

Case Report

Schizophrenia with Comorbid Idiopathic Parkinson's Disease: A Difficult Clinical Management Scenario

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ABSTRACT

Comorbidity of idiopathic Parkinson's disease (IPD) and schizophrenia is an uncommon and rare scenario, which often poses a difficult and challenging situation for management. Both the disorders have completely opposite pathophysiology and treatment of one disorder with available pharmacological agents can pose a threat to the other disorder. The situation becomes graver and risk of adverse side effects increases when an individual presents at a later age with both these disorders along with compromised physical and mental health. Of all the available psychopharmacological agents, clozapine has been found to be quite helpful for the management of psychosis without deterioration of existing movement problems of Parkinson's disease. In this case report, we present the case of a 60-year-old female with long-standing paranoid schizophrenia for the last 30 years, who later developed IPD and discuss the various management issues encountered during her treatment.

Key words: Management, Parkinson's disease, schizophrenia

INTRODUCTION

Available literature on comorbidity of idiopathic Parkinson's disease (IPD) and schizophrenia is limited to only a handful of case reports.^[1-8] This possibly suggests that this comorbidity is less common. This could be due to the completely opposite pathophysiology for these disorders, i.e., according to dopamine hypothesis of schizophrenia, positive symptoms are as a result of hyperdopaminergic transmission in the mesolimbic pathway of brain^[9] and symptoms of IPD are as a result of hypodopaminergic transmission in the substantia nigra of the brain. Some of the authors


suggest that comorbidity of both the disorders could be due to independent involvement of dopaminergic neurons in different areas brain (dopaminergic neurons projecting to the motor striatum and those projecting to association regions being affected independently) or the comorbidity could be due to variable vulnerability of dopaminergic neurons in different areas of brain to degeneration.^[1,10]

The management of both the disorders in the same patients is often a therapeutic challenge, as there can be relapse or exacerbation or destabilization of psychotic

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illness following treatment with antiparkinsonian dopaminergic agonists or anticholinergic agents. Most of the available literature highlights the emergence of psychosis induced by antiparkinsonian agents.^[11-14] However, little information is available on the management of schizophrenia among patients with IPD. In this case report, we present the case of a 60-year-old woman with paranoid schizophrenia, who later developed IPD and discuss the management issues.

CASE REPORT

Mrs. Y, a 60-year-old woman presented with acute exacerbation of psychotic illness. Exploration of history revealed that she has been suffering from paranoid schizophrenia since the age of 30 years. Initially, her symptoms were characterized by delusions of persecution and reference, auditory hallucinations (of commenting, commanding, and discussing type), somatic passivity, and irritability. For these symptoms, she was treated with tablet olanzapine 20 mg/day with which she achieved remission. However, over the years, she had multiple relapses due to poor compliance with medications. Over the years, she developed hypothyroidism at the age of 45 years and hypertension at the age of 48 years. At the age of 57 years, she developed neurological symptoms in the form of slowness in her daily activities, difficulty in walking, and would walk in short steps with reduced arm swing. Initially, there was mild improvement with reduction of dose of olanzapine to 10 mg/day along with addition of trihexyphenidyl 2 mg/day. However, within next 6 months, she developed tremors in both hands and there was worsening of gait difficulties. In addition, she had a relapse of psychotic symptoms. At this time, she was diagnosed with IPD and was started on tablet pramipexole 1.75 mg/day and antipsychotic medication was changed to tablet aripiprazole 20 mg/day. However, this change in medications did not lead to improvement in either the psychosis or the Parkinson's features. After a month, tablet syndopa (Levodopa plus Carbidopa) 187.5 mg/day was started along with change of antipsychotic to quetiapine 200 mg/day, following which there was significant improvement in both psychoses and Parkinson features over the next 2 months. However, within a year, her parkinsonian symptoms worsened and the dose of tablet syndopa had to be increased to 375 mg/day in divided doses. However, increase in the dose of syndopa was associated with relapse of psychosis with increased severity, i.e., had increased frequency of auditory hallucinations, somatic passivity, and delusion of persecution toward family members and had significant dysfunction. In addition, she developed perioral tremors and orofacial dyskinesia. Due to the continued symptoms, she was admitted to the inpatient unit.

