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Abdominal epilepsia partialis continua in a patient with astrocytoma treated with Lacosamide – value of repetitive EEG recordings

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Abstract. – OBJECTIVE: Isolated abdominal epilepsia partialis continua (EPC) without the involvement of other body parts is rarely seen. Abdominal EPC usually occurs either as a part of hemibody EPC or as an evolution of refractory EPC after initial treatment. As the isolated abdominal EPC was rarely reported up to date, the data regarding its pathophysiology and management are limited. Herein, we aimed to describe the clinical, neuroimaging, and electroencephalographic findings of a patient with abdominal EPC.

PATIENTS AND METHODS: A 48-year-old woman with a history of surgical resection for right posterior frontal astrocytoma was admitted with left abdominal EPC. Magnetic resonance imaging of the brain showed a residual mass lesion and encephalomalacia in the right frontoparietal region.

RESULTS: Although the initial electroencephalography (EEG) was normal, independent spikes were detected in the right frontal and parietal derivations in the second EEG. Although her EPC was refractory to levetiracetam, lamotrigine, phenytoin, and gabapentin, oral lacosamide treatment ceased the seizures.

CONCLUSIONS: The history of this patient emphasizes the necessity of repetitive recordings in case of a normal initial EEG. The independent spikes in her frontal and parietal regions suggested the presence of a large epileptogenic zone generating independent epileptiform activities in the pre-central motor cortex and the post-central sensory cortex as the pathophysiologic phenomena in persistent abdominal EPC. To the best of our knowledge, this is the first report presenting a patient experiencing an abdominal EPC due to a cerebral mass resolved with lacosamide suggesting this drug is a promising treatment option in resistant EPC.

Key Words:
Epilepsia partialis continua, Abdominal muscles, Astrocytoma, Epileptogenic zone, Lacosamide.

Introduction

Epilepsia partialis continua (EPC) is a rare kind of focal motor status epilepticus characterized by long-lasting repetitive episodes of muscle jerks with a various rate, rhythm, intensity, and territorial extent. It generally affects the facial and/or distal limb muscles for a minimum of an hour duration and recurs at intervals of no more than 10 seconds. EPC affecting abdominal muscles usually occurs either as a part of hemibody EPC or as an evolution of refractory EPC after initial antiepileptic treatment[1-5]. Isolated abdominal EPC without the involvement of face or limbs is seen rarely, most probably due to a smaller cortical representation area of abdominal muscles than ones of facial and limb muscles in the motor cortex[1,2,6,7].

The data regarding pathophysiology and management of the abdominal EPC are limited as it was rarely reported up to date. Moreover, the anatomical localization of the epileptogenic zone in abdominal seizures has not been clarified precisely. The previous reports[2,3,5,8] revealed that most of these patients had pre-central or parasagittal lesions accompanied by either epileptic discharges on frontocentral derivations in electroencephalography (EEG) corresponding to the motor cortex in the frontal lobe or spreading of these epileptiform activities from the derivations of adjacent lobes to there. Herein, we present a patient with EPC in the left abdominal muscles' insole, not spreading to the other body parts. The patient had a right frontal astrocytoma and surrounding encephalomalacia with independent epileptiform discharges in posterior frontal and parietal EEG derivations.

Case Report

A 48-year-old female patient was admitted to us on October 9, 2020, with continuous jerks in her left abdominal muscles. There was a surgi-

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cal resection of the right posterior frontal mass (46 x 40 x 67 mm in its maximum diameters) in past medical history, achieving complete tumoral excision in February 2019 (Figure 1). She was diagnosed with grade II astrocytoma. Prophylactic levetiracetam (1000 mg/day) therapy was introduced. She experienced a focal tonic-clonic seizure in her left arm and leg in September 2019, firstly, and the dosage of levetiracetam was increased to 1500 mg/day. Upon recurrent seizures twice a month with the same pattern, lamotrigine (100 mg/day) was introduced. However, her seizures were not ceased, and phenytoin (300 mg/day) was also added. Upon the recurrence of the tumor near the central sulcus (8x6x8 mm in its maximum diameters), she had a second operation in August 2020. Temozolomide chemotherapy, dexamethasone, and radiotherapy were started in September 2020, and the frequency of focal seizures was decreased in that time.

