CASE REPORT

Negative myoclonus secondary to paroxetine intake

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SUMMARY

Outside the context of overdose and serotonin syndrome, seizures and myoclonic movements attributed to selective serotonin reuptake inhibitors (SSRIs) are rare and poorly documented. We present a 77-year-old man, with no history of epilepsy, presenting in the emergency department with whole body jerks since that morning. Two days earlier, due to a prescription mistake, he was started on paroxetine 20 mg instead of his usual fluoxetine 20 mg. The patient's electroencephalogram (EEG), performed in the emergency department, revealed a bilateral synchronous parieto-occipital fast spike activity pattern, which correlated consistently with negative myoclonus. Two days after stopping paroxetine, the patient presented no seizures and no abnormalities in the EEG. We present an EEG documented case of drug-induced seizures, with a bilateral parieto-occipital pattern, secondary to paroxetine intake. A hyperexcitability of the primary somatosensory cortex inhibiting primary motor cortex output could explain the electroclinical correlation.

BACKGROUND

Seizures and myoclonus are known side effects of selective serotonin reuptake inhibitors (SSRIs), although the majority of cases are related to overdose,¹ often in the context of serotonin syndrome.² Some studies and case reports seem to indicate a slightly increased risk of seizures in patients taking SSRIs,³ although such data is called into question given that these drugs are clearly safe to use in patients with epilepsy.⁴ Myoclonus or myoclonus-like movements without other features of serotonin syndrome are described in some case reports;^{5,6} however, in none of them an electroencephalogram (EEG) correlate was identified. The pathophysiology of myoclonic movements in this context is poorly understood.

CASE PRESENTATION

A 77-year-old man presented to the emergency department (ED) with a history of jerks affecting the entire body since that morning, with no other complaints. He had been discharged 2 days earlier from the hospital, where he was admitted due to a posterior circulation stroke (2 weeks admission, with progressive improvement of the presenting symptoms of vertigo and gait imbalance). Due to a prescription mistake, at the time of the discharge, he was started on paroxetine 20 mg instead of his usual fluoxetine 20 mg. Before presenting to the ED, he did a total of two paroxetine intakes (previous day and that morning). The patient had

no known history of epilepsy or epileptic seizures. Besides the recent stroke, he had a history of type 2 diabetes and a gamma globulin peak detected in a protein electrophoresis, with a later diagnosis of monoclonal gammopathy of undetermined significance (MGUS). On neurological observation, the patient presented bilateral symmetrical myoclonic jerks, with a proximal predominance, involving the four limbs synchronously, only visible with the patient standing or with the arms outstretched, with no visible myoclonus with the patient lying down.

INVESTIGATIONS

The blood workup at the ED did not show any ionogram, renal or hepatic derangement. Cerebral CT scan showed no new lesions, besides the sequelae of past ischaemic strokes (right cerebellum, right mesial temporo-occipital and multiple lacunar lesions in the striatum-capsular region). He did an EEG in the ED which revealed a bilateral synchronous 18 Hz fast spike activity pattern in the parieto-occipital region (figures 1 and 2), which correlated consistently with the jerks, visible with the outstretching of the arms but completely absent with the patient resting (online Supplementary video 1). The patient also had these paroxysms in his lower limbs, although it was not shown in the video.

OUTCOME AND FOLLOW-UP

Two days after stopping paroxetine, the patient presented no seizures and no abnormalities in the EEG. He was restarted on fluoxetine and discharged. One month later he was re-evaluated at the outpatient clinic, with no further evidence of seizures.

DISCUSSION

Our patient illustrates a case of drug-induced negative myoclonus associated with a bilateral synchronous fast spike activity pattern in the parieto-occipital region. The present case report has some technical limitations, namely, the fact that we do not have an electromyography recording documenting the sudden brief loss of tone visible in the video, nor do we have somatosensory-evoked potentials or double magnetic stimulation for cortical inhibition evaluation. It is also worth noting that reports of drug-induced myoclonus with EEG correlate are lacking, so it is still unclear what electrophysiological patterns should be expected. Given these limitations and the unusual EEG pattern for myoclonus, we believe that the data is insufficient to assert that our patient had a true epileptic negative myoclonus,

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Figure 1 Electroencephalogram showing 18 Hz bilateral synchronous fast spike activity in the parieto-occipital region; these paroxysms correlated with the myoclonic events when the patient outstretched his arms. Bipolar montage.

Figure 2 Electroencephalogram showing 18 Hz bilateral synchronous fast spike activity in the parieto-occipital region; these paroxysms correlated with the myoclonic events when the patient outstretched his arms. Referential montage.

despite the suggestive semiology. We also cannot call the seizures 'atonic' given they do not have the necessary 1–2 s duration. In face of insufficient data, we cannot add further descriptors and therefore we have to classify them, according to the new International League Against Epilepsy (ILAE) 2017 Seizure Classification, 'unknown onset motor seizures'.⁷ Despite the fact that we think the seizures have a focal onset with a mesial generator, based only on scalp EEG (without an invasive EEG study), we cannot be certain that the seizures are not in fact generalised (ie, 'originating at some point within and rapidly engaging bilaterally distributed networks'); therefore, the classifier 'unknown onset' is warranted.

Given the temporal relation with paroxetine intake and the seizures self-limiting nature after discontinuation of the drug (and the absence of other systemic imbalance), we assume the causality of the SSRI. It is worth noting that a compounding effect with fluoxetine probably has taken place, given the long washout period of fluoxetine and its inhibition of CYP2D6 isoenzyme,⁸ which is the main enzyme responsible for paroxetine metabolism.⁸ This suddenly increased concentration of serotonin in the synaptic junction could justify a hyperexcitability of the somatosensory cortex, which has been demonstrated to be involved in the origin of negative phenomena through a direct or indirect inhibition effect on the tonic output of the primary motor cortex.^{9–10} The localised dysfunction of the somatosensory cortex, bilaterally, would explain the bilateral nature of the semiology, while having a regional pattern in the EEG. This hypothesis would explain the localisation of the ictal pattern documented in our case, which is, to the best of our knowledge, unique in its electroclinical correlation between EEG findings,

motor seizures in a patient without epilepsy and SSRI intake. We find implausible any direct causality between the seizures and the recent stroke, given the 16 days time gap between the stroke and the beginning of the myoclonus. However, there is evidence in the literature about the role of cerebellar dysfunction in the origin of cortical myoclonus.¹¹ These cases are related to neurodegenerative cerebellar pathology, in patients with chronic multifocal myoclonus. Nevertheless, our patient had evidence of vascular lesions in the cerebellum and cerebellar pathways, so we cannot rule out their role in increasing the patient susceptibility to the drug-induced reported event.

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Learning points

- Myoclonus and myoclonus-like movements can be a side effect of selective serotonin reuptake inhibitors (SSRIs), despite the absence of other serotonin syndrome symptoms. The movements might be of cortical origin, which means they are in fact of an epileptic nature.
- The long half-life of fluoxetine is a fact to remember when switching antidepressive therapy from fluoxetine to another antidepressant (SSRI or other classes).
- One mechanism of negative myoclonic motor seizures is a dysfunction of primary somatosensory cortex which can inhibit primary motor cortex function.

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