At this time, on physical examination, she was found to have increased muscle tone in all the limbs, rigidity in all the limbs, tremors in hands, perioral tremors, abnormal movements of mouth, and short stepping gait. On mental state examination, she was found to have decreased psychomotor activity, monotonous speech, blunted affect, delusion of persecution, auditory hallucinations, and poor insight. All the routine investigations (hemogram, liver function test, renal function test, fasting blood glucose level, serum electrolytes, and electrocardiogram) did not reveal any abnormality and magnetic resonance imaging of the brain revealed mild cerebral atrophy.

She scored 17 on the abnormal involuntary movement scale (AIMS) and positive and negative syndrome scale (PANSS) score was 68. Dose of tablet syndopa was reduced to 275 mg/day and she was started on tablet clozapine 12.5 mg/day which was gradually increased to 137.5 mg/day with biweekly monitoring of hemogram. There was a significant reduction in abnormal body movements (AIMS scored reduced to 4) and reduction in psychotic symptoms (PANSS-38) over the next 6 weeks. Parkinsonian symptoms also improved over this period. During this period, her antihypertensive medications and thyroid supplement were continued like before. She was discharged from the inpatient unit in an improved state. She continued to maintain well over the next 3 years in terms of psychotic symptoms on tablet clozapine (137.5 mg/day) without any hematological side effects. However, after 1 year after discharge, her parkinsonian symptoms started worsening, requiring increase in the dose of syndopa (500 mg/day). In addition, she developed features of dementia, for which she was managed with memantine and donepezil combination.

DISCUSSION

The two most common challenges faced by treating psychiatrists and neurologists in cases with comorbid schizophrenia and parkinsonism are to differentiate between antipsychotic-induced parkinsonism (AIP) and IPD and second is to balance the pharmacotherapy for these two disorders with opposite pathophysiology, so that treatment of one does not worsen the other disorder.^[10] Treatment in such cases becomes more complicated, when the age, physical comorbidities, and number of medications increase in the sufferer.

AIP is the second most common etiology of parkinsonism in elderly after IPD.^[15] It is often difficult to distinguish the two. However, certain clinical features, response to treatment and functional neuroimaging features can be of help. In contrast to AIP, parkinsonian symptoms in IPD are usually asymmetric and are frequently

associated with resting tremors whereas parkinsonian symptoms due to AIP are often symmetrical and less frequently have resting tremors. Further, IPD usually affects the entire body while on the contrary, AIP usually affects only the upper half of the body.^[15,16] In terms of response to treatment, if the parkinsonian symptoms do not disappear or reduce in intensity even after adequate interventions such as addition of anticholinergics or reduction in antipsychotic dosage and respond well to dopamine agonists such as levodopa; then, the clinical course and symptoms are considered to be more suggestive of IDP.^[10] Available data from few of the previous case reports, which had used single-photon emission computed tomography using dopamine transporter (DAT) tracer suggest a significant bilateral decrease of striatal DAT uptake in patients with IPD.^[1,2,17] Patients of AIP will have additional increased nigral signal extension. Thereby, these findings further support the notion that nigrostriatal and mesolimbic dopaminergic pathways largely function independently.^[1,2,10,18]

In the index case, reduction in the dose of antipsychotic medications did not lead to amelioration of parkinsonian features. Further, addition of anticholinergic agents such as tablet trihexyphenidyl did not lead to any change in the severity of parkinsonian symptoms. However, the changes done in the antipsychotic medications actually led to relapses in psychosis. In addition, there was development of tardive dyskinesia even while on

quetiapine which is otherwise known to have minimal extrapyramidal side effects and has been proved to be quite beneficial in treatment of psychosis in patients with IPD.^[19-22] However, there was significant improvement in parkinsonian symptoms after addition of syndopa. Thereby, in the index case, the diagnosis of independent IPD was not in doubt.

There are limited data on the management of cases with comorbid schizophrenia and IPD [Table 1].^[1-8,10,23-25]

As is evident from the Table 1, in majority of these cases, onset of IPD was quite early in the course of illness, with only few reports noting these comorbidities among elderly. The case reports, which have reported elderly cases, suggest that management of both disorders together in elderly individuals is more difficult and challenging like the index case.

