Epileptic aura continua: a case report with response to brivaracetam☆

Aura epiléptica continua: a propósito de un caso con respuesta a brivaracetam

Dear Editor:

In the broadest sense of the term, epilepsia partialis continua (EPC) is a form of focal status epilepticus associated with continuous motor, somatosensory, visual, olfactory, auditory, or cognitive symptoms, but preserved awareness, lasting ≥ 1 hour, and caused by locally restricted epileptiform activity.[1] Some authors use the term ''aura continua'' to refer to the non-motor form of EPC.[1–3] According to the International League Against Epilepsy's latest classification of status epilepticus, EPC is the motor form and aura continua belongs to the group of focal non-convulsive status epilepticus without impairment of consciousness.[4] No demographic data are available for aura continua; however, EPC is known to be a rare entity, with estimated prevalence of less than 1 case per million population.[5] EPC may be classified into 4 categories, according to disease progression: isolated episode, chronic repetitive non-progressive, chronic persistent non-progressive, and chronic progressive. It may be caused by a wide range of factors, including inflammation, infection, neurovascular processes, tumours, trauma, mitochondrial dysfunction, and metabolic disorders.[1,2] Treatment of this condition is highly challenging; furthermore, little evidence is available on the most appropriate drug due to its low prevalence. We present the case of a patient with somatosensory aura continua in the context of drug-resistant post-traumatic structural epilepsy.

Our patient was a 35-year-old right-handed man with history of head trauma at the age of 22 years, with right parietal haemorrhagic contusion secondary to the depressed skull fracture; he underwent surgery to remove bone fragments from the brain parenchyma. The neurological examination performed after the head trauma revealed right hemiparesis (4/5 strength on the Medical Research Council scale), right hemihypoaesthesia, and mild executive, visuomotor, and visuoconstruction impairment, which resolved completely over the following 6 months. He also presented focal motor seizures with preserved awareness, which were treated with phenytoin. Two months later, he began to present somatosensory symptoms in the form of paraesthesia, starting on the left side of the face and progressing to brachiocrural paraesthesia, followed by clonic movements in the left arm. Treatment was started with valproic acid. After 3 years of seizure freedom, the drug was progressively withdrawn, but the patient presented stereotyped, paroxysmal episodes consisting of fluctuating paraesthesia starting in the left thoracic region and progressing to the ipsilateral distal crural area and subsequently to the knee; episodes lasted between 1 and 5 hours and presented at a frequency of 10 episodes per month, usually in clusters. These findings suggest chronic repetitive non-progressive aura continua type 2a of structural aetiology,[2] originating in the right parietal lobe, or central neuropathic pain. Gabapentin achieved no improvement. Two interictal serial electroencephalography (EEG) studies did not detect epileptiform activity. Levetiracetam, valproic acid, and oxcarbazepine at optimal doses achieved no improvement. The patient presented adverse reactions to topiramate. Seizure frequency did not change at any point during the process, with 10 years of follow-up. Brivaracetam achieved a satisfactory response; the patient has remained seizure-free for 3 months, for the first time in 10 years of follow-up.

We present a case of aura continua, which is an infrequent entity with very few reported cases, especially in the case of the sensory type, making the condition a true diagnostic and therapeutic challenge.[1] While interictal EEG alterations are frequent, a lack of epileptiform activity does not rule out diagnosis.[2] In our patient, the stereotyped, paroxysmal nature of the seizures and their correlation with the traumatic brain injury enabled us to establish the diagnosis. The combination of hyperexcitability in a well-delimited focal area and preservation of mechanisms of lateral inhibition allows for the appearance of this epileptic phenomenon with limited propagation.[2,3] Treatment focuses on managing the underlying cause.[6] Little evidence is available on the efficacy of antiepileptic drugs, with topiramate and levetiracetam showing the best results.[1–3] Brivaracetam is a selective high-affinity synaptic vesicle protein 2A (SV2A) ligand; it shows 15 to 30 times higher affinity for SV2A than levetiracetam.[7] Furthermore, brivaracetam does not modulate α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors,[8] whereas levetiracetam does; this suggests that both drugs have different pharmacological profiles. Brivaracetam has been approved in the United States[9] and the European Union[10] as a complementary treatment for focal seizures with or without secondary generalisation in patients aged 16 years and older. This is the first reported case of aura continua showing fast response to brivaracetam, and suggests that the drug may be a treatment option for these patients. However, further evidence is needed to make recommendations.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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Treatment of patients with spinal muscular atrophy 5q: towards a new protocol☆

Tratamiento de pacientes con atrofia muscular espinal 5q: hacia un nuevo protocolo

Dear Editor:

In recent years, significant advances have been made in the treatment of spinal muscular atrophy (SMA) through the development of disease-modifying treatments.[1] The first treatment available in clinical practice is nusinersen, an anti-sense oligonucleotide that increases production of the SMN protein by the *SMN2* gene, and should be administered intrathecally. The drug was approved based on the results of 2 pivotal trials: ENDEAR, for type 1 SMA,[2] and CHERISH, for type 2 and 3 SMA.[3] In 2018, the Spanish Ministry of Health published a pharmacological and clinical protocol for the use of nusinersen to treat patients with muscular atrophy, based on a therapeutic positioning report gathering the evidence available until 2017.[4] This protocol has been used as a guideline to establish an efficient and equitable approach within the Spanish National Health System, both in terms of access to treatment and proper monitoring.

However, more accurate information on the long-term effects of this treatment has been obtained over the past 3 years,[5,6] as well as information from populations not initially included in the pivotal trials, such as presymptomatic and adult patients.[7,8] We also now have further information on the natural history of the condition, particularly on the development of motor assessment scales for type 2 and 3 SMA.[9–12] Furthermore, new treatments including risdiplam[13] and onasemnogene abeparvovec (Zolgensma®) will become available in the coming months.[14]

It is therefore particularly important to review the current therapeutic positioning, from the perspective of clinical practice and from that of the healthcare system. On the one hand, the review should address the clinical criteria for, among other things, favouring earlier treatment onset (when treatment is more efficacious), including during the presymptomatic stage of the disease; adapting therapeutic objectives to the functional status of each patient; better defining the indications in adolescent and adult patients; and monitoring the simultaneous use of other treatments. On the other hand, follow-up protocols should focus on improvements in patients' functional status and quality of life, beyond the observable changes in the motor scales used in every visit. Furthermore, this follow-up should be adjusted in line with the increasing evidence on the low frequency of some adverse effects, avoiding unnecessary and especially invasive tests in some populations, such as infants with type 1 SMA, and the possible occurrence of events associated with the neophenotypes resulting from treatment (for example, scoliosis). Finally, treatment with-

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