
*Corresponding author: enayetdmc@yahoo.com

Abstract Lafora body disease is one of the inherited progressive myoclonic epilepsy (PME) syndromes. It is an autosomal-recessive disorder with onset in late childhood or early adolescence. The disease is characterized by fragmentary, symmetric, or generalized myoclonic and/or generalized tonic-clonic seizures, visual hallucinations (occipital seizures), and progressive neurologic degeneration including cognitive and/or behavioral deterioration, dysarthria, and ataxia. The frequency and intractability of seizures increase over time. Status epilepticus is common. Emotional disturbance and confusion are common at or soon after onset of seizures and are followed by dementia. Dysarthria and ataxia appear early, spasticity late. Pathologically polyglucosan inclusion bodies (Lafora body) are seen which are pathognomonic of the disease and are not seen in any other types of PMEs. Electroencephalogram (EEG) reveals slowing of background and generalized spike/polyspike-and-waves and photosensitivity. Most affected individuals die within ten years of onset, usually from status epilepticus or from complications related to nervous system degeneration.

Keywords: *Lafora Body, progressive myoclonic epilepsy*

Cite This Article: Md Enayet Hussain, Afjal Momin, Mahmudul Islam, S R Haque, Mohammad Akter Hossain, Rajib Nayan Chowdhury, and Md Azharul Hoque, "Lafora Body Disease: A Rare Type of Progressive Myoclonic Epilepsy." *American Journal of Medical Case Reports*, vol. 4, no. 3 (2016): 80-82. doi: 10.12691/ajmcr-4-3-2.

1. Introduction

Progressive myoclonic epilepsies (PME) are a rare, symptomatic group of epilepsy with genetic origin. They progress clinically with progressive neurological deterioration including mainly stimulus-sensitive myocolonic seizures, tonic clonic seizures, cerebellar findings and mental failure [1,2]. The onset usually occurs in childhood or adolescence. They compose less than 1% of all epilepsies [3]. Lafora disease which is one of these epilepsies in this group was described by Lafora and Glueck [1] in 1911. It is a rare, autosomal recessive disease characterized by epilepsy, myoclonus, dementia and the presence of Lafora bodies in various tissues [1,4]. It can be observed worldwide, but it is most commonly seen in Mediterranean countries and Canada [1]. In this paper we present a case, who presented with treatment-resistant seizures and progressive mental failure and was finally diagnosed as Lafora Body disease.

2. Case Presentation

An 18 year old Bangladeshi boy of non consanguineous parents presented with the complaints of occasional, sudden, brief, jerky movement of the whole body followed by fall which started 2 years back. Initially the frequency of jerk and fall was once every 2-3 days which continued to increase in number. Two months later he had one attack of generalized tonic clonic seizure with tongue biting and incontinence of urine which lasted for 2-3 minutes followed by post ictal confusion and tiredness without any aura. He was put on sodium valproate which failed to bring significant relief of his jerks. With the course of time his parents rather noticed a decline in his memory and intelligence and an increase in the number of jerks which compelled him to restrict his movements. One year later he had three attacks of generalized tonic clonic seizure in a day and was managed in a local hospital as status epilepticus. Later he was referred to the National Institute of Neurosciences & hospital, a tertiary neurology referral center in Dhaka for further management. On admission the patient was confused and had frequent erratic spontaneous and stimulus (loud sound, touch) sensitive myoclonic jerks involving the whole body. He had no family history of such disease. General examination revealed all vital parameters were within normal limit. On neurological examination the patient was dysarthric, a bit confused with disorientation to time, place and person with frequent myoclonic jerk involving the whole body. So far the patient could be examined the other neuological findings were normal. Routine blood, urine and biochemical tests and magnetic resonance imaging (MRI) were unremarkable. EEG revealed abundant generalized almost symmetrical high-voltage polyspike-and-wave along with frequent bilateral independent posterior dominant (T6, O2//T5, O1) focal

spikes on a slow & disorganized background which aggravated on photic stimulation (Figure 1). CSF study including the anti measles antibody was normal. A provisional diagnosis of Progressive myolonic epilepsy (? Lafora type) was made. An axillary skin biopsy was done which revealed PAS positive intracytoplasmic inclusion body (Lafora body) in the epithelium of the sweat gland ducts (Figure 2). As the genetic testing is unavailable in Bangladesh it could not be done. The patient was discharged with appropriate counselling of his parents about the disease. He was put on sodium valproate (1500 mg/day) and Clonazepam (2 mg/day) with partial reduction of myoclonic jerks and without any significant improvement of cognition.

