CASE REPORT

Efficacy of Aripiprazole in Sulpiride-induced Tardive Oromandibular Dystonia

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Abstract

Tardive dystonia is a side effect of dopamine receptor-blocking agents, which are mainly used as antipsychotic drugs. The treatment of tardive dystonia is difficult and often unsuccessful. An 82-year-old woman experienced mandibular deviation to the left due to spasm of the masticatory muscles with involuntary chewing movement and Parkinsonism. She had been treated with sulpiride for motility disorder for 5 years. Parkinsonism almost disappeared after the withdrawal of sulpiride, but tardive oromandibular dystonia showed no improvement. Aripiprazole treatment at 3 mg/day improved tardive oromandibular dystonia without worsening Parkinsonism. Low-dosage aripiprazole may be effective for tardive oromandibular dystonia in patients with no other psychiatric disorder.

Key words: aripiprazole, tardive dystonia, oromandibular dystonia, sulpiride, Parkinsonism

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Introduction

Tardive dyskinesia is a syndrome of involuntary movements, consisting of abnormal, involuntary, irregular choreoathetoid movements in the muscles of the head, limbs, and trunk. This syndrome is usually associated with long-term exposure to dopamine receptor antagonists, particularly neuroleptic drugs (1). Tardive dystonia, a variant of tardive dyskinesia, is a persistent syndrome of sustained muscle contraction that appears after prolonged use of dopamine receptor-blocking agents (2). Tardive dystonia has numerous clinical manifestations that include twisting and repetitive movements or abnormal postures of the head, neck, back muscles, and other areas. Medical treatment of tardive dystonia is notoriously difficult and often unsuccessful. Oromandibular dystonia (OMD) refers to spasms of the masticatory, facial, and lingual muscles, resulting in repetitive and sometimes sustained jaw opening, closure, deviation, or any combination of these. OMD that develops after months or years of exposure to neuroleptic agents is known as tardive OMD (3).

Aripiprazole is a novel antipsychotic, acting as a modulating partial agonist of the dopamine-2 (D2) receptor. This drug has shown a profile of extrapyramidal side effects similar to placebo in clinical trials and demonstrated beneficial effects in delaying the onset of extrapyramidal symptoms in patients with psychiatric disorders, particularly schizophrenia (4). We report herein the case of a patient in whom tardive OMD improved following treatment with aripiprazole.

Case Report

An 82-year-old right-handed woman visited our hospital with a chief complaint of mandibular deviation to the left due to spasm of the masticatory muscles. She first noted mandibular deviation 1 year earlier, and consulted her local doctor, otolaryngologist, and dentist. Routine laboratory testing revealed no abnormalities. Various treatments, such as benzodiazepines and muscular relaxants, were attempted, but mandibular deviation continued to worsen. She had been treated for hypertension, gastrointestinal motility disorder, osteoporosis, and insomnia with nifedipine at 60 mg/day, sodium rabeprazole at 30 mg/day, sulpiride at 150 mg/day, alfacalcidol at 3 μg/day, and etizolam at 1.5 mg/day for 5 years. No pertinent family history was evident. Neurological examination revealed masked face, mild rigidity, and mild

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dyskinesia. The lower jaw deviated to the left with chewing movements. When she tried to return her lower jaw to a correct position, deflection to the left occurred immediately.

Parkinson syndrome and tardive OMD due to sulpiride were diagnosed. One month after withdrawing sulpiride, Parkinson syndrome had almost disappeared, but tardive OMD showed no improvement. Aripiprazole was then initiated at 3 mg/day and tardive OMD showed marked improvement within 1 month (Fig. 2), and Parkinson syndrome disappeared.

**Discussion**

Aripiprazole is a dopamine D2 receptor partial agonist with partial agonist activity at serotonin (5HT)1A receptors and antagonist activity at 5HT2A receptors. Aripiprazole exhibits agonist properties qualitatively similar to those of dopamine but quantitatively different. In the absence of dopamine, aripiprazole activates D2 receptors, resulting in a net increase in receptor activity. However, this activity is less than that elicited by dopamine. If dopamine is present, aripiprazole inhibits its binding to D2 receptors, thus decreasing receptor activity, although the intrinsic activity of aripiprazole means that activation of D2 receptors is not fully abolished (4).

Some reports have demonstrated the efficacy of aripiprazole in tardive dyskinesia (5-11) and Pisa syndrome, an atypical subtype of tardive dystonia manifesting as tonic lateral flexion of the trunk (12). The mechanism by which aripiprazole inhibits tardive dyskinesia remains unclear, but it may reverse D2 receptor hypersensitivity and restore cholinergic-dopaminergic balance via D2 partial agonist activity. Dosages of aripiprazole used in reported cases were ≥15 mg/day, typically to treat primary psychiatric disorders (mainly schizophrenia). A lower dosage of aripiprazole might improve tardive dyskinesia or dystonia. Aripiprazole at very low doses (0.625 mg/day) could be effective for L-dopa-induced dyskinesia (13); chronic tic disorders in children and adolescents have significantly improved with low doses of aripiprazole (mean dose, 3.3 mg/day) (14). Other reports have described various types of aripiprazole-induced involuntary movements, including acute dystonic reactions (15, 16), tardive dyskinesia (17-22), tardive dystonia (23-25), and Pisa syndrome (26). The dosages of aripiprazole used in those cases were ≥7.5 mg/day. In consideration of the potential risks and benefits, we initially prescribed aripiprazole at 3 mg/day, which is about half the minimum dose associated with the development of adverse reactions.

The results in the present case suggest that aripiprazole at 3 mg/day has potential for the management of tardive dystonia in patients with no psychiatric disorders, although the optimal total dose is unknown. Beginning with a low dosage of aripiprazole (i.e., <3 mg/day) in patients with tardive dyskinesia is important in consideration of the potential risk for aggravation of extrapyramidal symptoms.

**The authors state that they have no Conflict of Interest (COI).**

**References**

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