Periodic electroencephalogram discharges in a case of Lafora body disease: An unusual finding

Rajendra Singh Jain, Arti Gupta[1], Pankaj Kumar Gupta, Rakesh Agrawal

Department of Neurology, Sawai Man Singh (SMS) Medical College, Jaipur, Rajasthan, [1]Department of Pathology, Shyam Shah (SS) Medical College, Rewa, Madhya Pradesh, India

Abstract

Lafora body disease (LBD) is a form of progressive myoclonic epilepsy, characterized by seizures, myoclonic jerks, cognitive decline, ataxia, and intracellular polyglucosan inclusion bodies (Lafora bodies) in the neurons, heart, skeletal muscle, liver, and sweat gland duct cells. Electroencephalogram (EEG) findings in LBD may include multiple spikes and wave discharges, photosensitivity, multifocal epileptiform discharges, and progressive slowing in background activity. Periodicity in epileptiform discharges has not been frequently depicted in LBD. We herein report an unusual case of LBD who showed generalized periodic epileptiform discharges in EEG.

Key Words

Lafora body disease (LBD), periodic complexes, progressive myoclonic epilepsy

For correspondence:
Dr. Pankaj Kumar Gupta, Department of Neurology, Sawai Man Singh (SMS) Medical College, Jaipur, Rajasthan, India.
E-mail: pankajniw04@gmail.com

Ann Indian Acad Neurol 2016;19:269-271

Introduction

Lafora body disease (LBD) is a progressive myoclonic epilepsy, presenting with seizures, myoclonic jerks, cognitive decline, and ataxia.[1] It is an autosomal recessive fatal disorder characterized by the presence of intracellular polyglucosan inclusions in the neurons, heart, skeletal muscle, liver, and sweat gland duct cells called Lafora bodies. It usually starts in the age of adolescence.[2] Electroencephalogram (EEG) changes usually include generalized spike wave discharges, photosensitivity, and progressive slowing of background activity. Frequency of spike wave complexes also increase with the progression of illness.[1,3] Periodicity in epileptiform discharges has not been frequently described in LBD. We herein report a very unusual case of LBD who showed the periodic epileptiform discharges in EEG.

Case description

A 12-year-old boy born out of a nonconsanguineous marriage with an uneventful birth history and normal developmental milestones presented with a 5-month history of progressive cognitive decline in the form of poor scholastic performance, forgetfulness, and decreased speech output. He developed frequent myoclonic jerks and difficulty in walking in the form of swaying on both sides and dragging of feet 2 months after the onset of illness. There was a history of exanthematous illness at the age of 2 years. He was not vaccinated for measles. There was no history of a similar illness in the family. On examination, the pulse rate was 80/min, blood pressure was 100/70 mmHg, and temperature was 37°C. On neurological examination, he was conscious but disoriented and inattentive. Pupils and fundus examination were normal. Motor examination showed spasticity in all the four limbs. Deep tendon reflexes were exaggerated with positive Babinski sign bilaterally. Routine investigations including hematology, biochemistry, thyroid profile, x-ray of the chest, ultrasound abdomen, and electrocardiogram (ECG) were normal. Cerebrospinal fluid (CSF) examination

Access this article online

Quick Response Code:

Website: www.annalsofian.org

DOI: 10.4103/0972-2327.176862

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Jain RS, Gupta A, Gupta PK, Agrawal R. Periodic electroencephalogram discharges in a case of Lafora body disease: An unusual finding. Ann Indian Acad Neurol 2016;19:269-71.
Received: 24-08-15, **Revised:** 20-09-15, **Accepted:** 21-10-15