Majority of these available case reports suggest the use of clozapine for the management of psychosis.^[1,3-7,10,18] Clozapine by its unique and broad receptor profile, i.e., weak D2 and D1 antagonism, has very mild or no extrapyramidal side effects.^[26] The efficacy of clozapine in the treatment of dopaminergic drug-induced psychosis in IPD is also well established in several open-label and randomized controlled trials.^[27-31] In addition, the rationale for using clozapine in the index case was that the index case fulfilled the criteria for treatment-resistant schizophrenia and had tardive

Table 1: Case reports presenting cases of comorbid schizophrenia and idiopathic Parkinson's disease

Author	Patient profile	Psychosis during treatment with anti-PD medications	Antipsychotic used for treatment of psychosis
Friedman <i>et al.</i> ^[4]	32-year-old male with long-standing psychotic illness (autopsy confirmed diagnosis of IPD)	Worsening of existing psychosis	Clozapine
Lam ^[5]	58-year-old female with chronic schizophrenia (autopsy confirmed diagnosis of IPD)	Worsening of existing psychosis	Clozapine
Höflich <i>et al.</i> ^[23]	43-year-old female with schizophrenia	Worsening of existing psychosis	Clozapine + ECT
Orr <i>et al.</i> ^[3]	33-year-old female with schizophrenia	No relation with anti-PD drugs	Psychosis and IPD symptoms both responded to clozapine
Urban <i>et al.</i> ^[6]	47-year-old female with schizophrenia	No relation with anti-PD drugs	Increase in parkinsonian symptoms with FGA and SGA and good response to clozapine
Winter <i>et al.</i> ^[11]	35-year-old male with schizophrenia	No relation with anti-PD drugs	Clozapine
Habermeyer <i>et al.</i> ^[7]	64-year-old male with schizophrenia	Worsening of existing psychosis	Quetiapine
Fujino <i>et al.</i> ^[8]	71-year-old male with chronic schizophrenia	Worsening of existing psychosis	Aripiprazole improved both IPD and psychosis
de Jong <i>et al.</i> ^[10]	55-year-old male with schizophrenia	Worsening of existing psychosis	Clozapine
Gadit ^[2]	57-year-old male with schizophrenia	Worsening of existing psychosis	Risperidone low dose (1.5 mg)
Amorim ^[24]	70-years-old male with schizophrenia	Parkinson plus syndrome at 68 years of age and had worsening of psychosis with syndopa	Risperidone 1 mg/day+depot paliperidone 75 mg monthly
Stoner <i>et al.</i> ^[25]	52-year-old male with treatment-resistant schizophrenia	No relation with anti-PD drugs	Quetiapine

IPD – Idiopathic Parkinson's disease; PD –Parkinson's disease; SGA – Second-generation antipsychotic; FGA – First-generation antipsychotics; ECT – Electroconvulsive therapy

dyskinesia, both of which warrants the use of clozapine for symptom resolution. Further, use of clozapine in patients with IPD and psychosis has also been reported to improve dyskinesia^[3,32] and it is also considered as a second-line treatment for levodopa-resistant late-stage PD tremors in two small double-blind studies.^[27,33] Few case reports have also demonstrated the use of electroconvulsive therapy in treatment-resistant cases with comorbid schizophrenia and IPD resulting in significant improvement in both psychosis and parkinsonian symptoms.^[23,34-37]

To conclude, the index case shows that whenever a patient who has been treated with antipsychotics for a considerable time, develops parkinsonian symptoms during the chronic phase of treatment, at the same or lower dose, one should not only consider AIP but also consider IPD as a possible diagnosis and efforts must be made to differentiate between the two based on the clinical features, treatment response and if required using functional neuroimaging. Elderly individuals with both these disorders should be treated with more care so as to improve the quality of life and reduce suffering due to both disorders. A delicate balance must be made of medications so that symptoms of both disorders remain under control. Whenever possible, clozapine should be considered as an option because of its unique receptor profile and known efficacy in the management of psychosis.

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Conflicts of interest

There are no conflicts of interest.

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