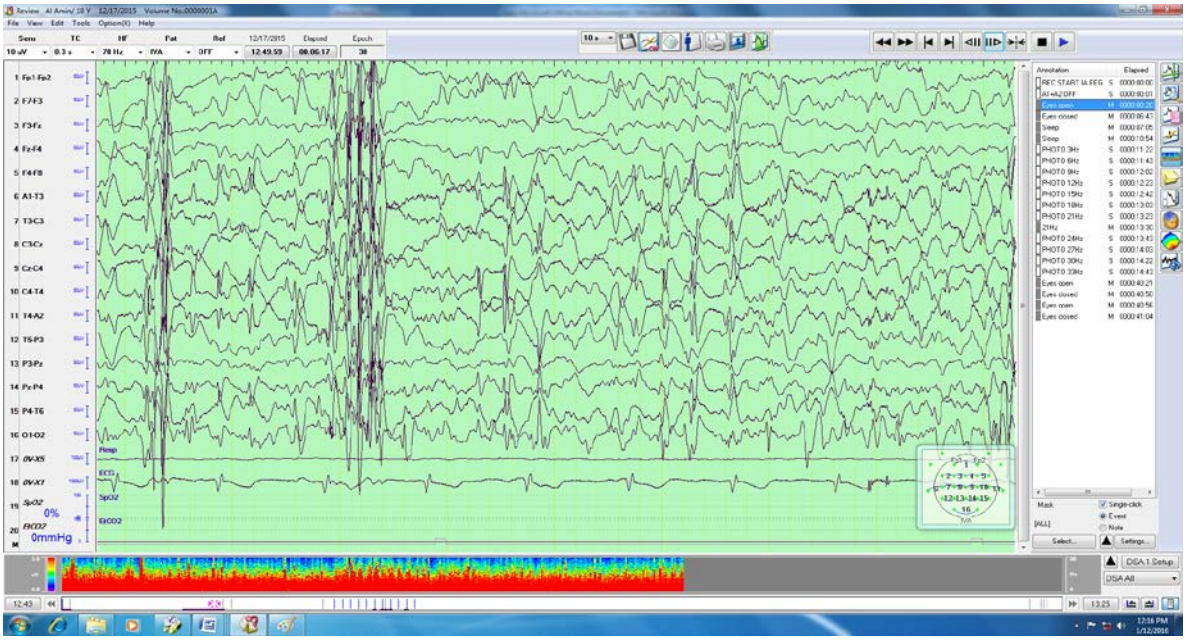

Figure 1. EEG: Generalized almost symmetrical high-voltage polyspikes-and-wave along with frequent bilateral independent posterior dominant (T6, O2//T5, O1) focal spikes on a slow & disorganized background which aggravated on photic stimulation

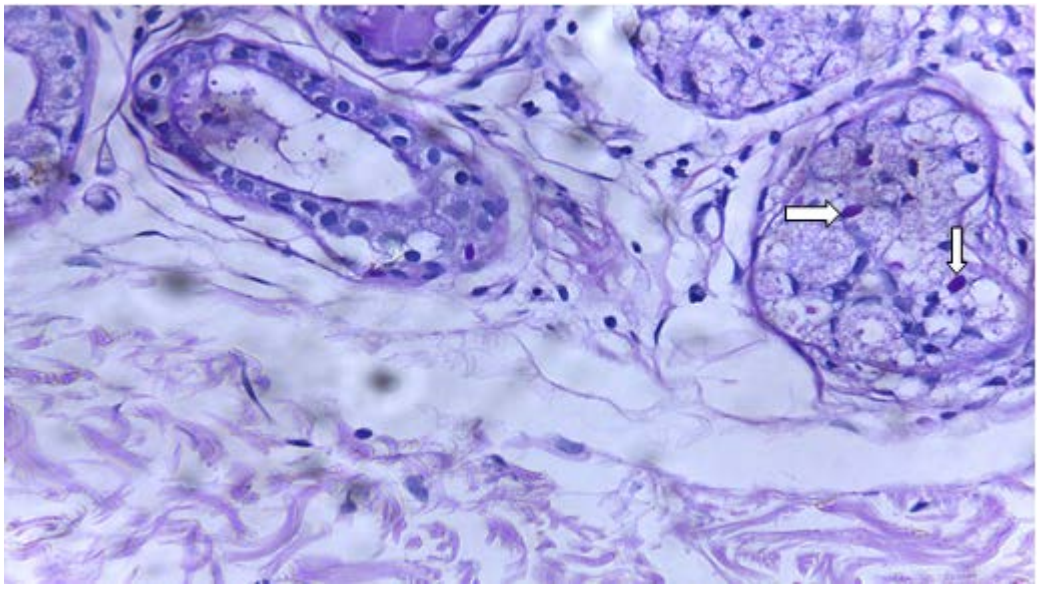

Figure 2. PAS positive polyglucosan intracytoplasmic inclusion body (Lafora Body) in the epithelial lining of the sweat gland ducts

