Delirium, psychosis, and visual hallucinations induced by pregabalin

Delírio, psicose e alucinações visuais induzidas pela pregabalina

José Luiz Pedroso[1,2], Gilberto Yoshinobu Nakama[2,3], Mario Carneiro Filho[2,3], Orlando G. Barsottini[1,2]

[1]Department of Neurology, Universidade Federal de São Paulo (Unifesp), São Paulo SP, Brazil;
[2]Hospital Israelita Albert Einstein (HIAE), São Paulo SP, Brazil;
[3]Department of Orthopaedics, Universidade Federal de São Paulo (Unifesp), São Paulo SP, Brazil.
Correspondence: José Luiz Pedroso; Rua Botucatu 740; 04023-900 São Paulo SP - Brasil; E-mail: zeluizpedroso@yahoo.com.br
Conflict of interest: There is no conflict of interest to declare.
Received 23 March 2012; Received in final form 05 June 2012; Accepted 12 June 2012

Pregabalin has emerged as a novel drug for neuropathic pain treatment. Few studies or case reports have demonstrated neurological side effects of its use[1]. The aim of this article was to describe cognitive disturbances induced by Pregabalin in a patient diagnosed with neuropathic pain due to lumbar herniated disc and radicular compression.

CASE REPORT

A 44-year-old woman presented to Albert Einstein Hospital with lumbar pain, irradiated to the posterior lower left limb. Neurological examination showed Lasègue's sign in the left leg. Lumbar brain magnetic resonance imaging (MRI) disclosed degeneration and bulging herniated disc with left extrusion component, compressing S1 root in the lateral recess. Patient refused surgery, therefore clinical treatment for neuropathic pain was started with anti-inflammatory (diclofenac 50 mg, 3 times daily) and muscle relaxants (ciclobenzaprine 10 mg, twice daily), associated with pregabalin 150 mg, and no side effects were observed. After seven days, the patient still complained of pain. Pregabalin was increased to 300 mg daily. In the third day, she developed structured visual hallucinations and psychosis, irritability, and acute confusional state (temporal and spatial disorientation). General blood exams excluded infection or metabolic abnormalities and the brain MRI was normal. Electroencephalogram showed temporal slow-waves abnormalities and delta waves in frontal regions. No epileptiform discharges were found. We discontinued Pregabalin, and the patient improved mental state after 24 hours. The free informed consent was got from the patient for this publication.

DISCUSSION

Pregabalin is a gamma-aminobutyric acid analogue in the treatment of neuropathic pain, partial-onset-seizures, fibromyalgia, and anxiety disorders[1]. Although this is originally an antiepileptic drug, Pregabalin seems to be an effective therapy for the neuropathic pain, and it has been widely used, but few reports have highlighted its neurological side effects.

Recently, Zaccara et al. performed a systematic review and a meta-analysis in a randomized controlled trial, describing the main side effects of Pregabalin use[2]. The main neurological side effects reported were dizziness, vertigo, incoordination, balance disorder, ataxia, diplopia, blurred vision, amblyopia, tremor, somnolence, confusional state, attention disturbances, abnormal thinking, euphoria, asthenia, and fatigue[2]. Side effects were more frequent with increasing doses[2].

In general, the emergence of acute confusional state or *delirium* in healthy young people leads to extensive diagnostic investigation for potentially serious illnesses, such as encephalitis, metabolic disorders and infections, however the side effects of drugs should also be considered. Only few reports have described acute confusion state during Pregabalin use[3]. Also, psychosis has already been described in one patient, but this is a rare condition[4].

The efficacy and safety of Pregabalin in the treatment of neuropathic pain have been documented in several recent data[5]. Hence, neurologists have prescribed Pregabalin more often in daily medical practice. We must be aware of the side effects reported in this article, such as delirium, psychosis and visual hallucinations, since its use has increased greatly in recent years.

In summary, the present report reinforces the idea that acute confusional state, psychosis, and visual hallucinations should be considered in the clinical spectrum of side effects due to Pregabalin use, especially in higher doses, and that the withdrawal of the medication usually improves symptoms.

