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CASE REPORT / OLGU SUNUMU

Effects of Lacosamide in Cerebral Tuberculoma–Induced Nonconvulsive Status Epilepticus: A Case Report


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Serebral Tüberküloma Bağlı Nonkonvülzif Status Epileptikusta Lakozamidin Etkisi: Olgu Sunumu

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Summary

Nonconvulsive status epilepticus (NCSE) is characterized by unexplained changes in behavioral and mental status accompanied by a continuous seizure activity seen on electroencephalography. The treatment is similar to that of status epilepticus. Lacosamide is one of the newer antiepileptic drugs that slows down the inactivation of voltage-dependent sodium channels. It has high oral bioavailability and low protein binding, and is primarily metabolized by the liver enzyme CYP2C19. Central nervous system (CNS) tuberculosis may present with signs of parenchymal lesions instead of meningitis. This study aimed to present a case study of a patient who was diagnosed with CNS tuberculosis a year ago with NCSE, which could be not controlled by levetiracetam. However, the use of lacosamide successfully resolved the NCSE condition.

Keywords: CNS tuberculoma; lacosamide; nonconvulsive status epilepticus.

Özet

Nonkonvülzif status epileptikus (NKSE) davranışlar ve mental durumda açıklanamayan değişiklik, elektroensefalografide (EEG) devamlı nöbet aktivitesinin eşlik ettiği tablodur. Tedavide status epileptikus tedavisi uygulanmaktadır. Lakozamid, voltaja bağımlı sodyum kanallarının yavaş inaktivasyonu ile etki eden, oral biyoyararlanımı yüksek, proteine düşük oranda bağlanan, karaciğerde başlıca CYP2C19 ile metabolize olan yeni antiepileptik ilaçlardan biridir. Merkezi sinir sistemi (MSS) tüberkülozu karşımıza menenjit şeklinde değil de parenkim lezyonları şeklinde çıkabilir. Bu yazıda, bir yıl önce MSS tüberkülozu nedeniyle tanı almış ve tedavi başlanmış olmasına rağmen yeni gelişen nonkonvülzif status kliniği ile başvuran, levetirasetam tedavisine yanıt vermeyen, lakozamid tedavisi altında tam nöbetsizlik sağlanan hasta literatür verileri eşliğinde sunuldu.

Anahtar sözcükler: MSS tüberkülomu; lakozamid; nonkonvülzif status epileptikus.

Intraduction

The nonconvulsive status epilepticus (NCSE) behavior is characterized by unexplained changes in the behavioral and mental status.[1] If this condition lasts for more than 5 min and is followed by a continuous seizure activity seen on electrocephalography (EEG), the diagnosis becomes clear.[2] Although different suggestions for NCSE classification are available, it is studied in two general parts.[3] The first one is called a generalized form (absence status epilepticus), and the second one is called a partial-focal form (complex partial status epilepticus).[3] In the Krumholz's classification, NCSE

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was associated with different clinical pictures, and all these forms were evaluated under the title of encephalopathies.[4] Kaplan classified NCSE cases according to their subtypes, such as generalized NCSE, localization-dependent NCSE, and uncertain NCSE, and noted that each subtype could be evaluated as light, moderate, and heavy coma scores.[5]

Lacosamide is an amino acid that has an acetamido-N-benzyl-3-methoxypropionamide structure, and it increases the inactivation of voltage-gated sodium channels selectively and reduces the pathological hyperstability without causing any changes in the physiological activity of neurons.[6–9]

It is a functionalized amino acid compound that binds to proteins at a low level (<15%) and has 100% oral bioavailability due to its pharmacokinetic characteristic. It can reach the peak blood concentration in 1–2 h, and its half-life is 13 h. It is usually excreted through kidneys and has no known drug–drug interaction.[10]

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis, which continues to threat public health and is a common disease in developing countries.[11–14] Central nervous system (CNS) impairments are seen in 5%–10% of cases with tuberculosis, and they may end up being meningitis, solitary tuberculoma, apse, infarct, or miliary parenchymal disease. Tuberculomas causing neurological findings due to local compression are less common. Tuberculomas generally respond to anti-tuberculosis treatment within 2–3 months.[15]

Case Report

A 53-year-old woman visited the outpatient clinic with complaints of vacant staring and not responding to questions for the past 2 weeks. She had started levetiracetam at a dose of 750 mg, twice a day (oral), treatment 1 week ago in another clinic, but no change was observed in her clinical picture. The neurological examination revealed that the condition that starts with blinking, vacant staring, and not responding to questions happened 10–20 times in an hour and lasted 30–40 s. She became conscious and co-operated between two seizures, and had no motor deficits.

