

Relapse of Tourette Syndrome with Clozapine in a Patient of Paranoid Schizophrenia

Sandeep Grover*, Prabhakar Pokhrel and Natasha Kate

Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India

Abstract

Tourette syndrome (TS) is characterized by multiple motor and vocal tics and is commonly associated obsessive-compulsive disorder (OCD). Comorbidity between TS and schizophrenia has been less commonly described. In this case report a case of schizophrenia with comorbid TS is described in which symptoms of TS relapsed when the patient was started on clozapine. Exacerbation of TS with clozapine has been reported in few case reports in the literature. Our case highlights the fact that clozapine should be used with caution in patients with schizophrenia who have tic disorder.

Introduction

Tourette syndrome (TS) is characterized by multiple motor and vocal tics occurring for at least one year. It is commonly associated with attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) [1,2]. Other comorbid psychiatric disorders reported to be seen in patients with Tourette syndrome include autistic disorder, Asperger's syndrome and bipolar disorder [3-5]. However, there is limited data on comorbidity of Tourette syndrome with schizophrenia [6,7]. Further, only few case reports suggest worsening of tics with clozapine [8-11].

In this case report we present a case who had Tourette syndrome prior to adolescence, which resolved on its own. Later the patient developed schizophrenia and while receiving clozapine, had a relapse of symptoms of Tourette syndrome.

Case Description

Mr X, 21 yr old, single, High school passed, presented to the inpatient unit with diagnoses of paranoid schizophrenia and akathisia while receiving olanzapine and aripiprazole. Detailed evaluation of the history revealed that since early childhood, he had motor tics in the form of jerky involuntary movements of the shoulder and hand along with vocal tics, which peaked prior to teen age and then reduced significantly. Initially motor tics were not associated with any dysfunction, but as the frequency and intensity of the tics increased, these were associated with marked social dysfunction. Additionally he had obsessive compulsive behaviour in the form of fear of contamination and repeated washing rituals since early childhood, which led to mild dysfunction. These symptoms gradually receded by the age of 12-13 years along with disappearance of motor tics.

Around the age of 15 years, without any precipitating factor, he developed symptoms characterized by suspiciousness, violent behaviour, delusion of reference, persecution, grandiosity, social withdrawal, anhedonia, apathy, amotivation, associated with academic decline and marked psychosocial dysfunction. He was seen by a psychiatrist after few months of onset of symptoms and was started on Tab amisulpiride which was continued for about 2 months, with which he showed no improvement in symptoms. Following this he was treated with adequate trials of aripiprazole, risperidone, olanzapine and a combination of aripiprazole and olanzapine. Further the history revealed that whenever he received olanzapine, either alone or in combination, he developed severe akathisia.

There was no family history of mental illness or tics. On examination, patient was restless and kept on pacing around. He had delusion of reference, persecution, grandiosity and thought insertion.

A diagnosis of paranoid schizophrenia (as per DSM-IV) and drug induced akathisia was made. His positive and negative symptom scale (PANSS) score was 75 and his Global Clinical Assessment of akathisia on Barnes akathisia rating scale (BARS) was 4. Tab aripiprazole and olanzapine were stopped. In view of the treatment history and side effects, clozapine was considered. Prior to starting clozapine his haemogram, liver function test, renal function test, serum electrolytes, lipid profile, fasting blood glucose level, electrocardiogram and electroencephalogram did not reveal any abnormality. Clozapine was started at the dose of 25 mg/day and gradually increased to 250 mg/day over the period of 4 weeks. Additionally he was treated with Tab clonazepam (up to 3 mg/day) and Tab propranolol 40 mg/day. With clozapine, patient showed significant improvement in his psychotic symptoms and akathisia also reduced significantly. By 6 weeks of clozapine therapy, his PANSS score came down to 41 and the Global Clinical Assessment of Akathisia on Barnes akathisia rating scale (BARS) was rated as 1 (i.e., questionable akathisia). All along his haematological monitoring did not reveal any abnormality. He was discharged from the inpatient unit at this time.

In follow up he reported occasional positive symptoms, following which the dose of clozapine was increased to 275 mg/day. Within few days of increase in the dose of clozapine to 275 mg/day, patient developed motor tics involving the shoulder and elbow along with vocal tics in the form of uttering some religious words. Over next few days he also developed obsessive compulsive symptoms, which were associated with marked distress. Following this clozapine was reduced to 250 mg/

***Corresponding author:** Dr. Sandeep Grover, Assistant Professor, Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India, Tel: 0091-172-2756807; Fax: +91-172-2744401, 2745078; E-mail: drsandeepg2002@yahoo.com

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day and a repeat electroencephalogram was done, which did not reveal any abnormality. Neurologist opinion was sought, who considered the possibility of a tic disorder (Tourette's syndrome). Following this he was started on Tab sertraline 50 mg/day, with which tics and obsessive compulsive symptoms reduced significantly over the period of 5-6 weeks. He has been now maintaining well with Tab clozapine 250 mg/day and Tab sertraline 50 mg/day and is functioning well.

Discussion

TS is associated with many comorbid psychiatric disorders. Among the various comorbidities, schizophrenia is less commonly reported. In a study involving 399 TS patients, schizophrenia was seen in 2.5% of cases [12]. Other studies have reported prevalence of schizophrenia like symptom in about 11-12% [7,13] and schizotypal or schizoid personality disorders in 13-15% of patients with TS [14,15].

In general it is reported that most of the patients with TS have reduction in tics and obsessive compulsive features by adolescence [16], as was in the index case. However, an interesting finding noted in the index case was relapse of symptoms of TS with clozapine. Similar relationship between worsening of tics with clozapine has been described in the form of case reports in the literature [8-11]. In another small study, authors reported exacerbation of TS in 4 out of 7 patients with starting of clozapine in low doses [17]. Although underlying mechanism is not known, some of the authors suggest that worsening of tics with clozapine may be related to an imbalance between the dopamine and serotonin systems [10].

In their review of literature, Marsalek [11] reported that there are 15 reported cases of tardive TS secondary to use of neuroleptic for more than 2 years in patients with schizophrenia. Another 2 cases of tardive TS were reported later [18]. Further, previous reports of tardive TS have reported the same while the patients were receiving an antipsychotic (8 cases) or after stoppage of neuroleptics (9 cases). In the index case, symptoms of TS had a relapse after being treated with clozapine for few months but shortly after increase in the dose from 250 mg/day to 275 mg/day, and symptoms reduced with reduction in dose of clozapine and addition of sertraline. As the index case had received multiple antipsychotics for duration of more than 5 years, possibility of tardive TS can also be considered in this case. However, none of the previous report had noted existent of the symptoms of TS prior to antipsychotic treatment as was seen in the index case. Hence, we considered the possibility of relapse of TS rather than the possibility of tardive TS.

Our case highlights the fact that TS patients can go on to develop schizophrenia later on and patients of schizophrenia, especially early onset schizophrenia may have history of comorbid TS. In view of the same when ever a patient presents with either of the diagnosis, proper evaluation should include evaluation for the other disorder. Additionally our case suggests that clozapine should be used with caution in patients with Tourette syndrome, as it can lead to worsening of the overall symptomatology. Further, in view the literature, it is important to remember than long term use of antipsychotic can lead to development of tardive TS.

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