Short-acting Intra-muscular Olanzapine-induced Seizure in a Patient with Dementia: A Case Report

A 69-year-old married woman patient with a three-year history of both Parkinson’s disease and Alzheimer’s disease. She had no pre-existing seizure disorder or history of head trauma. She had received amantadine 100 mg three times daily and the combined drugs of levodopa/benserazide (Madopar®) 125 mg three times daily for two years. At age of 67 years, she first visited our clinic presenting herself with psychotic symptoms including persecutory delusion, and the delusion of personal belongings being stolen. The result of neurological examinations revealed no focal sign of the brain. At that time, she received 50 mg of quetiapine per day at bedtime.

Moreover, the patient had suffered from progressive memory decline. Because of agitation, disturbing behavior, and exacerbation of psychotic symptoms (i.e., the delusion of personal belongings being stolen), she was brought to our emergency department and received 5 mg of olanzapine with short-acting intra-muscular (IM) injection. But her disturbing behavior and psychotic symptoms still persisted, and she received a repeated dose of olanzapine with IM injection 2 hours later. Subsequently, a seizure episode was developed with initial loss of consciousness, extension of the four limbs with tonic-clonic motions, and upward gazing, lasting for about 30 seconds with postictal confusion.

A blood laboratory study showed no electrolyte imbalance, metabolic disarrangement, or changes in blood cell counts. The results of an electroencephalographic examination on the following day revealed multifocal epileptiform discharges, and brain magnetic resonance imaging study was found no evidence of hemorrhage or mass lesions of the brain. We suspected that the short-acting olanzapine injection would induce the seizure attack, and the dose of 400 mg of valproic acid three times daily was prescribed. She subsequently received oral quetiapine, titrating slowly to 100 mg/day and Madopar® to 125 mg two times daily. Subsequently, no seizure-like symptom had been observed without the use of valproic acid.

Our patient was concurrently prescribed daily quetiapine 50 mg, amantadine 300 mg, and Madopar® 375 mg. Although these agents may have caused the seizure, those drugs were taken for a long time without any seizure activity, and our patient had no additional seizure after discontinuing olanzapine IM injection. Therefore, we suggest that olanzapine in IM injection was considered the leading suspect because it was newly used and the seizure occurred during upward adjustment of its dosage.

Comment

Olanzapine, a thiobenzodiazepine derivative, has similar pharmacological properties to clozapine, which is associated with seizures in a dose-dependent manner [1]. Except for patients with schizophrenia [2], oral olanzapine has been associated with clinical seizures in patients with neuropsychiatric disorders including Huntington’s disease and Alzheimer’s disease [3,4]. In contrast,
a previous double-blind study has observed no epilepsy seizure following rapid-acting IM olanzapine injection in treating agitation in 137 patients with Alzheimer’s disease or vascular dementia [5]. Therefore, the association between olanzapine and seizures in clinical practice has been reported only in cases involving oral olanzapine, but it is relatively uncommon in IM administration.

Other potentially contributing factors to cause seizures must be considered. Our patient had a neurodegenerative disease and was already taking quetiapine, amantadine, and Madopar®. A patient with Alzheimer’s disease can show spontaneous action myoclonus, typically as a late manifestation, and the estimated number of patients with seizures is 10%, or 10-fold more than predicted in persons in a reference population [6]. Quetiapine and amantadine are also associated with an increased seizure activity. Moreover, the combination of olanzapine with quetiapine or amantadine may have increased the risk of seizure activity because combination therapy has been identified as a factor for decreased threshold for seizures.

Our patient developed seizures after the olanzapine dosage was suddenly increased to 10 mg/day during a two-hour period, indicating a possible dose-dependent relationship. Based on the observations on our patient, we suggest that clinicians should be aware that IM injection of olanzapine might induce seizures in the elderly with dementia, particularly during the initial titration of olanzapine to a higher dosage. (The authors declare absence of conflicts of interest in writing this letter-to-the editor.)

References


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Received: March 27, 2016; revised: April 15, 2016; accepted: April 18, 2016

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