Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2016;29:173-176
DOI: 10.5350/DAJPN2016290210

Case Report / Olgu Sunumu

Lafora Disease Presenting with Acute Anxiety: a Case Report

Esra Ozdemir Demirci[1]

[1]Erciyes University, Faculty of Medicine, Department of Child and Adolescent Psychiatry, Kayseri - Turkey

ABSTRACT

Lafora disease presenting with acute anxiety: a case report

Psychiatric disorders are seen more frequently in patients with epilepsy than in the general population. Personality changes, psychosis, obsessive-compulsive symptoms and mood or anxiety disorders can occur in association with epilepsy. Anxiety disorders and depression are most common psychiatric disorders in patients with epilepsy. Lafora disease (LD) is a treatment resistant epilepsy with onset at the teenage period, followed by progressively worsening myoclonus, seizures, visual hallucinations and cognitive decline, leading to a vegetative state in status myoclonus and death. Different neuropsychiatric symptoms can be seen in patients with LD during the course of the disease. There are as yet no reports on how often patients with epilepsy, such as LD, presented with psychiatric symptoms to clinics at the first disease onset. No case of LD presenting with an anxiety disorder before seizures was reported in the literature. Herein, the case of a 14-year-old female adolescent who presented with acute severe anxiety before seizures, would be discussed.

Keywords: Adolescent, anxiety, epilepsy, lafora disease

ÖZET

Akut anksiyete ile ortaya çıkan lafora hastalığı: Bir olgu sunumu

Psikiyatrik bozukluklar epilepsili hastalarda genel topluma kıyasla daha sık görülmektedir. Kişilik değişiklikleri, psikoz, obsesif-kompulsif semptomlar ve duygudurum ya da anksiyete bozuklukları epilepsi ile ilişkili olarak ortaya çıkabilmektedir. Anksiyete bozuklukları ve depresyon epilepsili hastalarda en sık gözlenen psikiyatrik bozukluklardır. Lafora hastalığı (LH) ergenlikte başlayan, progresif miyoklonuslar, nöbetler, görsel halüsinasyonlar ile bilişsel yıkımın gözlendiği; bitkisel yaşam ile giden status miyokolonus ve ölüm ile sonuçlanan, tedaviye dirençli bir epilepsidir. LH olan hastalarda, hastalıkları süresince çeşitli nöropsikiyatrik semptomlar gözlenebilir. Bununla birlikte LH gibi epilepsili hastaların, hastalığın başlangıcında ne sıklıkla psikiyatrik semptomlarla kliniğe başvurdukları bildirilmemiştir. Literatürde nöbetlerden önce başlayan anksiyete ile başvuran bir LH olgusu bulunmamaktadır. Bu olgu sunumunda kliniğimize nöbetlerden önce akut gelişen şiddetli anksiyete ile başvuran 14 yaşındaki bir kız ergen sunulacaktır.

Anahtar kelimeler: Ergen, anksiyete, epilepsi, lafora hastalığı

Address reprint requests to / Yazışma adresi:
Esra Ozdemir Demirci,
Erciyes University, Faculty of Medicine,
Department of Child and Adolescent Psychiatry, 38039 Talas/Kayseri, Turkey

Phone / Telefon: +90-352-207-6666/20853

E-mail address / Elektronik posta adresi:
esra_z_d_r@hotmail.com

Date of receipt / Geliş tarihi:
July 3, 2015 / 3 Temmuz 2015

Date of the first revision letter /
İlk düzeltme öneri tarihi:
July 23, 2015 / 23 Temmuz 2015

Date of acceptance / Kabul tarihi:
September 9, 2015 / 9 Eylül 2015

INTRODUCTION

Lafora Disease (LD) is the most common and one of severe form of adolescent-onset, progressive myoclonic epilepsies (PMEs), a group of devastating inherited neurodegenerative disorders characterized by progressively worsening myoclonus, epilepsy, early dementia and death (1). Most patients are completely normal in childhood, with the exception of early learning difficulties in some (2). The earliest symptoms are headaches, decline in school performance, spontaneous and induced myoclonus, and convulsive seizures (1).

