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Case Report

Aripiprazole-induced tardive dyskinesia treated with quetiapine: a case report

Tomruk NB, Saatcioglu O, Yildizhan E, Alpay N. Aripiprazole-induced tardive dyskinesia treated with quetiapine: a case report.

Background: Tardive dyskinesia (TD) is a serious, potentially irreversible side effect of antipsychotics. Although the risk is smaller, atypical antipsychotics still pose a risk. Aripiprazole is an atypical antipsychotic with a unique mechanism of action. It has a partial agonistic effect on the presynaptic D2 dopamine autoreceptor and antagonistic effect at postsynaptic D2 receptors.
Method: There have been a few case reports of aripiprazole-induced TD. A case of aripiprazole-induced TD successfully treated with another atypical antipsychotic, quetiapine, is described and discussed in line with the recent literature.
Results: TD showed rapid improvement with discontinuation of aripiprazole and initiation of quetiapine.
Conclusion: Further studies are needed to ascertain the differential effects and side effects of second-generation antipsychotics in terms of TD.

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Introduction

Tardive dyskinesia (TD) is the most feared chronic extrapyramidal syndrome (EPS), which is associated with poor quality of life, non-adherence and increased medical morbidity and mortality. The mechanism of TD is poorly understood, but is thought to be a supersensitivity response to chronic dopamine blockade. The treatments are mostly unsatisfactory (1). Prevalence rates of 20% with the typical antipsychotics have been reported. Although the risk is smaller, treatment with atypical antipsychotic agents still poses a risk of TD. Current evidence supports a lower TD risk for second-generation antipsychotics than for first-generation antipsychotics (1).

Aripiprazole is an atypical antipsychotic drug with a unique mechanism of action; it inhibits central dopaminergic neuron activity by a partial agonistic effect on the dopamine autoreceptor and also acts as an presynaptic D2 antagonist at postsynaptic D2 dopamine receptors. It also acts as a partial 5-HT1A agonist and 5-HT2A antagonist. Although there have been reports of improvement of TD with aripiprazole (2), there have also been few case reports of aripiprazole-induced TD (3). These seemingly contradictory effects may be because of aripiprazole's both agonistic and antagonistic dopaminergic effects. There are very rare cases indicating the effectiveness of the atypical antipsychotics in the treatment of TD except clozapine (4).

Case

The case reported here was a 56-year-old female patient, married, with a 15-year history of schizoaffective disorder. She had five psychiatric hospitalisations, all of which were for depressive episodes with delusions of reference and persecution, auditory hallucinations and suicidal ideation. Although interepisodic clinical outcome was relatively good with improvement of the psychotic and depressive

symptoms, after the onset of her illness, she had retired for psychiatric disturbance 10 years ago. Her mother had a history of Parkinson's disease and one of her children had mental retardation.

At the onset of her depression, she had been first treated with *mirtazapine*, *sertraline* and *risperidone* (dosages unknown) as an outpatient. Her symptoms were not relieved and she had attempted suicide by hanging herself. During her first hospitalisation, she was treated with *haloperidole* 20 mg/day, *biperiden* 4–10 mg/day, *diazepam* 10 mg/day and seven sessions of electroconvulsive therapy (ECT). She was then given *risperidone* 4 mg/day, *biperiden* 4 mg/day and *diazepam* 10 mg/day as maintenance treatment. She stopped her medication 4 months later as her symptoms remitted.

A year later, she was hospitalised for her second depressive episode with psychotic features and was treated with *risperidone* 2 mg/day and *escitalopram* 10 mg/day and was given *valproic acid* 1500 mg/day as mood stabiliser.

During her third hospitalisation she was treated with *haloperidole* 20 mg/day, *biperiden* 4–10 mg/day, *diazepam* 10 mg/day. *Haloperidole* was later changed to *amisulpride* 800 mg/day because of EPS (bradykinesia and rigidity) which was then reduced to 400 mg/day. *Lithium* 900 mg/day was added as mood stabiliser.

Owing to poor compliance with outpatient medication, she was hospitalised for the fourth time and treated with *chlorpromazine* 100 mg/day, *biperiden* 4 mg/day and *haloperidole* 20 mg/day. After the first day, because of the development of acute distonia, *haloperidole* was changed to *aripiprazole* 10 mg/day and was titrated to 30 mg/day in 12 days. After relief from her depressive and psychotic symptoms, *biperiden* and *chlorpromazine* were also withdrawn and her maintenance treatment was only *aripiprazole* 30 mg/day for 1 year.

