Case Report
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Olanzapine-induced Concurrent Tardive Dystonia and Tardive Dyskinesia in Schizophrenia with Intellectual Disability: A Case Report

Young Min Choe[1,2], So Yeon Kim[2], Ihn-Geun Choi[2,3], Guk-Hee Suh[1,2], Dong Young Lee[4,5], Boung Chul Lee[2,6], Jee Wook Kim[1,2]

[1]Department of Neuropsychiatry, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, [2]Department of Psychiatry, Hallym University College of Medicine, Chuncheon, [3]Department of Neuropsychiatry, Hallym University Kangnam Sacred Heart Hospital, Seoul, [4]Department of Neuropsychiatry, Seoul National University Hospital, [5]Department of Psychiatry, Seoul National University College of Medicine, [6]Department of Neuropsychiatry, Hallym University Hangang Sacred Heart Hospital, Seoul, Korea

Tardive dystonia and tardive dyskinesia (TDs) are rare extrapyramidal side effects that develop after long-term use of antipsychotics, but they are different syndromes and rarely occur at the same time. Olanzapine is an atypical antipsychotic drug associated with a low risk of extrapyramidal side effects in schizophrenia, but its associations with tardive movements are not clear. We present a case of a 19-year-old Asian female patient with schizophrenia and intellectual disabilities who developed concurrent TDs after long-term use of olanzapine. At her 10-month follow-up examination, her concurrent TDs had been treated successfully with clozapine. This case demonstrates that although the use of olanzapine to treat psychosis and behavioral disturbances is increasing due to its high efficacy and low rate of extrapyramidal side effects, concurrent TDs should be carefully assessed after long-term use of this antipsychotic, especially in patients with schizophrenia and intellectual disabilities. Clozapine, by preventing or reversing the debilitating consequences of concurrent TDs, may be an effective treatment for these patients.

KEY WORDS: Olanzapine; Tardive dystonia; Tardive dyskinesia; Schizophrenia; Intellectual disability.

INTRODUCTION

Tardive dystonia is a syndrome characterized by sustained muscle contractions that frequently cause twisting and repetitive movements or abnormal postures [1,2]. It differs from tardive dyskinesia, the features of which include involuntary, irregular, stereotyped and choreiform or repetitive abnormal movements of the limbs, body and fingers [1,3]. Both tardive movement disorders are rare extrapyramidal side effects that begin after the long-term use of antipsychotics [1,2,4]; however, they are different disorders and rarely occur at the same time [5-7]. Olanzapine is an atypical antipsychotic associated with a low risk of extrapyramidal side effects in schizophrenia (SPR) [8]. In addition, some studies have shown that it improves the symptoms of tardive dystonia and tardive dyskinesia (TDs) [9-12], whereas others have found that olanzapine actually causes tardive dystonia or tardive dyskinesia [13-15]. There are no reported cases of olanzapine-induced concurrent TDs. In SPR patients with intellectual disabilities (IDs), the risk of TDs may be higher because SPR patients often require long-term treatment with antipsychotics, and IDs themselves may be a risk factor for TDs [2,16]. However, the effect of olanzapine on the development of these syndromes in SPR patients with IDs is unknown. Here, we report the case of a young female SPR patient with IDs who developed concurrent TDs while on long-term olanzapine. Treatment with clozapine resulted in the resolution of her concurrent TDs.

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Address for correspondence: Jee Wook Kim
Department of Neuropsychiatry, Hallym University Dongtan Sacred Heart Hospital, 7 Keunjaebong-gil, Hwaseong 18450, Korea
E-mail: kimakins@hanmail.net
ORCID: https://orcid.org/0000-0002-9570-4216

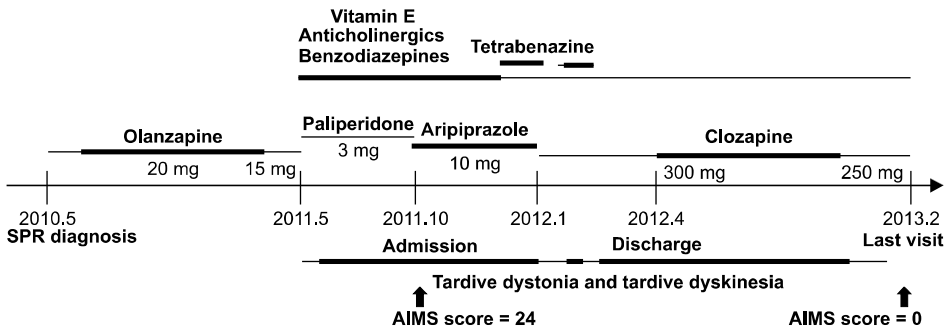

Fig. 1. Clinical timeline of the case. SPR, schizophrenia; AIMS, Abnormal Involuntary Movement Scale.