It was reported that comorbid anxiety disorders and major depression are more common than other psychiatric disorders in epilepsy patients. Researches have shown that anxiety disorders were seen more in female patients with epilepsy, and were associated to frequency of seizures (3). Obsessive-compulsive symptoms, common anxiety symptoms, panic seizures, and panic disorder were more frequently observed in patients with epilepsy than in healthy controls (4). The risk of an anxiety disorder is higher in cases with focal epilepsy than in other cases, and also anxiety disorders occur in those with frontal lobe epilepsies and generalized epilepsies (4). However,

there is no study showing how often patients with epilepsy are presented primarily with an anxiety disorder or depression.

Neuropsychiatric symptoms such as behavioral changes, depression, apathy, are also often present in LD as in other epilepsies (5). The frequency of anxiety disorders in treatment-resistant patients with epilepsy, such as patients with LD, who are scheduled for surgical treatment is 10%-44%, whereas the frequency is 11% in primary care among epileptic patients (6,7). However, it is not known definitely how often patients with epilepsy, such as LD, present with anxiety symptoms to clinics at the onset of disease. In the literature review, we could not come across with any cases with LD which presented with an anxiety disorder.

In this case, a 14-year-old female patient who presented with acute severe anxiety, and complaints of headaches, speech difficulties, decline in school performance, and whose anxiety symptoms did not improve after treatment with selective serotonin reuptake inhibitors (SSRI) is discussed. Her symptoms were followed by mutism and progressive convulsive seizures. With this case, we aimed to draw attention to differential diagnosis of underlying acute severe anxiety. Written informed consent was obtained from the patient and her family.

CASE

A 14-year-old female patient presented to Erciyes University, Faculty of Medicine, Child and Adolescent Psychiatry outpatient clinic in May 2012 with complaints of acute severe anxiety, headaches, speech difficulties and decline in school performance. She often worried that something bad would happen, had attacks which lasted about 10 minutes accompanied by sweating and palpitations twice a day and feared that she would die during an attack. She began to mispronounce letters and to stutter from time to time. She had headache accompanied by photophobia and visual hallucinations which did not responding to analgesics. Her concentration ability was decreased, so her school performance declined. Because of headaches, she could not attend school. Her complaints began suddenly in March 2012, except for headaches without any reason such as trauma. Previously, in 2008, she applied to a neurology outpatient clinic with her complaints and her preliminary diagnosis was made as migraine, so analgesic treatment was recommended. She was referred to our clinic with her family, because of increasing headache attacks and other complaints. She did not have any health problems until her complaints began. The patient and family histories were negative for mental and neurological diseases. Her blood analysis was within normal limits. The patient's Hamilton Anxiety Rating Scale (HAM-A) score was 32 points, and she described her anxiety as varying from a feeling of tension to an intense sense of fear and panic. As she had the preliminary diagnosis of panic attacks and unspecified anxiety disorder, and also she met the criteria for generalized anxiety disorder (GAD), except for duration of disorder, treatment with escitalopram 5mg/day and lorazepam 3mg/day was started. Because her headaches did not respond to analgesics and her panic attacks continued, neurology and cardiology consultation, electroencephalography (EEG) and magnetic resonance imaging (MRI) were performed. Her cardiologic assessment was normal. The escitalopram dose was increased to 10mg/day. Her anxiety symptoms did not improve with treatment of SSRI and benzodiazepine medication after 6 weeks, her HAM-A score increased from 32 to 35 points. Her symptoms were rapidly followed by mutism and progressive convulsive seizures for two months. EEG recording showed spikes over the temporal occipital regions and photosensitivity. Brain MRI was normal. Therapy with antiepileptics caused decrease in the frequency of seizures. Adjunctive therapy with clonazepam reduced the intensity of myoclonus. However, progressive worsening of cognitive and motor functions occurred within a few months. Skin biopsy was planned for the patient who was considered as having refractory epilepsy by the neurology department. Her diagnosis was made due to the presence of polyglucosan inclusion bodies (Lafora bodies) shown in skin biopsy performed in the axilla.