During the admission, she had continuous muscle jerks in the left abdominal muscles without propagation to the limbs or face persisting for the last three days. These unpainful contractions did not vary with sleeping, breath-holding, or positional changes. Intravenous diazepam infusion stopped them. Serum levetiracetam level was 22.2 μg/mL (6-46), and phenytoin level was 14.7 μg/mL (10-20). Lamotrigine was increased to 200 mg per day. However, EPC reoccurred in next day, and gabapentin was started (1200 mg/day). Upon the occurrence of abdominal rashes, lamotrigine was stopped, and gabapentin was increased to 1600 mg/day. Her seizures ceased. Interictal EEG was normal, and she was discharged on October 16, 2020. However, abdominal EPC reappeared on the evening of the next day. Lacosamide was added with a dosage of 100 mg (50 mg twice daily), and then the seizures stopped when she was awake but occurred intermittently when sleeping. Repetition of interictal EEG revealed frequent and independent spikes in the right posterior frontal and in parietal derivations with phase reversal patterns on F4 and on P4 electrodes, respectively (Figure 2). The nocturnal seizures ceased after lacosamide was increased to 400 mg/day (200 mg twice daily). She did not report any seizure during the follow-up visits for the last six months.

Discussion

EEG is an important auxiliary diagnostic tool in localizing or lateralizing the epileptogenic zone in patients with EPC. Initial scalp EEG could be normal in some instances, even if it is performed during the myoclonic movements. However, repetitive recordings could reveal either the epileptiform activities or the local background abnormalities in many cases[1,5]. The initial EEG was also normal in our case, but the second one recorded the frequent spikes in frontal and pari-

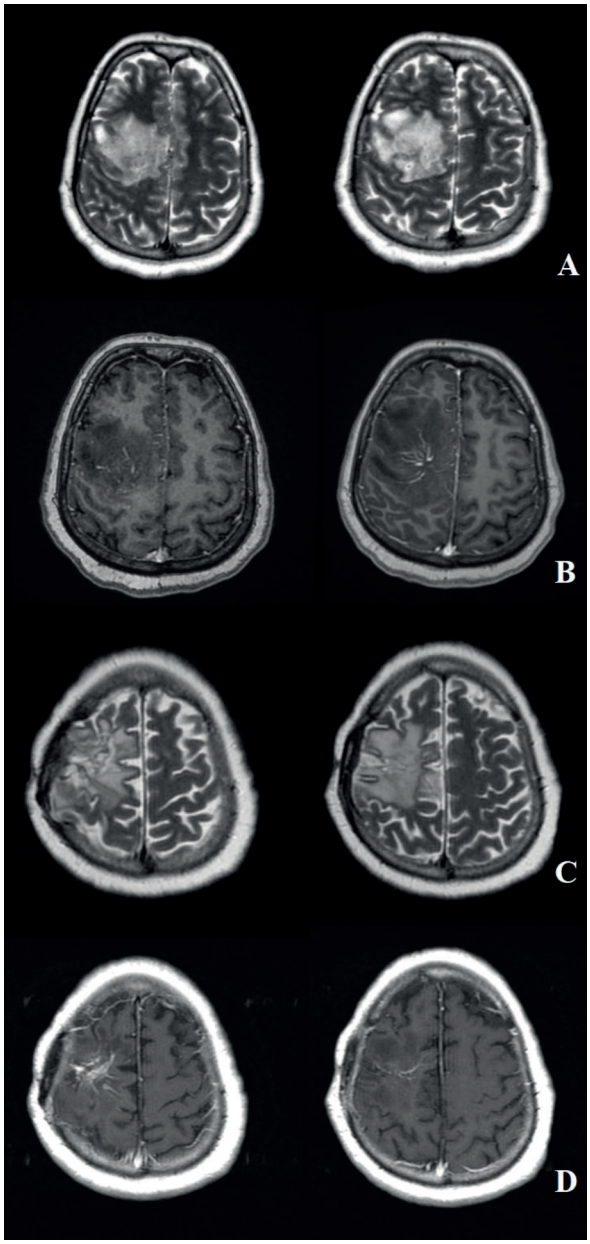

Figure 1. Preoperative magnetic resonance imaging (MRI) of the patient reveals a mass lesion at the right frontoparietal region on the axial T2 weighted sequence (**A**) and gadolinium enhancement on axial T1-weighted images (**B**). MRI after the second operation reveals a residual lesion at the same region on the axial T2 weighted sequence (**C**) and gadolinium enhancement on axial T1-weighted images (**D**).

