

## Tardive Blepharospasm and Meige Syndrome during Treatment with Quetiapine and Olanzapine

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### ABSTRACT

Meige syndrome, which has been presented in tardive syndromes, is a form of blepharospasm accompanied by oromandibular dystonia with manifestations over the face, jaw, and neck. A blepharospasm can be induced by antihistamines, dopaminomimetic or sympathomimetic drugs, or long-term exposure to dopamine antagonists. Atypical antipsychotics have less extrapyramidal side effects because of a weak dopamine D2 receptor binding affinity or a strong antagonistic effect to serotonin 5-HT<sub>2a</sub> receptor and have been known to cause less tardive dyskinesia than typical antipsychotics. Thus, in literature, atypical antipsychotics are recommended for the treatment of psychosis in cases of tardive dyski-

nesia. The potential risk factors associated with the development of tardive dyskinesia are extrapyramidal symptoms' history, diabetes mellitus, affective disorder, female gender, older age, and long-term therapy with neuroleptics at higher dosages. As reported below, a patient with an affective disorder who had quetiapine-induced oromandibular dystonia and olanzapine-induced Meige syndrome after antipsychotic augmentation in different stages of the disease process was presented.

**Keywords:** Atypical antipsychotics, tardive dyskinesia, tardive blepharospasm, Meige syndrome

### INTRODUCTION

Tardive dyskinesia (TD) is defined as a neurological, iatrogenic, and hyperkinetic movement disorder characterized by repetitive, involuntary, aimless choreoathetoid movements usually involving the mouth, face, tongue, and extremities. TD is usually associated with antipsychotic drug use because of schizophrenia or a major mental illness. The subtypes of TD include movement disorders such as tardive dystonia, tardive akathisia, tardive blepharospasm, tardive myoclonus, tardive tics/tourettism, tardive tremor, and tardive gait (1).

Among the tardive syndromes, tardive blepharospasm refers to a repetitive, persistent, and severe spasm of the orbicularis oculi muscle as an isolated condition. Meige syndrome, on the other hand, is a form of blepharospasm accompanied by oromandibular dystonia with manifestations in the face, jaw, and neck (2). There are reports showing that a blepharospasm can be induced by antihistamines, dopaminomimetic or sympathomimetic drugs, or long-term exposure to dopamine antagonists. The diagnosis of tardive blepharospasm is made on the basis of symptoms that develop during or within three months of the discontinuation of treatment with dopamine antagonists and a negative family history of dyskinetic blinking, blepharospasm, or other dystonias.

The symptoms of tardive blepharospasm may fluctuate. Eyelid spasm could be exacerbated by fatigue, anxiety, work, and light, whereas it could be relieved by sleep and rest (2,3,4,5). Atypical antipsychotics have fewer extrapyramidal side effects because of a weak dopamine D2 receptor binding affinity or a strong antagonistic effect on serotonin 5-HT<sub>2a</sub> receptor (6). Atypical antipsychotics are thought to cause less TD than typical antipsychotics. As reported by Tenback et al. (7), the incidence rate of TD triggered by atypical antipsychotics is 0.74%. In recent years, some studies comparing typical antipsychotics with atypical antipsychotics found no difference in the risk of developing TD, which has resulted in some controversies (8,9). Below, a patient who developed Meige's syndrome due to quetiapine augmentation to lithium and tardive blepharospasm due to olanzapine augmentation to lithium at different episodes of the illness is presented.

### CASE

A 32-year-old male worker with an 11-year-history of bipolar disorder was admitted to the outpatient clinic accompanied by his father. He had complaints of constant squinting and difficulty in keeping his eyes open. In his past medical history, he was treated with lithium 1200 mg/day, quetiapine 200 mg/day, and olanzapine 20 mg/day because of an exaggerated sense of self confidence believing that he was a wealthy person, excessive money spending, insomnia, feeling full of energy, and quarrelling with others for the last five months. It was mentioned that after his symptoms markedly resolved within one month, he continued his medications without any follow-up examination.



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His past history revealed no chronic diseases. He was a current smoker (1 pack per day for 10 years), but he did not have any history of alcohol or substance abuse. His family history revealed that his grandfather had been called "crazy" because of his impulsive and grandiose behaviors, but there was no diagnosis or treatment.

