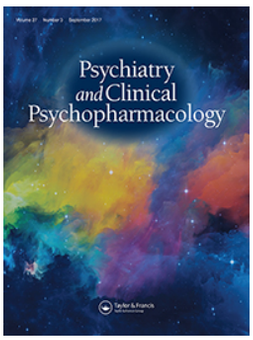

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CASE REPORT

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Relationship of levetiracetam and obsessive-compulsive disorder: a case report

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ABSTRACT

Levetiracetam has gained wide acceptance in the treatment of epilepsy due to its broad-spectrum efficacy, the lack of significant drug–drug interactions, and a relatively benign side effect profile. However, in recent years, the treatment of epilepsy using levetiracetam has been associated with psychiatric side effects such as anxiety, irritability, hostility, depression, hallucinations, and, in some rare cases, obsessive-compulsive disorder. In this case report, we present and discuss onset of obsessive-compulsive disorder symptoms in a 55-year-old epileptic female patient, who did not have any previous psychiatric disorder, including obsessive-compulsive disorder, and who received levetiracetam treatment.

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Epilepsy; levetiracetam; obsessive-compulsive disorder

Case report

The patient is a 55-year-old female, who is an elementary school graduate. She had her first seizure when she was 21 years old. Neurological examination, at that time, revealed no other pathologies, and neuroimaging studies showed no abnormalities. It was reported that the patient initially experienced generalized tonic-clonic seizures once a year, but later the frequency of seizures increased to once every three months. The patient was using carbamazepine 800 mg/day since the time she had the first seizure, but levetiracetam 1000 mg/day was added to the treatment because of the increased frequency of seizures in June 2012. The addition of levetiracetam ensured that seizures came under control, and did not recur. One month after the addition of levetiracetam, the patient started to show obsessive-compulsive behaviour first time in her life, such as thinking that her clothes are dirty and washing them repeatedly. She thought that her hands are dirty unless she washed them for at least 2 hours a day.

The patient presented to a psychiatry clinic with the abovementioned complaints and the treatment was initiated with citalopram 20 mg/day. Two months later, the patient was hospitalized in a psychiatry inpatient unit due to more frequent complaints. Nevertheless, she was discharged against medical advice, 15 days after the hospitalization, even before the planned treatments could be initiated. Afterward, the frequency and length of her obsessive-compulsive symptoms increased. Subsequently, citalopram dose was increased to 60 mg/day, and olanzapine 5 mg/day was added to the treatment, based on outpatient clinic visits. Apparently, the patient did not benefit from the modified treatment regimen, as she continued to spend about 8 hours a day, either washing hands or taking a shower.

Therefore, the patient was hospitalized back in the psychiatry inpatient unit due to a marked decrease in functionality and quality of life. A detailed examination revealed contact dermatitis on her hands, most probably due to excessive washing and cleaning. She also presented with increased anxiety, although perception was normal, and intellectual functions were clinically within acceptable range. A psychiatric examination revealed that she was obsessed with doubts and thoughts over contamination. However, her judgment, abstract thinking, and reality testing were normal. It was apparent that she was engaging in compulsive acts of decontamination, although her insights about this behaviour were acceptable.

There was no evidence of any psychiatric disorders in her family history. Although personal psychopathology was not determined, patient's routine laboratory tests and cranial MRI were unremarkable. She refused to undergo an electroencephalogram, seemingly due to her obsessive thoughts about getting contaminated. Subsequently, olanzapine treatment, started at the time of hospitalization, was discontinued, and the treatment with risperidone 2 mg/day was initiated. In addition, the dose of citalopram was increased to 80 mg/day. On the basis of treatment history, we noticed that obsessive-compulsive symptoms were noticed one month after the addition of

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levetiracetam to treat epilepsy. Therefore, in consultation with the neurology clinic, we decided to gradually discontinue the treatment with levetiracetam 1000 mg/day.