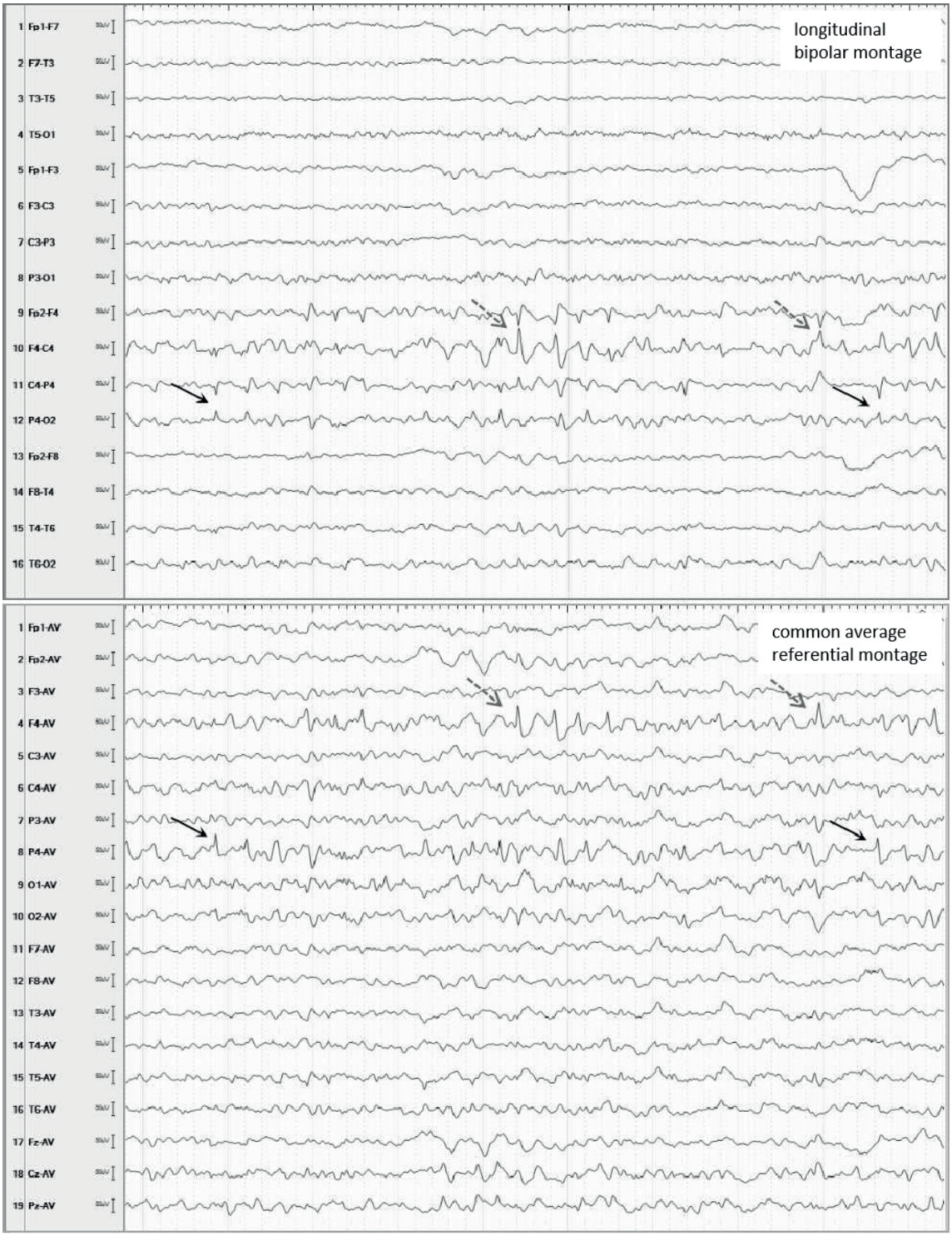

Figure 2. Interictal EEG trace revealing independent spikes on F4 (dashed arrow) and P4 (straight arrow) electrodes. EEG traces are given in a longitudinal bipolar (double banana) montage in the upper row and in a common average referential montage in the lower row; sensitivity: 7 μV; low-frequency filter: 0.3 Hz; high-frequency filter: 70 Hz. Speed: 10 seconds/page.

etal derivations corresponding to the localization of the cerebral mass.

In previous reports, epileptic clonic jerks in abdominal muscles were associated either with epileptic discharges originated from the motor cortex in the frontal lobe or the spread of these activities from adjacent lobes to there[2,3,5,7-10]. Pre-central or parasagittal lesions of the frontal lobe and medial parietal or occipital lesions with corresponding lateralizing or localizing epileptiform discharges have been documented in these patients.

