

A case of epileptic psychosis culminating in attempted suicide related to the use of antiepileptic

Antiepileptik kullanımıyla ilişkili intihar girişimiyle sonuçlanmış bir epileptik psikoz vakası

Hava Özlem Dede¹, İsmet Murat Melek², Asena Akdemir³, Taşkın Duman⁴, Esra Okuyucu²

¹ Dr., Mustafa Kemal University, Department of Neurology, Hatay, Turkey

² Asoc.Prof.Dr., Mustafa Kemal University, Department of Neurology, Hatay, Turkey

³ Prof.Dr., Mustafa Kemal University, Department of Psychiatry, Hatay, Turkey

⁴ Prof.Dr., Mustafa Kemal University, Department of Neurology, Hatay, Turkey

Abstract

Psychosis is seen in approximately 5.4% of epileptic patients, a rate which is eight times that of the normal population. The commonest type of seizure seen with epileptic psychosis is complex partial seizure which is resistant to treatment. It has been suggested that 2% of epileptic psychosis cases are related to the use of Lamotrigine, and suicidal thoughts have been reported in 0.43-1.84% of patients using antiepileptic drugs. In this article, a 45-year-old woman, who had been taking antiepileptic treatment for fifteen years, and who had idiopathic epilepsy with resistant generalised tonic-clonic seizures, was presented. Valproic acid and later Carbamazepine failed to bring her seizures under control, and in the past year, after the use of Lamotrigine was started, her seizure type changed to complex partial seizure. During the course of treatment with 250mg/day of Lamotrigine, monitoring by magnetic rezonans imaging, and checking that her electroencephalography was within normal limits, indications of psychosis began to be observed. The patient began to hear voices ordering her to kill herself, after which she made an attempt at suicide in which she made lateral cuts to both wrists and her neck. It was decided that this attack, which began after a change in antiepileptic medication, was epileptic psychosis related to Lamotrigine. Her antiepileptic treatment was changed and antipsychotic treatment was begun. This case is presented with the aim of making known and discussing this rare attempted suicide in an epilepsy patient using Lamotrigine, and the severe consequences of psychosis related to the drug.

Key words: Suicide, antiepileptic drugs, toxic psychoses

Özet

Psikoz, epileptik hastaların yaklaşık %5,4'ünde gözlenir ve bu oran normal populasyondan sekiz kat daha fazladır. Epileptik psikozda en sık görülen nöbet tipi; tedaviye dirençli kompleks parsiyel nöbetlerdir. Epileptik psikoz vakalarının %2'sinin Lamotrigine kullanımına bağlı olduğu düşünülmektedir ve antiepileptik ilaç kullanan hastaların %0,43-1,84'ünde intihar düşünceleri rapor edilmiştir. Bu makalede 45 yaşında, onbeş yıldır antiepileptik tedavi alan ve idiopatik epilepsi ile birlikte dirençli generalize tonik-klonik kasılmaları olan kadın hasta sunulmuştur. Valproik asit ve ardından kullanılan Karbamezapin nöbetlerini kontrol altına almada yetersiz kalmış, ve son yıl içerisinde kullanılmaya başlanan Lamotrigine sonrası nöbetleri kompleks parsiyel şekle dönmüştür. 250 mg/gün dozunda sürdürülen Lamotrigine tedavisi sırasında; magnetik rezonans görüntülemesi ve elektroensefalografi kontrolleri normal sınırlarda olan hastada, psikoz gözlenmeye başlandı. Hasta, kendini öldürmesi gerektiğine dair sesler duymaya başlamasından sonra, her iki el bileği ve boynuna yaptığı kesilerle intihar girişiminde bulundu. Bu atağın, epileptik tedavideki değişim sonrası Lamotrigine kullanımına bağlı gelişen epileptik psikozla ilgili olduğu düşünüldü. Antiepileptik tedavisi değiştirildi ve antipsikotik tedavi başlandı. Bu makale, Lamotrigine kullanan hastalarda nadirde olsa ortaya çıkabilecek intihar girişimlerinin ve bu ilaca bağlı psikozun ciddi sonuçlarının bilinmesi ve tartışılması amacıyla sunulmuştur.

