

Status Epilepticus Associated with Ecstasy

Ekstazi İlişkili Status Epileptikus

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Summary

Status epilepticus (SE) is a life-threatening emergency condition. In addition to well-known etiological factors, many rare causative factors have also been defined. Ecstasy (3,4-methylenedioxy-N-methylamphetamine) is an amphetamine derivative known to cause SE. Presently described is a case of recurrent SE in which ecstasy was an etiological factor.

Keywords: Ecstasy; epilepsy; status epilepticus.

Özet

Status epileptikus hayatı tehdit edebilen bir acil durumdur. İyi bilinen sık etiyolojik faktörlerin yanı sıra nadiren görülebilen birçok neden tanımlanmıştır. Ekstazi (3,4-methylenedioxy-methamphetamine) bir amfetamin türevidir ve status epileptikusa neden olduğu bilinmektedir. Bu yazıda, tekrarlayan status epileptikus tablosu gelişen ve etiyolojisinde ekstazinin sorumlu tutulduğu bir olgu sunuldu.

Anahtar sözcükler: Ekstazi; epilepsi; status epileptikus.

Introduction

Status epilepticus (SE) is a neurological condition with high morbidity and mortality if not treated urgently.^[1] There are many well-known common causes, such as cerebrovascular disease, central nervous system (CNS) infection, metabolic disorder, and sudden withdrawal of antiepileptic drugs, as well as rare etiological factors, including drugs and toxins. One such drug is 3,4-methylenedioxy-N-methylamphetamine (MDMA/ecstasy), a synthetic amphetamine derivative, which has increasingly been abused as a psychostimulant by the young population.^[2] Presently described is a case of a patient who twice developed SE that was determined to be associated with ecstasy use.

Case Report

A 20-year-old female was brought to the emergency department in October 2013 due to contractions in her arms and legs, foaming at the mouth, and cyanosis lasting for two minutes, repeating twice within one hour. While she was undergoing an examination in emergency room, a generalized tonic-clonic (GTC) seizure was observed by a neurologist. She had a body temperature of 38.1°C, a white blood cell count of 23,900/μL, creatinine level of 1.27 mg/dL, and creatinine kinase (CK) of 1905 mg/dL. On the first neurological examination, she was lethargic and had uncertain nuchal rigidity. Bilateral extensor plantar response was present (occasionally spontaneous) and spontaneous nys-



tagmus was detected in both eyes. Bilateral Achilles clonus and Hoffmann's sign were observed. Brain computerized tomography (CT) was normal. Due to recurrent seizures, the patient was admitted to the neurology clinic and oral valproic acid (VPA) 1000 mg/day treatment was administered. Another GTC episode was observed during clinical follow-up, as well as another two GTC episodes that occurred without recovery of consciousness between them, and the patient was considered to have status epilepticus (SE). She did not respond to 10 mg intravenous diazepam; clinical seizures stopped after loading diphenylhydantoin (20 mg/kg). At about four hours after the end of the seizures, infrequent, generalized, sharp, sharp-slow wave activity was observed on electroencephalography (EEG) with rapid ground activity. A neurological examination after becoming clinically stable revealed lethargy, bilateral extensor plantar response, brisk deep tendon reflexes, bilateral Achilles clonus and Hoffmann's sign findings. CK was 11,140 mg/dL and creatinine was 1.58 mg/dL. Other routine biochemical parameters were normal. Examination of the cerebrospinal fluid was clear and no cells were observed.

According to the information received from the patient and relatives, there was no known disease or history of epileptic seizure, no alcohol use or drug addiction. She was taking venlafaxine 150 mg/day for three months for depressive disorder and smoked approximately five or six cigarettes per day.

