Epileptic Disord 2019; 21 (1): 92-6

Tonic status epilepticus in a centenarian woman

José L. Fernández-Torre [1,2,3], Javier Riancho [2,3], María Martín-García [1], Gonzalo Martínez-de las Cuevas [4], Pilar Bosque-Varela [5]

[1] Department of Clinical Neurophysiology, Marqués de Valdecilla University Hospital, Santander
[2] Department of Physiology and Pharmacology, University of Cantabria (UNICAN), Santander
[3] Biomedical Research Institute (IDIVAL)
[4] Department of Internal Medicine, Marqués de Valdecilla University Hospital, Santander
[5] Department of Neurology, Marqués de Valdecilla University Hospital, Santander, Spain

Received September 09, 2018; Accepted November 18, 2018

ABSTRACT – Generalized tonic status epilepticus (TSE) is a rare epileptic condition. It occurs usually in the context of symptomatic generalized epilepsy, in particular, in subjects with a diagnosis of Lennox-Gastaut syndrome, atypical forms of idiopathic (genetic) generalized epilepsy, or as a paradoxical effect during treatment with diverse antiepileptic drugs. Herein, we describe the case of an elderly woman on chronic treatment with psychotropic drugs who developed an episode of generalized TSE. Motor manifestations were subtle and difficult to recognize as seizures, and a detailed video-EEG importantly contributed to accurate and prompt diagnosis. TSE was initially refractory to conventional anti-seizure drug therapy including levetiracetam and valproate but was finally controlled with lacosamide. Our case indicates a potential therapeutic effect of lacosamide on TSE in the elderly after treatment failure with first-line anti-seizure drugs. [*Published with video sequence on www.epilepticdisorders.com*]

Key words: tonic status epilepticus, video-EEG, elderly patient, lacosamide

Tonic status epilepticus (TSE) is a rare epileptic condition. It occurs usually in the context of symptomatic generalized epilepsy, in particular, in subjects with a diagnosis of Lennox-Gastaut syndrome or atypical forms of idiopathic generalized epilepsy (IGE) (Kobayashi *et al*., 2005). Moreover, TSE has been also described as a paradoxical effect during treatment with diverse antiepileptic drugs (Prior *et al*., 1972; Capocchi *et al*., 1998; Grande-Martín *et al*., 2016). Herein, we describe the case of a centenarian woman who developed an episode of generalized TSE, possibly secondary to chronic use of psychotropic drugs.

Case study

A 102-year-old woman, partially dependent in daily-life activities, with antecedents of hypertension and atrial fibrillation, was admitted to our hospital because of general deterioration and dyspnoea. She was on chronic treatment with trazodone, amiloride, hydrochlorothiazide, pantroprazole, and bromazepam. On general

VIDEO ONLINE

Correspondence:
José L. Fernández-Torre
Department of Clinical Neurophysiology, Marqués de Valdecilla University Hospital, Avda. Valdecilla, 25, 39008 Santander, Cantabria, Spain
<jlfernandez@humv.es>
<ftorrenfc@hotmail.com>

doi:10.1684/epd.2019.1031

physical examination, she was haemodynamically stable with a temperature of 36.0° C. Routine laboratory tests were within normal limits except for the presence of severe bacteriuria. With these results in mind, she was diagnosed with urinary tract infection, and oral treatment with amoxicillin-clavulanic acid was started for five days. On Day 5 of admission, after finishing the antibiotic treatment, she complained of "funny" movements as a "tremor" of both lower limbs. These episodes were interpreted as anxiety and nervousness, and treatment with clonazepam and risperidone was initiated. The next day, these "funny" episodes in both legs persisted and the patient was evaluated by our neurologists. On neurological examination, she was awake and alert, but disoriented to time. No focal motor or sensory deficits were seen. She reported self-limited involuntary movements in the lower limbs. These movements were synchronous, fast, and were not accompanied by cognitive disconnection, automatisms or loss of consciousness. On some occasions, she acquired a certain tonic aspect in both feet, but "funny" movements were not clearly tremulous. At that moment, a video-electroencephalogram (v-EEG) study was requested. On v-EEG, recurrent generalized bursts of rhythmic, high-voltage, sharp, well-defined, sinusoidal, beta activity, lasting from 2 to 6 seconds, were observed (*figure 1*). Simultaneously, the patient experienced a subtle increase in tone and stiffness involving the axial musculature and both lower limbs (*see video sequence*). Occasionally, she also experienced subtle jerks in both feet. Autonomic manifestations were not evident. Irregular theta and delta waves were seen between bursts. The episodes recurred continuously in clusters along the recording and, therefore, a diagnosis of generalized TSE was suggested. A computed tomography (CT) scan of the brain disclosed diffuse and symmetric cortico-subcortical atrophy and subcortical hypodense lesions compatible with chronic small vessel ischaemia. Treatment with intravenous levetiracetam (LEV) (1,000 mg/day) was initiated. During the following four days, tonic seizures were less frequent but were not completely controlled and intravenous valproate (VPA) (800 mg/24 hours) was added to her anti-seizure drug (ASD) therapy. On Day 11, tonic seizures worsened involving also upper limbs and the dose of VPA was increased (1,000 mg/24 hours). One day later, the episodes of stiffness persisted and intravenous lacosamide (LCM) (100 mg/24 hours) was included in the ASD therapy. After the onset of treatment with LCM, tonic seizures were completely controlled, and clinical improvement persisted for the next days. On Day 14, the patient was discharged under chronic ASD therapy with LEV (750 mg/24 hours), VPA (1,200 mg/24 hours), and LCM (100 mg/24 hours) with follow-up via neurology consultation.