In an earlier report, Chalk et al[9] reported a 66-year-old man with cryptococcal meningitis manifesting as left abdominal EPC. His CT and MRI of the head showed only mild atrophy, whereas the EEG revealed right parasagittal periodic sharp wave discharges with close relation in time with left abdominal muscle jerks. In another report, Lim and colleagues reported a 31-year-old male with the clinical picture evolved to EPC in the left lower limb and abdomen after the treatment of a generalized tonic-clonic seizure[5]. His brain MRI demonstrated a venous angioma in the right cingulate gyrus. Although the EEG during his myoclonic movements did not reveal any epileptiform activity, a second study performed two days later identified an ictal focus over the right anterior temporal region. More recently, Aljaafari et al[10] reported ictal and interictal EEG recordings of a young man with chronic medically refractory epilepsy having right-sided abdominal seizures with or without a few clonic movements of the right arm and head deviation toward the right side with a frequency of 1-4 events per month. Abdominal seizures were associated with ictal EEG changes recorded over the contralateral parietal region. Brain MRI demonstrated areas of left peri-insular and parietal atrophy, and dipole source solution of the averaged early ictal sharp waves in EEG monitoring localized the focus to the posterior wall of parietal lobe gyrus which is posterior to the postcentral gyrus.

On the other hand, Fernández-Torre et al[8] reported a 77-year-old woman having continuous twitches on abdominal muscles prominent in the left side not spreading to face or limbs after treatment of initial left hemibody EPC[8]. She had lung cancer having multiple metastases in the right frontal lobe, right temporal pole, right cerebellar cortex, and left parasagittal frontal region. Her video-EEG polygraphic study was reported to reveal periodic lateralized epileptiform discharges consisting of the burst of sharp waves and irregular sharp-and-slow wave complexes involving the right central, mid-temporal, and parietal areas and occasionally spreading to the left parietooccipital region. These focal changes demonstrated a phase reversal in the C4 and T4 electrodes when displayed in a longitudinal bipolar montage and maximum electronegativity in C4 in the common reference montage. These epileptiform discharges were associated simultaneously in the EMG with contractions of both abdominal recti muscles, notably more prominent on the left side.

Recently, Casciato et al[3] reported rhythmic spikes and spike-wave discharges involving right frontal and centro-parietal areas with early spreading over the temporal regions in EEG of their patient experiencing abdominal EPC after brain tumor surgery. Diffusion-weighted imaging (DWI) sequences of brain MRI scan, acquired during sustained epileptic activity, showed a focal restricted signal mainly involving the right frontal and parietal cortex, whereas follow-up DWI sequences showed no areas of diffusion restriction after EPC resolved. In another report, Oster et al[11] reported a man with clonic contractions on his abdomen and trunk having a gliotic lesion in the cortex of the pre-central gyrus in MRI. Neurolite ictal single-photon emission CT study showed intense uptake in the left superior lateral frontal lobe and moderate uptakes in the right anterior frontal lobe, temporal lobes, and cingulate region. They suggested that the primary focus of seizure onset occurs in the motor cortex, which correlates with intense focal uptake in the motor area, and the areas with moderate uptakes might represent secondarily propagated pathways[11]. In similar, Lizarraga et al[12] reported a patient with recurrent focal seizures as intermittent, short-lasting episodes of involuntary, painless abdominal movements for the last three days with a left medial parietal hemorrhage and adjacent cortical cytotoxic edema extending cranially through the medial aspect of the left parietal lobe to reach the postcentral and central sulci near the vertex corresponding to the somatotopic localization of the sensorimotor areas of the trunk. Continuous video-EEG monitoring demonstrating interictal epileptiform activity in the medial parietal and left parieto-occipital regions (Pz, P3, and O1) that propagates to medial central and left frontocentral regions (Cz, C3, Fz, and F3). During another episode of abnormal abdominal movements, this interictal epileptiform activity evolves into an ictal pattern in the medial parietal and left posterior quadrant regions (Pz, P3, T5, and O1), propagating anteriorly to medial central and left frontocentral regions (Cz, C3, and F3). The authors postulated that the epileptogenic zone most likely

corresponded to the medial parietal region and the symptomatogenic zone to the primary sensorimotor representation of the trunk. They hypothesized that an epileptic activity arising in medial brain regions spread through the non-eloquent cortex to eventually reach the primary sensorimotor region corresponding to the trunk without involving other primary sensorimotor areas.

As a difference from the above-mentioned reports, interictal EEG of our case revealed frequent but independent epileptiform activities on the right frontal (F4) and the right parietal (P4) derivations just over the locations of astrocytoma over the motor cortex in the right frontal lobe and cerebral damage involving the adjacent parietal lobe caused by unintentional damages during surgery and radiotherapy. In other terms, the epileptiform activities on frontal derivations of our case exist independently from the spikes on the parietal region not occurred as a spreading activity from this zone. Therefore, a presence of a large epileptogenic zone generating independent epileptiform activities from multifocal origins in parasagittal regions of the pre-central motor cortex and post-central sensory cortex could be postulated as underlying pathophysiologic phenomena in cases with chronic persistent EPC restricted in abdominal muscles.