revealed cell count 02/Cu mm (all lymphocytes), protein 20 mg/dL, sugar 65 mg/dL (corresponding blood sugar 122 mg/dL), and chloride 126 meq/L. Measles antibody titers were negative. Ziehl-Nielsen stain, Gram stain, and India ink stain were negative. Polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* and herpes simplex virus was also negative. Magnetic resonance imaging (MRI) of the brain was normal. EEG showed generalized spike and wave epileptiform discharges of 110-150 microvolts amplitude, 1.5-2 Hz frequency, lasting for 1-2 s with a periodicity of 20-24 s [Figure 1]. Punch biopsy of the skin from the right axilla was obtained. Histological examination showed the presence of periodic acid-Schiff (PAS)-positive inclusion bodies (Lafora bodies) in the sweat glands [Figure 2]. We had planned and discussed genetic testing but the patient's relatives were not willing for the same. On the basis of clinical presentation and investigations including histopathological examination of the skin biopsy, diagnosis of LBD was confirmed. The patient was managed with antiepileptics (sodium valproate and clonazepam) for myoclonic jerks, baclofen, and physiotherapy for spasticity. Myoclonic jerks were partially controlled but there was no improvement in walking. He was discharged in a stable condition. The patient's relatives were explained about the course and prognosis of the disease. The patient did not come back for follow-up. On telephonic enquiry with family members, we came to know that the patient had expired following a seizure.

Discussion

Periodic EEG patterns include various forms of discharges, usually epileptiform, and may also consist of waves or complexes occurring in a sequence at an approximately regular rate or intermittently regular intervals. Periodic EEG changes are commonly seen in critical patients.[4] They are usually classified as periodic lateralized epileptiform discharges (PLEDs), bilateral independent PLEDs or BIPLEDs, generalized epileptiform discharges (GPEDs), and triphasic waves. PLEDs can be subclassified into PLEDs-proper and PLEDs-plus, and GPEDs into periodic short-interval diffuse discharges (PSIDDs) having a periodicity of less than 4.0 s and periodic long-interval diffuse discharges (PLIDDs).[4] In PLEDs-proper, the periodicity of discharges is relatively stable and there are no associated rhythmic discharges and in PLEDs-plus, the periodicity of discharges is variable and there is an associated low amplitude rhythmic activity.[4] PLEDs are indicative of an acute nonspecific brain dysfunction or unilateral brain lesion, usually destructive. They have been commonly described in cerebral infarction, fast-growing brain tumors (as glioblastoma multiforme), brain abscesses, viral encephalitis (especially related to Herpes simplex virus), Creutzfeldt-Jakob disease (CJD) and hematomas.[4] BIPLEDs arise when PLEDs are seen in both hemispheres. They occur in an independent and asynchronous manner. They are mostly evident in anoxic encephalopathy and central nervous system infection, with a high incidence in comatose patients.[4] GPEDs are characterized by periodic complexes occupying at least 50% of a standard 30-min EEG, projected over both the hemispheres in a symmetric, diffuse and synchronous manner. PSIDDs are usually less specific than PLIDDs and seen in toxic-metabolic encephalopathies, anoxic brain injury, CJD, and subclinical or nonconvulsive status epilepticus. EEG patterns in CJD are usually characterized by PSIDDs with biphasic or triphasic sharp waves, with a duration of 100-300 milliseconds and recurring at 0.7-1.5-s interval.[4] PLIDDs (periodicity of at least 4.0 s) are more specific and have been depicted in some toxic encephalopathies (baclofen or ketamine), anoxic brain injury, and subacute sclerosing panencephalitis (SSPE).[4] EEG changes in SSPE are characterized by periodic or quasiperiodic, bilaterally symmetrical, synchronous, high voltage (200-500 mv), stereotyped sharp and slow wave complexes occurring at a regular interval (usually 5-15 s) and having a constant relationship to myoclonus, it make this one of the most characteristic and disease-specific of all EEG patterns.[4-6] Triphasic waves are periodic and generalized with typically frontal predominance. They include generalized periodic sharp waves or sharply contoured delta waves with a triphasic morphology (classically with a negative/positive/negativity polarity, with each phase lasting longer than the prior phase), recurring at 1.0-3.0 Hz. This pattern may occur in any toxic-metabolic or structural encephalopathy but may have been mostly depicted in hepatic encephalopathy, renal failure, and anoxic injury.[4]