References

1. Tassone DM, Boyce E, Guyer J, Nuzum D. Pregabalin: a novel gamma-aminobutyric acid analogue in the treatment of neuropathic pain, partial-onset seizures, and anxiety disorders. Clin Ther 2007; 29:26-48.
2. Zaccara G, Gangemi P, Perucca P, Specchio L. The adverse event profile of pregabalin: a systematic review and meta-analysis of randomized controlled trials. Epilepsia 2011;52:826-36.
3. Hickey C, Thomas B. Delirium secondary to pregabalin. Gen Hosp Psychiatry. 2011 [Epub ahead of print].
4. Olaizola I, Ellger T, Young P, Bösebeck F, Evers S, Kellinghaus C. Pregabalin-associated acute psychosis and epileptiform EEG-changes. Seizure 2006;15:208-210.
5. Baron R, Freynhagen R, Tölle TR, et al; A0081007 Investigators. The efficacy and safety of pregabalin in the treatment of neuropathic pain associated with chronic lumbosacral radiculopathy. Pain 2010;150:420-427.

Recurrent post-ictal hyperthermia

Hipertermia pós-ictal recorrente

Sofia Rocha, Filipa Sousa, João Pinho, Ricardo Maré, Álvaro Machado

Department of Neurology, Hospital of Braga, Braga, Portugal.

Correspondence: Sofia Rocha; Serviço de Neurologia, Hospital de Braga; Sete Fontes / São Victor; 4710-243 Braga - Portugal; E-mail: sofiarocha99@hotmail.com

Conflict of interest: There is no conflict of interest to declare.

Received 14 May 2012; Received in final form 18 May 2012; Accepted 29 May 2012

Hyperthermia is a well-known precipitant of seizures, especially in susceptible individuals and in children[1,2]. Its occurrence following epileptic seizures or exclusively peri-ictally is rarely described[2].

CASE REPORT

An 80-year-old hypertensive man, with epileptic seizures of unknown etiology, since his 70th's, was observed for 3 times in 4 years with self-limited right focal motor seizures with impairment of consciousness. In all these episodes, he had post-ictal global aphasia, right homonymous hemianopsia, right hemiparesis and hyperthermia (38–39.6°C). Complete clinical workups during these events (including C reactive protein, sedimentation rate, leukocyte count, thorax radiograph, urinalysis, and lumber puncture) ruled out an infection. Brain magnetic resonance imaging and computerized tomography showed old lacunar basal ganglia infarcts and generalized atrophy. Electroencephalogram (EEG) obtained in two of these episodes revealed in one of them slow background activity of 6–7 Hz, with continuous slow theta/delta activity in left fronto-temporal region, with paroxysmal activity (spikes and sharp waves) in the same localization. The patient was treated with valproate and antipyretics (paracetamol and lysine acetylsalicylate). The hyperthermia did not respond to these drugs, but resolved spontaneously in 12–18 hours and the neurological deficits recovered within 24 hours.

DISCUSSION

Transient post-ictal hyperthermia may follow generalized convulsive status epilepticus[2,3]. In our case, over four years of follow-up, the patient presented three episodes of right focal motor seizures with consciousness impairment and a prolonged post-critic with aphasia, right homonymous hemianopsia, right hemiparesis, and hyperthermia. There was no fever preceding seizures or convulsive status epilepticus. In all of them, an infectious cause of hyperthermia was exhaustively investigated. Such research was always negative. Therefore, we interpreted hyperthermia as a post-ictal manifestation.

Post-ictal hyperthermia seems to be a quite infrequent symptom and it has been rarely described[2]. Rossetti et al.[2] reported two cases and reviewed the literature of the last 40 years. They found another eight reports of peri-ictal fever, which were mainly related to non-convulsive seizures, involving all age groups (5–83 years old), display a relatively short duration (8–96 hours) and showed mostly bi-temporal EEG alterations.

The exact mechanisms that underlie the onset of hyperthermia in the peri-ictal period are not well established. It seems possible that the thermoregulatory center in the hypothalamic pre-optic area may be affected by spreading epileptic activity, and thus cause elevated body temperature[3-5]. The mesial temporal lobe structures have extensive connections with the neuroendocrine hypothalamus portion, and a discharging temporal focus can possibly alter hypothalamic function[3]. Another mechanism may involve vagal nerve nuclei (nucleus tractus solitarius) modulation during seizures[2]. Seizure-induced production of pyrogens in several brain regions, such as neocortex, amygdala, and hippocampus, appears as an alternative[2].

The knowledge of the existence of post-ictal hyperthermia could improve the medical management of subjects presenting with. Indeed, fever does not always imply infection, inflammation or malignancy, even though they are still the most common causes[4]. Whilst a seizure occurring in a febrile context should generally prompt investigations to detect an infectious etiology, repetitive occurrence of this feature should raise the suspicion of a post-ictal symptom.