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Successful management of clozapine-induced restless legs syndrome with gabapentin enacarbil

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To the Editor: Treatment of antipsychotics-induced restless legs syndrome (RLS) is conducted primarily by decreasing or discontinuing dosage of responsible medication [1]. However, the concurrent need to treat the underlying psychiatric disorder renders decreasing or discontinuing medication difficult. In such cases, antipsychotics-induced RLS is treated in line with idiopathic RLS, using medications such as dopamine agonists and benzodiazepines [2]. The effect of dopamine agonists and benzodiazepines for secondary RLS were reported in several studies [2], but the effect of gabapentin enacarbil (GE) for secondary RLS was reported in only one study [3]. In the present report, we detail a case wherein GE proved effective in treating clozapine (CLZ)-induced RLS. The written consent has been obtained from the patient for submission of the report.

The subject of the case study was a 40-year-old male with no history of notable conditions, including idiopathic RLS. He also had no history of typical risk factors for secondary RLS, including hypoferric anemia, renal failure, or diabetes. At age 16, the patient began to experience persecutory delusions, and at age 23, according to DSM-IV-TR criteria, he was diagnosed as suffering from paranoid schizophrenia. Antipsychotic monotherapy with 15 mg/day haloperidol, 250 mg/day chlorpromazine, and 50 mg/2-week risperidone long acting injections was initiated, but none of these treatments proved effective. At age 36, because of resistance to other therapies, the patient was placed on CLZ as the primary treatment. When the dosage was increased to 300 mg/day, the patient reported paresthesia in his lower limbs accompanied by the irresistible urge to move his legs. These symptoms worsened at night and were ameliorated by touching his feet or walking. Antipsychotic induced akathisia was ruled out because the patient's symptoms were restricted only to the legs and diurnal variation. Based upon structured evaluation, the patient was fulfilled the International Restless Legs Syndrome Study Group diagnostic criteria for RLS [4]. The patient was diagnosed CLZ-induced RLS as the patient had no previous history of idiopathic RLS and developed RLS after CLZ administration. At this time, the patient's psychiatric symptoms were highly marked, making it difficult to decrease CLZ dosage. The patient was unsuccessfully treated for CLZ-induced RLS, with a combination of 1 mg/day clonazepam and 3 mg/day lorazepam. After obtaining the patient's consent, 600 mg/day GE was added to his treatment regimen, leading to complete resolution of his RLS symptoms within several days, following which the dose of CLZ was increased from 300 mg/day to 600 mg/day, although no recurrence of RLS was observed. Clonazepam and lorazepam were successfully discontinued, and the increased dosage of CLZ aided in controlling the patient's neuropsychiatric symptoms.

To our knowledge, the present report is the second

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one to demonstrate successful treatment of antipsychotic-induced RLS by using GE, and that GE may increase the therapeutic potential of CLZ by controlling the restlessness. While treatment for antipsychotics-induced RLS has not been fully established, it is often treated in line with idiopathic RLS [1, 2]. For patients with treatment-resistant schizophrenia, discontinuation of CLZ is generally difficult. Our findings suggest that, for cases in which conventional treatments for antipsychotic-induced RLS fail, GE may be an effective treatment option, and that the combination of GE and CLZ may be indicated as a clinical option for the treatment of schizophrenia.

Conflicts of interest

All authors declare no conflict of interest associated with this letter.

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