LBD is an autosomal recessive inherited rare disorder characterized by generalized tonic-clonic seizures (GTCS),

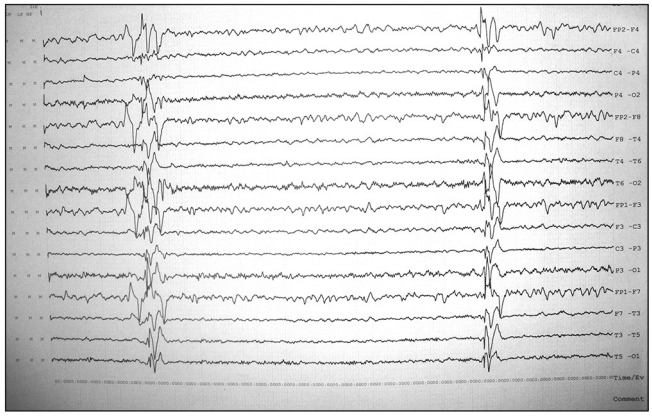

Figure 1: Electroencephalogram of the patient showing generalized periodic epileptiform discharges at an interval of 24 s

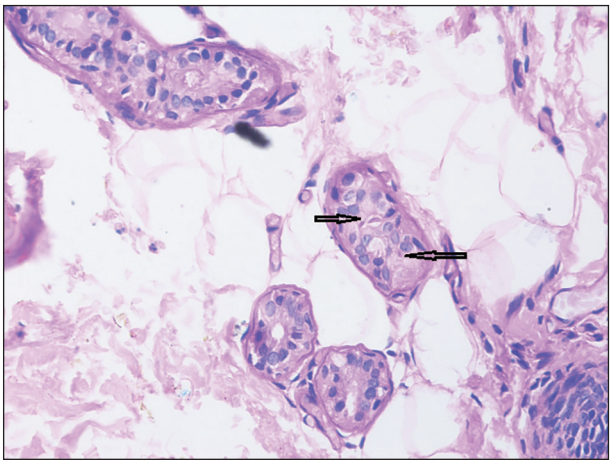

Figure 2: Histological examination of axillary skin biopsy showing periodic acid-Schiff (PAS) positive Lafora bodies in the sweat glands

resting and action myoclonus, ataxia, dementia.[7] It is caused by mutation in the PME 2 gene (EPM2A) on chromosome 6q and EPM2B Gene. The age of onset ranges from 5 years to 20 years but most of the patients present at 13-14 years of age with seizures and myoclonic jerks as the first symptom. Myoclonic jerks are often fragmentary, asymmetric, arrhythmic, and progressively disabling.[7] Occipital seizures with transient blindness and visual hallucinations, atypical absences, and atonic and complex partial seizures have also been described in LBD. Seizures become refractory and are more intractable with disease progression. Death usually occurs within 10 years of onset.[8] At the initial stage, EEG findings include a well-organized background with multiple spikes and wave discharges, and photosensitivity is common. In the next few months to years, with disease progression, the background activity deteriorates. Multifocal epileptiform discharges, mainly occipital in location, appear in addition to generalized bursts. In longitudinal EEG studies, the spike and wave pattern changes from a slow frequency of 3 Hz in the early stages to faster frequencies of 6-12 Hz as the disease progresses.[1,8] Periodicity in EEG changes has not been frequently described in LBD and other progressive myoclonic epilepsy syndromes. Riehl *et al*. depicted the periodic discharges on EEG in a 12-year-old girl with Unverricht-Lafora's disease.[9] Mancardi *et al*. also reported the periodic recurrence of EEG changes in LBD.[10] Correlation between periodicity and clinical state has not been established in LBD; however, Natsumi Isobe *et al*. described the prominence of periodic epileptiform discharges and synchronized paroxysmal activity in a child — onset of Huntington's disease (HD) and dentatorubral-pallidoluysian atrophy (DRPLA) with the progression of the disease.[11] Diagnosis is determined by the analysis of EPM2A gene mutation or demonstration of PAS-positive Lafora bodies in tissues of neurons, skin, liver, and muscles. Examination of the sweat glands in the axillary skin biopsy specimen is a convenient and effective method.[8,12] Currently, no curative treatment is available for LBD. Palliative treatment is given in the form of antiepileptics to control the seizures and myoclonic jerks.[8,13]