CASE

The patient was a 19-year-old Korean woman with moderate IDs. An intelligence test revealed a full-scale intelligence quotient of 39 on the Wechsler Adult Intelligence Scale. As shown in Figure 1, she was diagnosed with SPR and treated with 20 mg/day olanzapine, which led to complete remission of her psychotic symptoms of delusion and auditory hallucinations. One year later, during which time she continued olanzapine treatment, her neck started turning intermittently and involuntarily to the left. This severe, frequent, and spasmodic torticollis (also called cervical dystonia) caused her marked distress. In addition, she experienced aberrant eye blinks, abnormal tongue movements, and involuntary and irregular stereotyped choreiform or repetitive abnormal movements of the neck, trunk, face, and upper extremities. Her total Abnormal Involuntary Movement Scale (AIMS) score was 24. A neurologic exam with electroencephalography and blood tests, including plasma Cu^{2+} levels, was performed to rule out Wilson's disease and other metabolic diseases. The results were negative. She had no history of alcohol or substance abuse and no family history of psychiatric or neurologic disorders. After olanzapine therapy was discontinued, we started 3 mg paliperidone and later switched to 10 mg aripiprazole to prevent worsening of the psychosis. Treatment with 12 mg trihexyphenidyl, 2 mg benztropine, 3 mg lorazepam, 3 mg clonazepam, and 800 IU vitamin E in combination with 3 mg paliperidone or 10 mg aripiprazole was ineffective, and her concurrent TDs persisted without improvement. During tapering of her anticholinergics or benzodiazepines, 75 mg tetrabenazine was added to her drug regimen, which resulted in a dramatic but still partial improvement of her concurrent TDs. However, she experienced prominent psychomotor retardation and a dull sensation. Therefore, clozapine treatment was initiated and the dose titrated to 300 mg/day, and her other medications were discontinued. At her 10-month follow-up examination, her concurrent TDs had completely disappeared, and she felt no distress. Eventually, her condition was successfully treated with 250 mg clozapine, 1 mg benztropine, and 1 mg clonazepam. Her final AIMS score was 0.

DISCUSSION

Our young female SPR patient with IDs developed concurrent TDs while on long-term olanzapine. Her concurrent TDs fully resolved after she started clozapine.

This case differs from previous reports of antipsychotic-induced TDs. First, it suggests that a diagnosis of SPR in patients with pre-existing IDs increases the risk of concurrent TDs while on long-term antipsychotic treatment. IDs are common in individuals with SPR [17], and they increase the risk of TDs [16,18]. Therefore, our patient, with both SPR and IDs, was at high risk of tardive movements. Second, the patients suffered from concurrent TDs. According to one study, the relationship between the two extrapyramidal syndromes suggests that having tardive dyskinesia increases the probability of developing tardive dystonia [19]. However, whether tardive dyskinesia is specifically related to tardive dystonia is unknown. Since tardive dyskinesia causes intense suffering in affected patients, the strong possibility of concurrence suggests that these patients should also be carefully monitored for tardive dystonia.

Both the baseline diagnosis and the medication used for its treatment may contribute to tardive movements. Olanzapine is an atypical antipsychotic associated with a low risk of extrapyramidal side effects, including tardive movements, in SPR, but the exact relationship between olanzapine and tardive movements is unknown. Regard-

ing the pathophysiology of olanzapine-induced concurrent TDs, olanzapine at therapeutic doses is associated with a higher D_2-receptor occupancy compared with clozapine which is not associated with tardive movements [20]. Thus, olanzapine may have been responsible for the development of concurrent TDs in our patient.

Previous studies have suggested that aripiprazole is an effective treatment for tardive dyskinesia [21-23]; however, this drug did not lead to a significant improvement in our patient. Aripiprazole has a high affinity for D_2-receptors and a weak affinity for D_1-receptors, which could lead to an imbalance between D_1- and D_2-mediated striatal outputs [1,23,24]. While chronic neuroleptic use results in high D_2-receptor blockade, a lower occupancy rate of D_1-receptors may lead to sensitization of D_1-mediated striatal output and, in turn, to abnormal movements [25].

In our patient, while the concurrent TDs improved in response to anticholinergics, benzodiazepines, vitamin E, and tetrabenazine, there was a more substantial improvement with clozapine. Clozapine is associated with absent or fewer extrapyramidal symptoms and tardive movements than are other antipsychotics [26]. Clozapine also has a lower D_2-receptor occupancy [27] and higher D_1-receptor occupancy. This profile may have contributed to the restoration of the D_1- and D_2-receptor balance [25].

In conclusion, olanzapine is increasingly being used to treat psychosis and behavioral disturbance because of its high efficacy and low risk of extrapyramidal side effects. However, this case report highlights the need for careful assessment of concurrent TDs in patients with long-term use of olanzapine, especially patients with SPR and IDs. Clozapine may be an effective approach for patients with concurrent TDs, either in preventing or reversing the debilitating consequences of this condition.

■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Young Min Choe, So Yeon Kim, Ihn-Geun Choi, Guk-Hee Suh, Dong Young Lee, Jee Wook Kim. Data acquisition: So Yeon Kim, Ihn-Geun Choi, Guk-Hee Suh, Boung Chul Lee, Jee Wook Kim. Supervision: Jee Wook Kim. Writing—original draft: Young Min Choe, So Yeon Kim, Jee Wook Kim. Writing—review & editing: Young Min Choe, So Yeon Kim, Ihn-Geun Choi, Guk-Hee Suh, Dong Young Lee, Boung Chul Lee, Jee Wook Kim.

■ ORCID

Young Min Choe https://orcid.org/0000-0002-9263-876X
So Yeon Kim https://orcid.org/0000-0002-8123-4030
Ihn-Geun Choi https://orcid.org/0000-0002-9183-2827
Guk-Hee Suh https://orcid.org/0000-0003-4303-0368
Dong Young Lee https://orcid.org/0000-0001-8976-8320
Boung Chul Lee https://orcid.org/0000-0002-0968-087X
Jee Wook Kim https://orcid.org/0000-0002-9570-4216

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