As the patients with isolated abdominal EPC referring the abdominal muscle jerks without the involvement of facial or limb muscles have been rarely reported up to date, the experiences regarding their managements are very limited[1,2,6,8,9]. As the other types of EPC, abdominal EPC is also hard to handle in most cases and generally resistant to antiepileptics. Benzodiazepines, phenytoin, and levetiracetam were the most commonly used drugs in the management of these patients in previous reports. However, the prognoses of the abdominal seizures seem to depend largely on the underlying etiology rather than introduced antiepileptics, and better in central nervous system infections or surgically treatable structural causes as expected. EPC secondary to malignant lesions is hard to manage and generally controlled hardly with a combination of the targeted treatments for tumor (surgery, radiotherapy, chemotherapy, etc.) and the multiple antiepileptics as in the presented case. Our patient experienced EPC while already using levetiracetam, lamotrigine, and phenytoin and was not relieved with the addition of gabapentin. However, it revealed a clear response to lacosamide.

Lacosamide is a functionalized amino acid that enhances the slow inactivation of voltage-gated sodium channels. Therefore, its administration results in stabilization of hyperexcitable neuronal membranes, inhibition of neuronal firing, and reduction in long-term channel availability without affecting physiological function. In 2008, it was approved in the European Union and in the USA for the usage in add-on therapy for focal seizures with/without secondary generalization in epileptic adults and adolescents. In addition, the US Food and Drug Administration (FDA) approved its usage as monotherapy in focal epilepsy in 2014[13]. Its intravenous formulation is also reported to be useful in the treatment of status epilepticus, with the overall success rate ranging from 33% to 81% when used as a third-line drug[14,15]. However, the experiences regarding its usage in EPC are very limited. In 2013, Spalletti et al[16] reported a 39-year-old male patient suffering from EPC as left-arm focal motor seizures eight days after the surgery for right chronic subdural hematoma[16]. It was continued against the usage of diazepam, midazolam, levetiracetam, and phenytoin. Ictal focal epileptiform discharges arising from right central areas were associated with the Jacksonian motor spread of the seizure to the upper left limb. Contralateral spreading of ictal discharges was variable but associated with brief impairment of consciousness. Between seizures, right central periodic lateralized epileptiform discharges (PLEDs) were observed on the EEG, which were myoclonus-related (cortical myoclonus, lasting for 100-120 ms). Immediately before the seizures, PLEDs were more abundant and enriched with fast activity (PLEDs-plus). The authors reported that intravenous lacosamide (200 mg) ceased the motor seizures within an hour. The patient was discharged with oral LCM therapy (200 mg bid), and he was seizure-free with lacosamide monotherapy during his six months follow-up period.

More recently, Asranna et al[7] reported a 25-year-old man with cysticercal granuloma in the left pre-central gyrus presented with a sudden onset abdominal EPC as arrhythmic focal myoclonic movements lasting between 20 minutes and an hour. Ictal EEG recording did not reveal any epileptiform discharges. His persistent abdominal EPC was reported to be controlled with the usage of oxcarbazepine, levetiracetam, and lacosamide.

Conclusions

Although the intermittent jerks on the facial and/or upper extremity muscles are the most frequent seizure types of EPC, persistent myoclonic

jerks of abdominal muscles insole, referred to as abdominal EPC, could rarely be seen as in our patient. History of the present case also re-emphasizes the necessity of repetitive recordings for the patient with normal initial EEG as the epileptiform spikes could be observed with the second EEG recording. We suggested the frequent and independent spikes in the right frontal derivations corresponding to the pre-central motor cortex and the parietal derivations in EEG of our patient as the indicators of the presence of a large epileptic zone generating independent epileptiform activities in the pre-central motor cortex and the post-central sensory cortex could be the underlying pathophysiologic phenomena in cases with chronic persistent EPC restricted in abdominal muscles. Although the EPC of our case was refractory to other antiepileptic drugs, it was resolved with the usage of oral lacosamide therapy. Considering this clear response seen in our case, together with its effectiveness in EPC of a few previously reported cases, this drug could also be a promising option in add-on therapy for the resistant EPC. However, further observations are warranted to clarify this issue.

Author's Contribution

M.A. examined the patient, considered the laboratory, neuroimaging and EEG findings, and wrote the manuscript.

Conflict of Interest

The author declares that he has no competing interests or any financial support for this study.

Acknowledgment

An informed consent was obtained from the patient for this report. This work has not been published previously, and it is not under consideration for publication elsewhere.

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