Although properly using aripiprazole 30 mg/day, a month before her last hospitalisation disturbing biting and chewing movements in her mouth emerged, and *venlafaxine* 75 mg/day and *hydroxyzine* 25 mg/day were added because of the relapse of her depressive and psychotic symptoms. Also at the same time disturbing biting and chewing movements in her mouth emerged. After 2 weeks of outpatient treatment she was hospitalised as her symptoms and suicidal ideas persisted.

She had dysphoria and prominent delusions of persecution, ideas of reference with no evidence of hallucinations and no cognitive impairment. Her reality testing and abstract thinking were impaired and she had poor insight. Hamilton Depression Rating Scale (HDRS) and Abnormal Involuntary Movement Scale (AIMS) scores were 39 and 12, respectively. Her cranial magnetic resonance imaging (MRI) was unremarkable and her oral dyskinesias were diagnosed as TD because of the use of *aripiprazole* and then it was confirmed by neurology consultation. Her treatment was rearranged as *quetiapine* 200 mg/day, *venlafaxine* 150 mg/day and *diazepam* 10 mg/day. *Venlafaxine* was stopped because of hypertension and *escitalopram* was titrated up to 20 mg/day in 1 week. Following 25 days of hospitalisation, she was discharged with a complete relief of the depressive/psychotic symptoms and with improvement in oral dyskinesia. Informed consent was obtained from the patient.

Discussion

There are several known risk factors such as female gender, advanced age and affective illness for TD in our case. Although she had been treated previously with relatively high doses of typical antipsychotics which pose greater risk for TD, it seems likely that TD is related to long-term and high-dose aripiprazole use (2). Although our patient had been exposed to several other antipsychotic agents, because of partial refusal of medication, their uses were confined mainly to her hospitalisations which are relatively short compared with her 1-year-long aripiprazole use.

Aripiprazole has been associated with a significantly reduced risk of new-onset TD when compared with haloperidole, and there have been case reports on improvement of TD with aripiprazole, we report a case of TD associated with the use of it. Although studies with aripiprazole have shown a low liability for extrapyramidal side effects, there are some case reports concerning extrapyramidal side effects, which include TD, parkinsonism and rabbit syndrome associated with aripiprazole (4).

A TD case associated with the use of aripiprazole 15 mg/day for 18 months for refractory depression was reported where symptoms of TD resolved within several weeks of discontinuation of the medication (5). Another case report describes early onset TD during treatment with aripiprazole in a patient with a history of acquired brain injury (6). In another case in which symptoms of TD developed following 9 months of treatment with aripiprazole 15 mg, the symptoms disappeared rapidly upon discontinuation of aripiprazole and switch to quetiapine (7).

In a 54-year-old female with schizoaffective disorder who had breast cancer while receiving hormonal therapy with tamoxifen for 4 years developed TD 10 months after initiation of aripiprazole 20 mg/day. Her dyskinetic movements completely resolved within 1 month after the discontinuation of aripiprazole. She was successfully maintained on quetiapine without return of dyskinesia for 1 year (8).

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Quetiapine is a 5-HT2A antagonist and a 5-HT1A partial agonist with transient dopamine receptor occupancy, a property shared with clozapine. This transient occupancy hypothesis may partially explain its mechanism of action and the low liability for EPS and TD associated with quetiapine. Three patients with schizophrenia who showed improvement of TD following treatment with quetiapine were reported. They showed marked, prompt and enduring improvement in TD with quetiapine treatment (300–800 mg doses). Clozapine failed to diminish these symptoms in two of the cases (9).

Quetiapine was administered to a patient who had persistent choreoathetoid movements that developed during treatment with conventional antipsychotics and remained unimproved during long-term treatment with risperidone. During 10 weeks of monotherapy with quetiapine, his AIMS score fell from 11 to 3. He was subsequently switched back to risperidone and his movements returned. The addition of quetiapine to his risperidone regimen once again resulted in a decrease of his TD symptoms (10).

Similar to the cases reported in the literature as discussed above, the TD showed rapid improvement with discontinuation of aripiprazole and initiation of quetiapine. The quick onset of dyskinesia suppression in our patient resembles that described in several reported cases of quetiapine treatment of TD.

TD is a serious, potentially irreversible side effect of antipsychotics. Although the risk is smaller, atypical antipsychotics still pose a risk. And it is important to note that aripiprazole can be associated with TD. Further and long-term follow-up studies are needed to ascertain the differential effects of quetiapine and other second-generation antipsychotics in patients with TD.

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