The patient's clinical history revealed that she underwent a cerebrovascular disease 3 years ago; multiple lesions were detected in her brain using magnetic resonance imaging (MRI), which was performed because of headache, nausea,

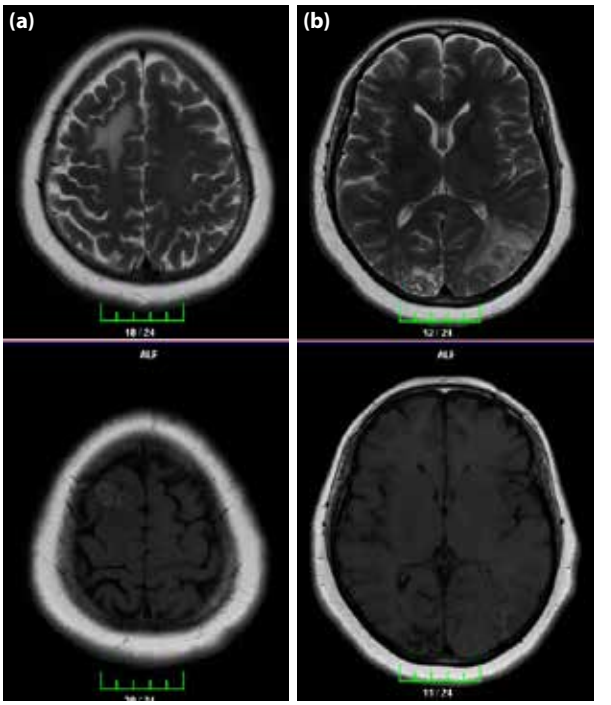

Fig. 1. **(a, b)** Multiple lesions of 1.5 cm diameter.

and vomiting complaints (Figure 1a and 1b). At that time, the desired markers of the patient in terms of paraneoplasia and vasculitic processes were normal. The computed tomography (CT) of thorax and abdomen was requested due to a metastatic mass with unknown primary origin. Her abdominal CT revealed a 12×13 mm^2 hypodense lesion that did not lead to mass expansions in the liver. No features were detected in her positron emission tomography (PET) scan done for determining the disease etiology. The patient was diagnosed with tuberculosis after taking a biopsy sample from the hypodense lesion in her liver, and anti-tuberculosis (anti-tbc) treatment was started. The patient visited the clinic due to the development of present complaints while she was under anti-tbc treatment. She was using levetiracetam 1500 mg/day, isoniazid (INH) 300 mg/day, ethambutol 1500 mg/day, rifampicin 600 mg/day, morphozinamide 2000 mg/day, and clopidogrel 75 mg/day when she visited the clinic. Her routine blood test parameters were as follows: hemoglobin, 10.1 mg/dL; erythrocyte sedimentation rate, 80 mm/hour; and C-reactive protein, 26 mg/dL. (Her other biochemical analyses, thyroid function tests, antibodies, and tumor markers were normal.).

High-amplitude, generalized, multiple-spike, slow wave activities were detected in her EEG (Figure 2a and 2b). Her brain MRI showed lesions at left occipital and right frontal