Since then, no epileptic seizures were noted during hospitalization. The patient was discharged, at her own request, in week 11 of the hospitalization with the prescriptions of citalopram 60 mg/day, risperidone 2 mg/day, and carbamazepine 800 mg/day. After discharge, the patient visited the clinic for regular follow-ups, and the dose of risperidone was tapered off. The patient continued on citalopram 40 mg/day and displayed euthymic and positive mood during the last psychiatric examination. Although there was a significant decrease in the frequency of overall obsessive-compulsive behaviour, the obsessive thoughts about contamination and compulsive acts of decontamination lasting for about 30 min in a day were still observed. Patient's eating and sleeping routines have been improved and no epileptic seizures have been noticed since 2011 while she continued to be treated for epilepsy with only carbamazepine 800 mg/day.

Informed consent had been obtained from the patient for using her personal information and medical history.

Discussion

The relationship between antiepileptic drugs and obsessive-compulsive disorder is complex and still unclear. For instance, it was reported that some anticonvulsants such as valproic acid, carbamazepine, and phenytoin have been used for the adjuvant treatment of obsessive-compulsive disorders. On the contrary, it was also reported that zonisamide and topiramate can induce or aggravate obsessive-compulsive disorder [1,2].

In fact, some inferences can be made on the relationship between anticonvulsant drugs and obsessive-compulsive disorder on the basis of neurochemical links. Some neurochemical neurotransmitters, such as glutamate, are known to be associated with the pathophysiology of obsessive-compulsive disorder [3] and epilepsy [4,5]. Despite the uncertainty about the mechanism of action of levetiracetam, recent studies have shown that levetiracetam works by binding to synaptic vesicle protein (SV2A), and exerts its antiepileptic effect by controlling SV2A-mediated glutamate release from presynaptic neurons [6].

Levetiracetam is an anticonvulsant that is associated with a number of psychiatric side effects, which include new-onset mood and anxiety symptoms, but rarely, psychotic symptoms [7–9]. A previous study in 288 epileptic patients using levetiracetam showed adverse psychiatric side effects in 37% of the patients, which included poor seizure control, mental retardation, and impulsivity [10].

Recently, obsessive-compulsive disorder and behavioural changes associated with the use of levetiracetam have been reported [10–13]. In a case report, a 14-year-old female epilepsy patient was reported to show obsessive-compulsive disorder following the addition of levetiracetam 1500 mg/day to carbamazepine therapy [14]. Following the levetiracetam treatment, seizure control was ensured, but the patient started to show obsessive-compulsive behaviour, which lasted for a significant amount of time every day. However, all such symptoms disappeared two months after the discontinuation of levetiracetam, but seizures re-occurred. In another case report, a 21-year-old male patient exhibited obsessive-compulsive symptoms following the addition of levetiracetam to the treatment for seizure control [11]. The type of seizures was generalized tonic-clonic, which was similar to this present case report. On the contrary, there are few other case reports where levetiracetam has been shown to be effective in the treatment of the refractory obsessive-compulsive disorder [15].

In the present report, seizures of our patient were successfully controlled by treatment with levetiracetam and carbamazepine, and we observed that obsessive-compulsive symptoms were only associated with levetiracetam. Notably, there was a clear association between the use of levetiracetam and the occurrence of obsessive-compulsive disorder symptoms, with the severity of symptoms decreasing after tapering off levetiracetam treatment. However, it should be noted that the patient still experiences mild obsessive-compulsive symptoms despite the fact that the dose of levetiracetam was tapered off.

In summary, levetiracetam is a very useful and commonly used anticonvulsant. Yet, it is important to recognize that levetiracetam may increase behavioural side effects and obsessive-compulsive symptoms. Future studies on the inter-relationship between obsessive-compulsive disorder and glutamatergic system may help us better understand the aetiopathogenesis of obsessive-compulsive disorder, a chronic and long-lasting psychiatric disorder.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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