Anahtar kelimeler: İntihar, antiepileptik ilaçlar, toksik psikozlar

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Introduction

Although the precise mechanism of the formation of psychotic findings in epilepsy patients is not known, there are many hypotheses. It is thought that epileptic

activity plays a role in the physiopathology of cell loss in the amygdala and other limbic areas, degenerative processes such as gliosis, increasing synaptic transition, and a reduction in stimulation threshold (1). The use of antiepileptic drugs can cause psychotic symptoms in ways which have not yet been defined. In particular,

psychosis cases have been reported with the use of the new generation of antiepileptic drugs such as Lamotrigine, Levatiracetam, and Topiramate (2). In Turkey, studies have been performed on the child patient population on the side effects of antiepileptic drugs of a tendency to depression and attempted suicide (3).

Case

The 45-year-old female patient had been receiving anti-epileptic treatment for 15 years. When she was first diagnosed, her seizures were generalised tonic-clonic in nature, and she did not describe an aura. There was no history of epilepsy in her family and she had no history of head trauma, feverish illness or metabolic disease. She was given Valproic acid at a dose of 1000mg/day and blood drug levels were monitored at the upper limits but the seizures were not brought under control and therefore Carbamazepine treatment was added. At a Carbamazepine dose of 800 mg/day, thrombocytopenia was observed and Carbamazepine was gradually reduced and stopped; almost one year ago treatment with Lamotrigine was started. With a treatment of 250 mg/day of Lamotrigine, the number of her seizures was reduced and the type of seizure changed to a complex partial seizure type. In the last month; almost daily complex partial seizures were identified accompanied by motor automatism and stereotypical movements, although oromandibular automatism was not observed. Those close to her, reported that the patient had become more irritable and disagreeable in the past year. In the past three months she had begun talking to herself and had started talk about imaginary people. She had hallucinations of a sexual nature at night after which she said the devil had entered her and tried to make her do bad things. She said that she heard a man's voice ordering her to kill herself, and she injured herself with horizontal cuts to both wrists and her neck. After this attempted suicide, the patient was brought by her family to our outpatients' clinic. Cranial magnetic resonance (MR) images and electroencephalography (EEG) were within normal limits. It was concluded that her complaints, which had begun with the use of Lamotrigine, were (epileptic) psychosis with organic causes developing in connection with unwanted side-effects of the anti-epileptic. The skin rash expected as a side effect of the use of Lamotrigine was not observed, but the rare side effect of epileptic psychosis and suicide attempt was seen. An assessment was made together with the Psychiatry Department and the patient was transferred under observation to antipsychotic treatment. 10mg of Aripiprazol was started and when the side-effect of tremor was observed, treatment was changed to 10mg of Olanzapine. After treatment with

Lamotrigine had been reduced and stopped, the patient's psychotic delusions lessened. The aural and visual illusions stopped completely. Her cooperativeness increased. Treatment with Levatiracetam was started and increased gradually to a dose of 3000 mg/day. The frequency of the patient's complex partial seizures, which had been 1-2 a day, was reduced to once a month. There were no generalised tonic-clonic seizures.

Discussion

Following the recognition that epilepsy is an organic disease relating to the neurobiology of the central nervous system, the reasons for the personality changes seen in epilepsy patients have not been identified in detail even though accompanying psychiatric findings have been observed (4). The first among the suggested mechanisms is the great social burden of epilepsy as a disease and the patient's ejection and isolation from society. The cerebral pathologies that cause epilepsy may be the cause of the psychiatric illnesses. In the neurobiology of psychotic disorders focal points of gliosis in the medial temporal lobe and the amygdala have come to the fore as lesions in common (5,6,7,8). Degeneration caused by epileptic activity in the amygdala and limbic areas has been considered to be the cause of the psychosis seen in epilepsy patients (9). Psychotic symptoms can be seen in connection with epilepsy in ictal, postictal and interictal periods. It has been emphasised that psychosis in the post-ictal period may begin in the ictal period. Also, in conditions where pathological findings are not seen in scalp EEG examination, changes may be observed by stereoelectroencephalography (SEEG) relating to limbic seizure activity. It is generally difficult to distinguish interictal psychosis from primary schizophrenia. In seizures which cannot be brought under control, interictal psychosis can cause a permanent psychotic condition in 5% of cases. Complex partial status epilepticus, in particular when it is of temporal lobe origin, can be confused with primary psychosis. The observation of epileptic activity by SEEG, the patient's nearly 10 years of history of epilepsy, in particular temporal lobe epilepsy, the time relationship between the most recent attacks and the psychiatric symptoms, the short psychotic attacks and the increased frequency of generalised tonic-clonic seizure before the psychotic symptoms are characteristics indicating epileptic psychosis (1,10,11).