On the second day of hospitalization she was intubated and put on mechanical ventilation as a result of developing hypoxemia. The x-ray showed patchy density in the middle and lower zones of the lungs. The patient had a high fever and her urine culture was negative. Thorax tomography revealed bilateral pleural effusion and consolidation areas with air bronchograms in the parenchyma and peribronchial patchy densities. On the sixth day of hospitalization, a fever of 38°C was still present. She was extubated after 5 days. Contrast-enhanced brain magnetic resonance imaging was normal. Neurological examination was normal except bilateral extensor plantar response, bilateral Achilles clonus and Hoffman's sign. During this period, bilateral, temporal and frontotemporal slow (theta and infrequent delta) wave paroxysms were observed on EEG, predominantly on the right side (Figure 1). A neurological examination was normal on the 14th day of the hospitalization and she was discharged with valproic acid (VPA) 750 mg/day treatment.

Approximately two months later, the patient was brought back to the emergency department with another SE episode. Sudden cardiac arrest developed during diphenylhydantoin infusion. After resuscitation, the patient was monitored for five days in anesthesia intensive care unit and transferred to our clinic. Neurological examination revealed bilateral extensor plantar response and brisk deep tendon reflexes in the lower extremities. A thoracic CT showed

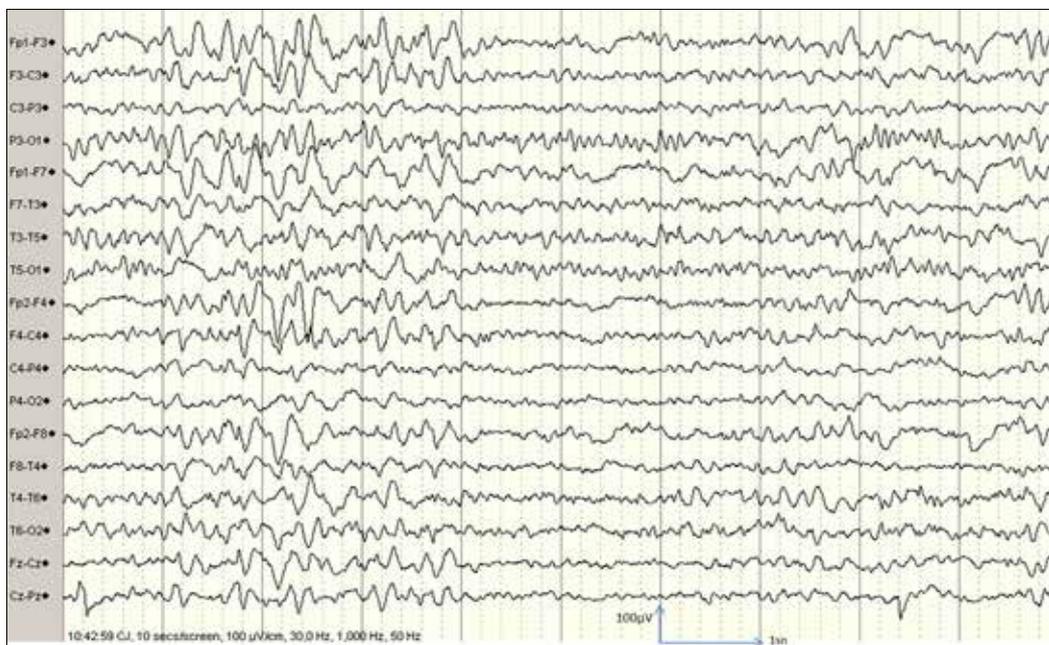


Figure 1. Bilateral, temporal and frontotemporal slow wave paroxysms observed on EEG.

pleural effusion consolidation areas and frosted glass densities in the thorax, both pulmonary lower lobes, the left upper lobe, and the right upper lobe. Alveolar hemorrhage and vasculitis were considered in differential diagnosis. Her medical history was negative in terms of vasculitis and all vasculitis markers were negative. Bronchoscopy revealed hemorrhagic fluid in the left lower lobe aspiration. In the histopathological examination of the fluid, iron deposition was observed in macrophages using a special staining method with Prussian blue that was evaluated as compatible with old alveolar hemorrhage. In the toxicological evaluation of the patient using cloned enzyme donor immunoassay method, urine specimen was positive for amphetamine/MDMA (ecstasy). Upper limit value for amphetamine was determined to be 500 ng/mL and the value of urine sample was 1691.3 ng/mL. The patient was also assessed for psychiatric conditions. It was determined that recurrent SE was associated with ecstasy use. Hypoxemia-required mechanical ventilation of her first hospitalization was thought to be ecstasy-related diffuse alveolar hemorrhage.

