

Perampanel-Induced Psychotic Disorder: a case report

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Dear Editor,

Patients with epilepsy have increased vulnerability to psychiatric comorbidity, including psychotic disorders, imposing additional disease burden [1]. Among the types of psychotic disorders in epilepsy, antiepileptic drug (AED) induced psychotic disorder (AIPD) represents an iatrogenic adverse drug reaction, which prevalence ranges from 1% to 8,4% in clinical trials of AEDs [2]. By definition, the definitive diagnosis of AIPD can only be made retrospectively [1].

Perampanel (PER), a noncompetitive antagonist of the α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor, is the first agent developed as an adjunctive therapy for adults with focal seizures with or without secondary generalization [3]. The profile of adverse reactions has been extensively studied, with emphasis on psychiatric side effects. The development of acute psychotic disorders as a side effect rarely occurs, ranging from 0,1% to 1,3% according to different studies [3-5] and is poorly described.

Here we report a clinical case of a 57-year-old female with drug-resistant temporal and left front-opercular epilepsy, with limbic mesial involvement, excluded from surgical treatment due to language area involvement, who developed an acute psychotic disorder about two weeks after increasing the dosage of PER to 12 mg per day.

Behavioural and psychopathological changes were reported by her family, lasting from two weeks prior to admission and in relation to dosage increase of PER to 12 mg per day. The patient had felt controlled by the television (which talked to her), and by piped water/water meters. She smelt toxic gases spreading throughout the house, which burned her hands (that she protected by placing a pillow between the TV and her hand).

The patient had no personal or family history of psychiatric illness, as well as no toxophilic habits (tobacco, illicit substances or alcohol). Her medical comorbidity was epilepsy, since the age of 14, which was always difficult to manage, sometimes with multiple crises with secondary generalization. Recently, she was medicated with topiramate 100 mg twice daily, clonazepam 2 mg twice daily, lacosamide 100 mg twice daily, and had improved considerably with the introduction of PER and its titration up to 12mg/day. The last epileptic seizure was over a month before her psychiatric admission.

Initial mental examination revealed a hostile contact and extreme irritability. The patient was conscious and oriented, exhibited disorganized thought, persecutory and self-referential psychotic symptoms, together with multiple delusional

interpretations and perplexity. She also suffered from auditory-verbal, olfactory and somatic hallucinations. Critical judgement was not maintained.

Neurological examination did not show focal deficits, routine laboratory tests and brain computed tomography scan were performed and did not reveal any changes. Her previous electroencephalogram (EEG) evidenced left temporal paroxysmal activity.

For acute management, we reduced the dosage of PER to 6 mg per day, and maintained the other usual AEDs. She was also given a low dosage of an antipsychotic: risperidone 2mg per day, plus lorazepam 2,5mg. Psychotic symptoms gradually diminished and after one week ceased completely. The patient did not suffer any other convulsive episode during her hospitalization.

She was discharged to the Psychiatry Day Hospital, where she was partially hospitalized during three months. Due to extrapyramidal effects, risperidone was switched to quetiapine 200 mg per day. The patient did not present any psychotic symptoms, returning to her premorbid state.

In patients with partial seizures, treatment with PER up to 12 mg caused a dose-related increase in psychiatric treatment emergent adverse events (TEAE) [4]. It is important to consider that epilepsy-related variables may contribute to TEAE, such as location of the seizure focus or neurochemical changes related to neuronal excitation and seizure inhibition, that may predispose patients to psychiatric phenomena [6]. Additional studies have shown that variables related to epilepsy implicated in TEAE of AED can include limbic system dysfunction, hippocampal sclerosis, neuronal channel dysfunction or forced normalization [7]. The presence of complex partial seizures and AED polytherapy are also significantly associated with development of psychosis [8]. Female gender and temporal lobe involvement are significant risk factors for AIPD [1].

Our intention is to draw attention to AIPD as a psychiatry adverse effect of PER. After the dose reduction of PER and the addition of an antipsychotic drug, the clinical picture improved promptly and our patient was discharged within a short period of time.

We suggest that patients should be counseled regarding the potential for psychiatric adverse effects when initiating treatment with PER, and physicians should monitor them closely after careful consideration of the risks and benefits for the patient, particularly in cases of polytherapy or the presence of risk factors for the development of psychotic symptoms.

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