Discussion

It is well known that tonic seizures and TSE typically occur in patients with intellectual disability and severe symptomatic epilepsy. However, the occurrence of episodes of generalized TSE is fairly rare in adults and elderly subjects without antecedents of epilepsy. Nevertheless, Kobayashi *et al*. (2005) drew attention to the possibility that status epilepticus (SE) with minor tonic seizures may occur in IGE.

The case of our centenarian patient without antecedents of epilepsy shows a different scenario. Previously, Garmel *et al*. (1992) described an episode of unresponsiveness in a 73-year-old woman as secondary to generalized TSE. These authors emphasized the complexity of diagnosis since motor manifestations may be subtle and difficult to recognize. Our findings support this conclusion because in the case report described here, tonic seizures were initially interpreted to result from the patient's anxiety. More recently, Ostrow and Kaplan (2011) reported a young woman with prolonged TSE which evolved into a stimulus-induced diffuse voltage attenuation (SIDVA) pattern in the setting of aseptic meningoencephalitis. This was the first report of a SIDVA pattern in an adult without a history of epilepsy. The ictal EEG pattern observed in our patient consisted of recurrent generalized bursts of rhythmic, sinusoidal, beta-like activity, lasting several seconds without spike-wave complexes. This ictal EEG pattern resembled that typically observed in tonic seizures of Lennox-Gastaut syndrome (Prior *et al*., 1972).

TSE is more difficult to recognize than other forms of SE. This is because, firstly, TSE is rare in adults or elderly subjects, in comparison with generalized tonic-clonic SE or partial motor SE, and secondly, motor symptoms may be subtle and the fact that increased tone or stiffness in isolation may have an epileptic origin is not widely known. Thus, fine tonic seizures may only be evident with careful video analysis or with the use of muscle recording electrodes. The description of our case may help to emphasize that TSE may occur in the elderly population and, in particular, in patients with chronic psychotropic drug therapy.

We cannot rule out that the treatment with amoxicillin-clavulanic acid could have precipitated the episode of TSE. However, we believe that this was unlikely because the clinical manifestations occurred once the treatment was completed. Moreover, in a recent article in which the current evidence for seizures associated with the use of antibiotics was systematically reviewed, the authors did not find reports or studies confirming a seizure threshold-lowering effect of amoxicillin-clavulanic, and an association with seizures or SE was not demonstrated (Sutter *et al*., 2015). The confluence of multiple factors seems more plausible.