The patient has been seizure free for 2 years since discharge with VPA 750 mg/day.

Discussion

This case report is a rare example of drug abuse causing SE. Common etiological causes of SE include cerebrovascular disease, CNS infection, intracranial tumor, head trauma, metabolic disorder, alcohol-related conditions, and sudden withdrawal of antiepileptic drugs.^[3] It is relatively easy to establish the presence of these factors and they are less likely to be overlooked during routine investigations for SE etiology. However, clinicians should also be mindful of rare conditions.

Tan et al. identified 181 rare causes after an extensive examination of 558 articles in a review. These are classified in five categories: immunological disease, mitochondrial disease, infectious disease, genetic disease, and drugs and toxins. Approximately 70 drugs and toxins can cause or facilitate SE.^[3] It is important to evaluate each patient individually. Among rare causes, ecstasy should be considered, especially in young patients.

Ecstasy may cause hyperthermia, coagulopathy, rhabdomyolysis, renal failure, hyponatremia (due to inappropriate antidiuretic hormone secretion syndrome and excessive

fluid intake), and have proconvulsant effects at toxic doses.^[4] It also plays a role in formation of seizures by acting on monoamine system in the brain, especially through serotonin (5HT).^[5] MDMA acts as a stimulant, entactogen, and hallucinogen.^[5] Abuse of MDMA has become widespread in recent years.^[6] Epileptic seizures may occur spontaneously or be provoked by particular factor. Acute metabolic changes can trigger seizures. Primate studies have demonstrated chronic depletion of 5HT terminals after prolonged use of MDMA had proconvulsive effect.^[7]

Brown et al. compared patients with amphetamine-associated first seizure (44 patients) with two other first-ever seizure control groups. The first control group (126 patients), included patients with first seizure due to proconvulsive non-amphetamine drug use, drug or alcohol withdrawal, or metabolic and other systemic diseases. In the second control group (401 patients) there were patients with first-ever seizure without trigger factor. SE was observed in 2% (3 patients) in the first control group, 1% (5 patients) of the second control group, and was not observed in the study group with patients who abused amphetamine. All amphetamine-associated seizures were generalized seizures, while the rate was 98% in the first control group and 96% in the second control group.^[8]

Our patient did not have any seizures during the two-year follow-up period. The prognosis for amphetamine-associated seizures is good, recurrence is rare, and is often associated with re-exposure. The likelihood of developing epilepsy is low (7%).^[8]

In cases of intoxication resulting in SE, in addition to abuse of stimulants, the possible role of antidepressant drugs is also significant. These include bupropion, amoxapine, fluoxetine, clomipramine, amitriptyline, citalopram, and fluvoxamine, as well as venlafaxine.^[3] Venlafaxine has an interesting aspect. Psychostimulant effects of venlafaxine have been described as mixture of entactogenic, euphoric mood and live dreams. Some users even describe venlafaxine as "baby ecstasy".^[9] Our patient had used venlafaxine for 3 months. It was an interesting association, and it is likely that venlafaxine lowered seizure threshold and facilitated development of SE following MDMA use.

Diffuse alveolar hemorrhage following oral amphetamine intake is a rare condition.^[10] In our case, during the first epi-

sode of SE, the cause of sudden hypoxemia could not be explained clearly, but bronchoalveolar lavage and pathological examination revealed it was consistent with alveolar hemorrhage.

Although the patient was questioned in detail with regard to toxic substance intake, the cause of SE could not initially be determined. Analysis of toxic substance provided an explanation of the patient's seizures and conducting such analysis in addition to routine examinations in patients with their first episode of seizure should be kept in mind.

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