3. Discussion

Lafora body disease—also called progressive myoclonic epilepsy type 2 (EPM2) is named after the Spanish neuropathologist Gonzalo Rodriguez Lafora (1887-1971), who first reported the presence of spherical inclusions in brains of patients with myoclonic epilepsy, which are known as Lafora bodies. These inclusion bodies later proved to be the key factor in distinguishing Lafora disease from other myoclonic epilepsies. It is characterized by myoclonus, tonic–clonic seizures, visual hallucinations, intellectual decline and progressive neurologic deterioration [5]. The age of onset is usually 12–15 years, but an earlier onset variant begins at the age of 5 years [6,7]. Lafora body disease is caused by mutations either in the EPM2A gene (encoding for laforin, a dual-specificity protein phosphatase) or in the EPM2B (NHLRC1) gene (encoding malin, an E3- ubiquitin ligase) [7]. These two proteins interact and, as a complex, regulate glycogen synthesis. Lafora body disease is, therefore, a disorder of carbohydrate metabolism resulting in polyglucosan inclusion bodies in neural and other

tissues [8]. Tissue biopsy (axillary skin, brain and spinal cord, heart and liver, skeletal muscle) reveals Lafora bodies, which are aggregates of polyglucosans (poorly constructed glycogen molecules). Lafora bodies are pathognomonic and do not occur in any other condition [9,10,11,12]. In the differential diagnosis: subacute sclerosing panencephalitis (SSPE), progressive myoclonic ataxia (PMA), progressive encephalitis (GM2 gangliosidosis, Nieman Pick, Gaucher disease), juvenile myoclonic epilepsy, nonketotic hyperglycemia should be considered [13]. No curative treatment is available for Lafora disease. Valporate, phenobarbial, benzodiazepines, levetiracetam and zonisamine in combination may be beneficial in the early period for myoclonus. To prevent worsening of myoclonus carbamazepine, phenytoin, gabapentin, pregabalin and lamotrigine should be avoided. Perampanel, a relatively newer antiepileptic drug, has shown some promising results in seizure control and improvement of neurological dysfunction in Lafora disease [15,16]. In the future, gene therapy will be an option [2,14]. LD has an unfavorable prognosis, and patients usually die within 10 years of the clinical findings at onset.

4. Conclusion

We presented the case because of the rarity of the disease and because of its profound clinical similarity with that of Subacute sclerosing panencephalitis (SSPE) which is more common in our country. So far our knowledge goes this is the first reported case of Lafora Body disease in Bangladesh.

References

[1] Baykal BB, Özemir ZA. Progresif miyoklonik epilepsiler. ‹çinde: ‹brahim Bora, Naz Yeni, Candan Gürses, (yazarlar). Epilepsi. ‹stanbul: Nobel t›p kitabevleri, 2008: 271-90.

[2] Panayiotopoulos CP. A clinical guide to epileptic syndromes and their treatment. Second edition. Springer, Oxfordshire, 2007: 475-82.

[3] Baykal B. Progresif miyoklonik hastal›klar- Lafora hastal. Epilepsi 2008; 14: 17-51.

[4] Kaplan KJ, Nelson BL. Pathologic quiz case myoclonic epilepsy and cognitive decline in a 19-year old man. Arch Pathol Lab Med 2003; 127: 231-2.

[5] Couarch P, Vernia S, Gourfinkel-An I, et al. Lafora progressive myoclonus epilepsy: NHLRC1 mutations affect glycogen metabolism. J Mol Med 2011; 89: 915-25.

[6] Singh S, Ganesh S. Lafora progressive myoclonus epilepsy: a meta-analysis of reported mutations in the first decade following the discovery of the EPM2A and NHLRC1 genes. Hum Mutat 2009; 30: 715-23.

[7] Turnbull J, Girard JM, Lohi H, et al. Early-onset Lafora body disease. Brain 2012; 135: 2684-98.

[8] Spuch C, Ortolano S, Navarro C. Lafora progressive myoclonus epilepsy: recent insights into cell degeneration. Recent Pat Endocr Metab Immune Drug Discov 2012;6:99-107.

[9] Acharya JN, Satishchandra P, Asha T. Lafora's disease in South India: A clinical, electrophysiologic, and pathologic study. Epilepsia 1993; 34: 476-87.

[10] Carpenter S, Karpeti G. Sweat gland duct cells in Lafora disease: diagnosis by skin biopsy. Neurology 1991; 31: 1564-8.

[11] Nishimura RN, Ishak KG, Reddick R, Porter R, James S, Barranger JA. Lafora disease: diagnosis by liver biopsy. Ann Neurol 1980; 8: 409-15.

[12] Kaufmann MA, Dwork AJ, Willson NJ. Late onset Lafora's disease. Neurology 1993; 43: 1246-48.

[13] Comoglu S, Ozbakir S, Pesinci E. Diagnosis of Lafora Body Disease by Axillary Skin Biopsy. Turk J Med Sci 2006; 36: 235-237.

[14] Striano P, Zara F, Turnbull J, et al. Typical progression of myoclonic epilepsy of the Lafora type. Nature clinical practice neurology 2008; 4: 106-11.

[15] Dirani M, Nasreddine W, Abdulla F, Beydoun A. Seizure control and improvement of neurological dysfunction in Lafora disease with perampanel. Epilepsy & Behavior Case reports 2014; 2: 164-166.

[16] Schorlemmer K, Bauer S, Belke M et al. Sustained seizure remission on perampanel in progressive myoclonic epilepsy (Lafora disease). Epilepsy & Behavior Case reports 2013; 1: 118-121.