Our case presented with progressive cognitive decline with myoclonic jerks with a history of exanthematous illness in childhood and he was not vaccinated for measles. EEG showed generalized periodic epileptiform discharges recurring at 20-24 s (PLIDDs). Initially, it appeared to be subacute sclerosing panencephalitis; however, measles antibody titer was negative and therefore, we planned axillary skin biopsy, which came out to be positive for Lafora bodies.

This case was very unusual, as the periodic discharges in EEG have not been frequently reported in LBD. Our case, which appeared to be subacute sclerosing panencephalitis at presentation, turned out to be LBD after histological examination of skin biopsy. We postulate that possibly periodic discharges in EEG might indicate a fulminant course of the disease as was seen in our case. Patients, particularly children and adolescents, with progressive cognitive decline, myoclonic jerks, and negative measles antibody titer should be investigated for Lafora bodies, even in the presence of periodic discharges in EEG.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Yen C, Beydoun A, Drury I. Longitudinal EEG studies in a kindred with Lafora disease. Epilepsia 1991;32:895-9.
2. Franceschetti S, Gambardella A, Canafoglia L, Striano P, Lohi H, Gennaro E, *et al*. Clinical and genetic findings in 26 Italian patients with Lafora disease. Epilepsia 2006;47:640-3.
3. Smith SJ. EEG in the diagnosis, classification, and management of patients with epilepsy. J Neurol Neurosurg Psychiatry 2005;76(Suppl 2):ii2-7.
4. Andraus ME, Andraus CF, Alves-Leon SV. Periodic EEG patterns: Importance of their recognition and clinical significance. Arq Neuropsiquiatr 2012;70:145-51.
5. Praveen Kumar S, Sinha S, Taly AB, Jayasree S, Ravi V, Vijayan J, *et al*. Electroencephalographic and imaging profile in a subacute sclerosing panencephalitis (SSPE) cohort: A correlative study. Clin Neurophysiol 2007;118:1947-54.
6. Garg RK. Subacute sclerosing panencephalitis. Postgrad Med J 2002;78:63-70.
7. Satishchandra P, Sinha S. Progressive myoclonic epilepsy. Neurol India 2010;58:514-22.
8. Shahwan A, Farrell M, Delanty N. Progressive myoclonic epilepsies: A review of genetic and therapeutic aspects. Lancet Neurol 2005;4:239-48.
9. Riehl JL, Lee DK, Andrews JM, Brown WJ. Electrophysiological and neuropharmacological studies in a patient with Unverricht-Lafora's disease. Neurology 1967;17:502-11.
10. Mancardi GL, Primavera A, Leonardi A, De Martini I, Salvarani S, Bugiani O. Tendency to periodic recurrence of EEG changes in Lafora's disease. Case report. Eur Neurol 1979;18:129-35.
11. Isobe N, Sakai Y, Kira R, Sanefuji M, Ishizaki Y, Sakata A, *et al*. Periodic epileptiform discharges in children with advanced stages of progressive myoclonic epilepsy. Clin EEG Neurosci 2015. [Epub ahead of print].
12. Striano P, Zara F, Turnbull J, Girard JM, Ackerley CA, Cervasio M, *et al*. Typical progression of myoclonic epilepsy of the Lafora type: A case report. Nat Clin Pract Neurol 2008;4:106-11.
13. Ünver O, Demirkesen C, Uysal S. Lafora disease: A progressive myoclonic epilepsy. Turk Arch Ped 2011;46:161-3.