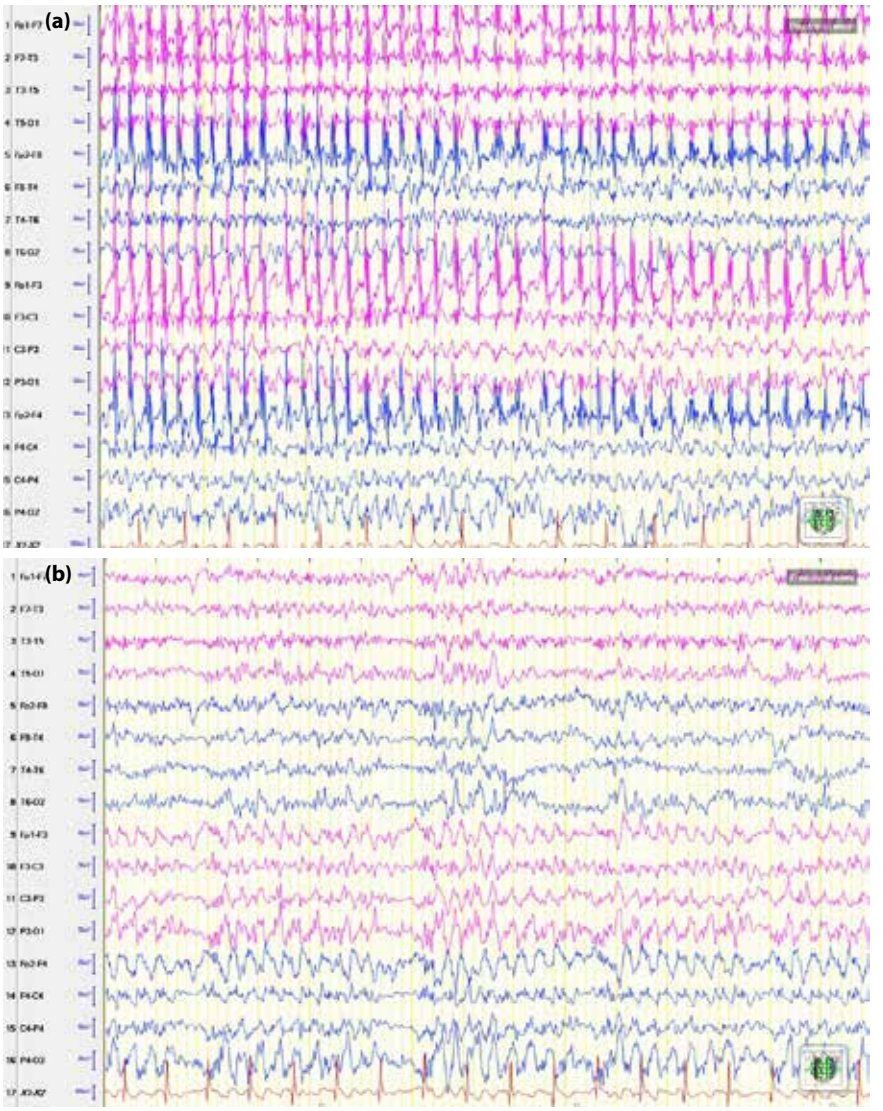

Fig. 2. **(a, b)** EEG showing multiple-spike, slow wave activities with high amplitude originating from the frontal hemisphere.

regions. The patient's levetiracetam dose was increased to 3000 mg/day. Since seizures continued, an oral lacosamide 50 mg, twice a day, treatment was added. She had 2–3 seizures in the second day of her treatment; then they did not reoccur. The patient with normal control EEG was still followed as seizure-free.

Discussion

Tuberculoma should also be considered in the differential diagnosis of the patients who live in areas where tuberculosis is endemic, such as in our country, and who have space-occupying lesions in the CNS. The intracranial tuberculoma is similar to the tumors that the granulation tissue forms in the brain parenchyma. Tuberculomas, which usually occur as multiple lesions, rarely solitary, can affect as a mass when they are very large. Early diagnosis and appropriate medical treatment are important to prevent mortality and reduce morbidity.[12] Radiological imaging techniques play an important role in following up diagnosis and treatment response. However, no exact radiological analysis method is available for the diagnosis. In isolated CNS tuberculomas with no primary origin, the clinical picture is better than CNS tuberculosis associated with military tuberculosis. Some silent clinical and spontaneous reemissions were reported in some rare cases. Tuberculomas vary according to patholog-

ic stages in MRI.[14–18] Although signs and symptoms of the intracranial tuberculomas are usually asymptomatic, they can mimic space-occupying lesions when the intracranial pressure increases depending on the localization.[19–21]

The most common symptoms are focal and generalized seizures, cranial neural paralysis (stroke), papilledema, and headache.[21–24] The present case was diagnosed with CNS tuberculosis 1 year ago, and the treatment was started with four anti-tbc drugs. Since vacant staring and nonresponse complaints had started when she was under treatment, her clinical condition was assessed again. The generalized NCSE was considered with the patient's clinical and EEG features. Although the association of tuberculoma and convulsive status epilepticus has been reported in previous studies, the NCSE association was rare.[25] In another case, the association of NCSE and tuberculosis meningitis was also reported.[26] In the present case, no features were detected in the analyses regarding NCSE etiology, but it was observed that the old lesions shrank and some atrophic changes were added. Although some INH toxicity–related status epilepticus cases have been reported, it rarely resulted in a seizure in therapeutic doses.[27] In the present case, tuberculomas were thought to be the reason behind the etiology of NCSE.

It was observed that the condition that started with blinking during EEG and continued with vacant staring and not responding lasted for 30–50 s and was accompanied by highly generalized multiple-spike, slow wave activities, which originated from the frontal hemisphere as shown in the EEG. As the present case could not benefit from 1500 mg/day levetiracetam treatment, the dose was increased to 3000 mg/day. However, no change occurred in the patient's clinical condition. The patient's EEG recovered with the addition of 50 mg, twice a day, oral lacosamide in the first day of the treatment. Lacosamide treatment can be applied in the cases that do not respond to standard treatments of NCSE and status epilepticus treatments or in the cases where standard treatment steps are skipped due to other diseases and drug interactions.[28,29] This case was reported because it was a generalized NCSE clinical condition after she was diagnosed with CNS tuberculoma, with a dramatic lacosamide treatment response.

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