Lafora bodies were seen in cell types related to the sweat glands, specifically the duct cells of the eccrine glands and the myoepithelial cells surrounding apocrine glands. Also, a homozygote NHL repeat containing 1 (NHLRC1) mutation and novel homozygous epilepsy progressive myoclonus type 2A (EPM2A) mutation were detected in the patient. In the following six months, her mental decline continued without a decline resulting in severe disorientation, akinesia, hypertonia, and inability to feed, which was her clinical state prior to her admission for status epilepticus and death.

DISCUSSION

LD classically starts in adolescence in otherwise neurologically normal individuals, and usually with action and stimulus-sensitive myoclonus as well as tonic–clonic, absence, atonic, and visual seizures. The first symptoms can be dysarthria, mutism, headaches, attention deficits, depression, spontaneous and induced myoclonus, and convulsive seizures, with EEG showing background slowing and occipital-based irregular spike-wave discharges (1). The initial symptoms are followed by rapidly progressive dementia, refractory status epilepticus, psychosis, cerebellar ataxia, dysarthria, mutism, and respiratory failure which lead to death within about a decade (5,8). In our case, consistent with the literature, a 14 years old adolescent patient who was completely normal in the childhood, presented with panic attacks and GAD symptoms, and complaints of headaches, speech difficulties and decline in school performance. These initial symptoms were followed by rapidly progressive spontaneous and induced myoclonus, convulsive seizures and death.

In adults with epilepsy, depression and anxiety are the most prevalent psychiatric disorders (9). Many studies have been performed on children and adolescents with epilepsy. Ettinger et al. (10) assessed depression and anxiety with quantitative scales in a population of children and adolescents aged from 7 to 18 years with epilepsy and reported that 26% of patients had increased depression scores, and 16% had anxiety symptomatology. Oguz et al. (11) reported that adolescents with epilepsy aged between 12 and 18 years of age had higher depression and anxiety scores when compared with the control group. Dunn et al. (12) reported that 23% of 115 adolescents with epilepsy aged between 12 and 16 years had symptoms of depression. It was reported that GAD was most frequently observed in patients with epilepsy (13). Also, ictal anxiety disorders complicated severely the differential diagnosis of psychiatric diseases. Fear could occur as the only symptom of a simple partial seizure different from other ictal phenomena, and it could also be the aura of a complex partial seizure (14). There may be autonomic symptoms associated with fear during a simple partial seizure, such as palpitations, epigastric disorder, nausea, and increase in respiratory rate, paleness or flushing as in panic attacks. It was reported that patients with epilepsy who had structural lesion on the right temporal lobe were erroneously diagnosed as having panic attack disorder (15). Despite all information in the literature, it is not known definitely how often patients with epilepsy present with an anxiety disorder or depression at onset of the disorder. Our case who was presented with acute severe anxiety, met the criteria for panic attacks and also GAD except duration of the disorder before epilepsy.

The frequency of anxiety disorders in treatment-resistant epileptic patients who are scheduled for surgical treatment is 10%-44%, whereas the frequency is 11% in primary care among patients with epilepsy (6,7). Also, it is known that (4) the amygdala and right temporal focus play an important role in the formation of temporal-derived anxiety symptoms, and epileptic discharges. Some cases with complex partial status epilepticus described anxiety symptoms treated with right temporal lobectomy (16). Ictal fear was reported in about 50% of patients with epilepsy and amygdala volume was lower in patients with ictal symptoms of anxiety (4). Consistent with the literature, in our case, anxiety symptoms were not improved with treatment by SSRI, and benzodiazepines. Besides, EEG recording showed spikes over the temporal occipital regions and photosensitivity. However, the volumes of the

amygdala and the temporal region were measured normal by MRI examination. It was thought that this might be due to acute onset of the disease. Also, anxiety symptoms which patient experienced before seizure initiations could be another reason.

In a conclusion, clinicians should be aware that patients who develop acute symptoms of anxiety, especially panic attacks or GAD symptoms, may have a differential diagnosis underlying anxiety. Treatment resistant patients with anxiety symptoms could have a clinical tendency for a more severe disorder including LD.

Contribution Categories	Name of Author
Follow up of the case	E.O.D.
Literature review	E.O.D.
Manuscript writing	E.O.D.
Manuscript review and revisation	E.O.D.

Conflict of Interest: Author declared no conflict of interest.

Financial Disclosure: Author declared no financial support.

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