Epileptic psychosis can be seen in connection with use of the new generation of antiepileptic drugs such as Topiramate, Levatiracetam and Lamotrigine. Antiepileptic drugs are effective through many different

mechanisms (12). One of the best known mood regulator mechanisms has serotonergic effects and also negative psychotropic effects (13). The antiepileptic which is thought to reduce the risk of attempted suicide, Carbamazepine, is thought to have this effect by raising extracellular serotonin levels. Antiepileptic drugs such as Phenobarbital, Clonazepam, Clobazam, Valproate, Gabapentin and Tiagabine are effective by raising aminobutyric acid (GABA) levels or potentializing its effect. Levitiracetam on the other hand reduces GABA levels. Gamma aminobutyric acid is a neurotransmitter which has a direct effect on the state of mind. It has been emphasised that the group of drugs which either raise or lower GABA levels can increase suicide attempts. There are studies showing that Valproate has a positive effect on the state of mind but results are not conclusive. It has been suggested that in researching the effects of the drug, the effect which would form the patient's basal state of mind was being shown (14).

In a 13-year monitoring of 1400 patients receiving Lamotrigine treatment, 6 patients showed development of epileptic psychosis characterised by generally schizophrenia-like paranoid hallucinations (15). Cases of epileptic psychosis where negative symptoms were in the foreground are rarer (1). The dose in Lamotrigine treatment for patients who develop psychosis is 300-700mg. The toxic dose limit in Lamotrigine treatment is >0.8mg/kg. Psychotic signs are observed independent of dose. It has been shown that there are risk factors of temporal lobe epilepsy and psychiatric comorbidity when psychosis develops when Lamotrigine is used (14). In this case, psychosis was observed with advancing positive symptoms in the foreground of irritability, talking to herself, auditory and visual hallucinations; beginning when Lamotrigine 250mg/day treatment was started.

Epileptic psychosis is treated with Risperidone 4-6 mg/day, Olanzapine 5-15mg/day, Quetiapine 400-600 mg/day, Amisulpride 400-800 mg/day or Clozapine 300-700 mg/day (1). The use of Ziprasdone and Aripiprazole are recommended (1). This patient was treated with 20 mg/day Olanzapine and 10mg/day Aripiprazole for her psychotic symptoms. Treatment with Lamotirigine was progressively terminated and at the same time treatment with Levitiracetam was started, after which the psychotic symptoms were observed to recede from the first week. In a check-up at the end of the first month, there were no generalised tonic-clonic seizures and the frequency of complex partial seizures had decreased. Her cooperativeness had increased, her auditory and visual hallucinations had ceased. Levitiracetam, the anti-epileptic chosen for the treatment of this patient, is reported to depress the

emotional state and increase the risk of attempted suicide (13). The best choice with regard to suicide attempts, Carbamazepine, was not used with our case because of side-effects, and treatment was successful with Levitiracetam. Following the suicide attempt, the patient was monitored for a year, during which her psychotic features almost completely disappeared, and no further attempts at suicide were seen. Antipsychotic treatment was reduced under the monitoring of the Psychiatric Department. No generalised tonic-clonic were seen. In the last six months, partial attacks of automatism involving hand-wringing were observed twice.

Conclusion

This case indicates that the psychotic symptoms seen in epilepsy patients can be caused by the new generation of anti-epileptic drugs. It was presented to emphasise the importance of careful monitoring of patients under treatment for epilepsy for psychotic symptoms which may develop and the necessity of keeping in mind the possibility of serious results such as attempted suicide. The risk of attempted suicide is rising with all anti-epileptic drugs. According to Food and Drug Administration (FDA) data for 2008, an increase of the risk of attempted suicide of 2.43% has been seen with Levitiracetam, 2.57% with Topiramate, 1.96% with Zonisamide, 1.78% with Lamotirigine, and 1.52% with Pregabalin. It was determined that the increased risk was least with Carbamazepine at 0.66% (14, 16).

When planning anti-epileptic treatment, it is advantageous to take into account the drug's effect on increased risk of suicide and to evaluate the risk of suicide in at-risk patients in a clinical check-up.

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İletişim:

Dr. Hava Özlem Dede

Mustafa Kemal Üniversitesi Tıp Fakültesi

Nöroloji Anabilim Dalı Hatay-Türkiye

Tel: +90.505.2869346

e-mail: havaozlemdede@hotmail.com