As reported by his family members, his first episode began as bipolar mania with psychotic features characterized as insomnia, talking too much, increased self-confidence, suspiciousness, mumbling to himself, hearing voices, thoughts of being a rich commander, and expecting an outbreak of war during his military service in August 2001. It was learned that he was treated with haloperidol, biperiden, and carbamazepine during that episode, but these drugs were stopped because of side effects such as walking like a robot, agitation, and restlessness. He was therefore started on diazepam. After the signs of parkinsonism and akathisia subsequently disappeared, lithium 900 mg/day was prescribed. Under treatment with lithium 900 mg/day, he experienced two manic episodes with psychotic features that recovered with quetiapine augmentation (with a dosage adjustment of 100–800 mg/day) between the 2001 and 2004. In 2004, olanzapine (20 mg/day) was added to the therapy because the symptoms were not well controlled under the current therapy. It was learned that he was admitted to a hospital presenting with a difficulty in swallowing, hoarseness, and tongue protrusion resulting from oromandibular dystonia after one month. It was mentioned that his symptoms were resolved with benzodiazepine and biperiden two months after the discontinuation of his other drugs. In 2009, he was once again given lithium 1200 mg/day and quetiapine 600 mg/day for four months because of a manic episode; he had developed oromandibular dystonia again, in addition to blepharospasm characterized as eyelid spasm and had difficulty in keeping his eyes open. All drugs were stopped, and he improved within one month. It was confirmed by his family members that he took lithium 1200 mg/day as a maintenance therapy, and he continued to regularly take his medications. The blepharospasm relapsed during the tapering down of quetiapine, which was received at a dosage of 600 mg/day for another manic episode in 2011. In March 2012, all his drugs were stopped by another psychiatrist because his symptoms were in remission. Unfortunately, he had another manic episode with psychotic features in September 2012 and was given lithium 1200 mg/day, olanzapine 20 mg/day, and quetiapine 200 mg/day.

In his last admission in January 2013, he was under these medications at the same dosages for five months, and he complained of blepharospasm for the last three days. Upon psychiatric examination, he was conscious and oriented. He was euthymic but anxious. He had no active hallucinations and delusions. The ophthalmological consultation was unremarkable for any visual abnormalities, and the neurological consultation did not reveal any movement disorder, except for the blepharospasm. Complete blood count and routine biochemical tests were normal. Cranial magnetic resonance imaging (MRI) and electroencephalography (EEG) were also normal. The blepharospasm was assessed as a tardive syndrome, upon which olanzapine and quetiapine were ceased on the same day, and diazepam 20 mg/day, E vit 1200 mg/day, and C vit 250 mg/day were started. The blepharospasm markedly improved within 15 days. Although he was under regular lithium therapy, he continued to have manic episodes for which his treatment was arranged as lithium at a dosage of 900 mg/day and sodium valproate at a dosage of 500 mg/day. Under this treatment, he had no manic episode or any side effects after one year. An informed consent was obtained from the patient for the publication of the manuscript as a case report.

## DISCUSSION

According to the DSM-IV criteria, TD was diagnosed with at least four-week history of choreiform, athetoid, or rhythmic involuntary movement and a

history of use of neuroleptic medications for at least three months (or one month in individuals aged 60 years or older). In DSM-V, the duration for the diagnosis of TD is not specified, but it is stated to be at least few weeks in duration, in addition to the history of use of neuroleptics for at least few months. On the other hand, it was stated that TD developing upon neuroleptic withdrawal, substitution, or dose changes should develop within 4–8 weeks. The potential risk factors associated with the development of TD were reported as the presence of a past medical history of extrapyramidal symptoms, diabetes mellitus, affective disorders, female gender, older age, and long-term therapy with neuroleptics at higher dosages (9).

Here we presented a patient who developed Meige syndrome due to quetiapine augmentation with lithium during his manic episodes, and tardive blepharospasm due to olanzapine augmentation with lithium and quetiapine therapy because of an inadequate response at his last manic episode. According to the review of TD associated with second-generation antipsychotics, quetiapine is known to have the lowest risk (10). However, there are some case reports indicating that quetiapine and olanzapine could be used in the treatment of psychosis in the presence of comorbid blepharospasm (11,12). Additionally, there are some other reports suggesting olanzapine to be an appropriate choice of treatment in Meige syndrome (13). Also, there are few case reports about TD with olanzapine, and only a few cases of blepharospasm due to olanzapine have been reported (14,15,16,17). While Meige syndrome is thought to be related to olanzapine, which has a strong D2 receptor binding affinity in comparison with clozapine and quetiapine, the presented patient developed tardive blepharospasm related to the use of quetiapine and olanzapine for long periods and in high doses and also upon withdrawal of the drug. We thought that dopaminergic hypersensitivity caused such side effects in our patient. In literature, there are only few case reports of acute Meige syndrome related to olanzapine and quetiapine (18,19). In our patient, the presence of the diagnosis of affective disorder may constitute a risk factor for developing TD. In the management of his treatment, all ongoing antipsychotics were discontinued, benzodiazepines were added, and lithium was decided to be continued for maintenance therapy as a mood stabilizer. In literature, it is observed that ongoing antipsychotics are primarily stopped, and after adding trihexsifenidil or clonazepam/diazepam, clozapine is used for maintenance therapy because most patients are schizophrenic (17,18,19).

This case shows that atypical antipsychotics may also cause Meige syndrome and tardive blepharospasm. As the anamnesis was not taken in detail for all medications and side effects, it was found that the patient sought new treatment options for the same clinical condition. Another issue highlighted by this report is that clinicians should get detailed information on the history of past illness, drug use, and side effects, and the patient follow-up should be performed by a single center.

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