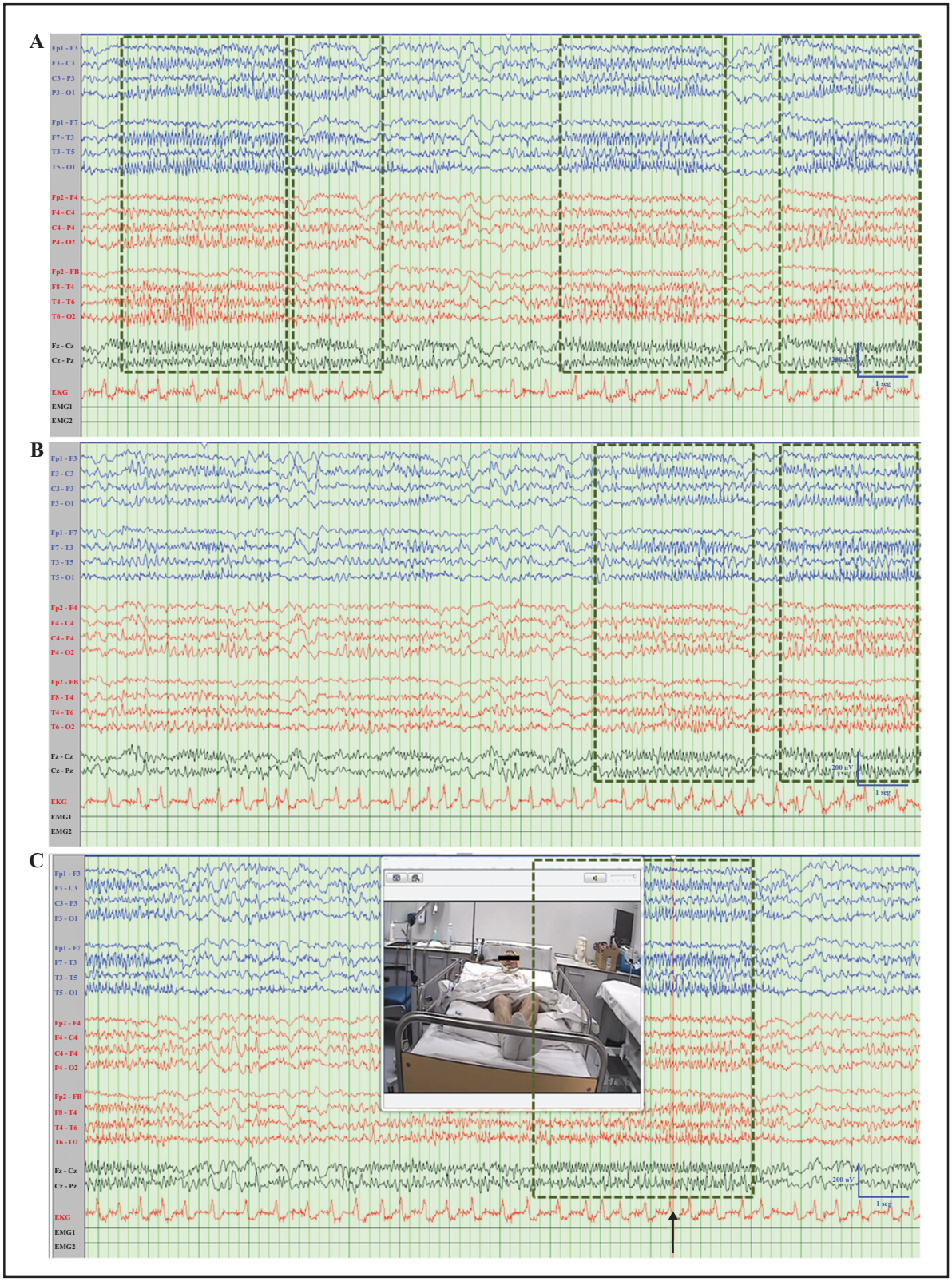

Figure 1. (A, B) The presence of a recurrent burst of sharp, sinusoidal, high-voltage, beta activity lasting from 2 to 5 seconds (green dashed line), compatible with the diagnosis of generalized TSE. (C) Tonic contraction of both legs coinciding with ictal EEG changes (arrow and green dashed line). Low filter: 0.53 Hz; high filter: 70 Hz; notch filter: 50 Hz.

Our patient had a chronic vascular disorder and she was a chronic consumer of psychotropic medication. It is possible that under these circumstances, a homeostatic imbalance secondary to urinary tract infection could account for the occurrence of SE.

In this case, TSE was refractory to conventional ASD treatment. It is well known that tonic seizures and TSE, particularly associated with Lennox-Gastaut syndrome, can be aggravated by benzodiazepines. We used VPA and LEV as first-line treatment in order to prevent this potential complication. Although initially, tonic seizures improved after several days, the seizures remained uncontrolled and we therefore added LCM to her antiepileptic treatment. LCM is a relatively new ASD therapy that has become a well-established anticonvulsive medication for the treatment of focal-onset seizures, with and without secondary generalization. Treatment with LCM has demonstrated efficacy in patients with absence SE in whom VPA and LEV have previously failed (Reif *et al*., 2018). Moreover, LCM was noninferior to fosphenytoin as treatment for nonconvulsive seizures in critically ill patients (Hussain *et al*., 2018). Conversely, the use of high doses of LCM combined with other antiepileptic drugs in a case of super-refractory TSE was ineffective (Thompson and Cock, 2016). The patient was a 24-year-old man with autistic spectrum disorder and learning disability with an electroclinical picture reminiscent of Lennox-Gastaut syndrome, who responded to a rapid increase in rufinamide.

In summary, TSE may occur in elderly patients under chronic psychotropic drug treatment. Motor manifestations can be subtle and, therefore, a detailed v-EEG contributes to accurate and prompt diagnosis. Our case indicates a potential therapeutic effect of LCM on TSE in the elderly after treatment failure with first-line ASDs. □

Legend for video sequence

Recurrent and continuous episodes in which there is flexion of the patient's entire body along with hip, knee and ankle flexion of both lower limbs. Note the flexion of the left arm during the second sequence.

Key words for video research on www.epilepticdisorders.com

Phenomenology: status epilepticus (convulsive)/tonic seizure
Localisation: generalized
Syndrome: not applicable
Aetiology: toxics abuse

Supplementary data.
Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.
None of the authors have any conflict of interest to declare.

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TEST YOURSELF

(1) List three epileptic conditions associated with tonic status epilepticus.

(2) What is the most frequent ictal EEG pattern during tonic status epilepticus in patients with Lennox-Gastaut syndrome?

(3) Which antiepileptic drug can trigger tonic status epilepticus in generalized epilepsy?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".