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Case Report

De novo Tardive Tourette-like syndrome after prolonged combination depot and oral neuroleptic therapy

Yogaratnam J, Xu C, Thinn DSS, Yoong LK, Khoo CL, Sim K. *De novo* Tardive Tourette-like syndrome after prolonged combination depot and oral neuroleptic therapy.

Introduction: Tardive Tourette-like syndrome is recognised by the observation of several motor and vocal tics often in individuals receiving psychotropic medications and can happen within 1–3 months of treatment.
Clinical case: We report a case which is unique in its onset of Tardive Tourette-like syndrome comprising of vocal, motor tics and coprolalia after more than three decades of treatment with combination depot and oral neuroleptics.
Discussion: Use of the Naranjo Adverse Drug Reaction Probability Scale indicates a probable relationship between the onset of Tardive Tourettism and the antipsychotic therapy in this patient. This was in contrast to earlier reports which noted earlier onset and partial reversal with termination or change of medications. Clinicians need to pay heed to the emergence of late-onset Tourettism in order to better manage its manifestation and prevent its worsening in the context of holistic care for patients with neuropsychiatric conditions including schizophrenia.

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Keywords: late onset; neuroleptic therapy; Tardive Tourette syndrome

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Introduction

Tardive Tourette-like syndrome is recognised by the observation of several motor and vocal tics often in individuals receiving psychotropic medications for a sustained period of time and the first reports observed the onset of Tourette's disorder in association with administration of methylphenidate (1) and L-dopa (2). Subsequent reports noted the occurrence of Tardive Tourette-like syndrome within patients suffering from a variety of neuropsychiatric conditions such as autism (3), affective disorder (4), cerebral palsy (5), epilepsy (6,7) and schizophrenia (8–11). In terms of treatment features, previous reports were characterised by the onset of Tardive Tourette-like syndrome mostly within a few years of treatment (8,9) with oral psychotropic medications including psychostimulants (1), anticonvulsants (4,6,7), antidepressants (12) and neuroleptics (8,9). To the best of our knowledge, this is the first report of an individual patient with *de novo* development of Tardive Tourette-like syndrome following treatment with combination depot and oral neuroleptic therapy for more than three decades.

Case report

Ms T is a 59-year-old female with a longstanding history of schizophrenia for more than 35 years, and a medical history of hypertension and hyperlipidaemia. She first presented to a psychiatric hospital in her twenties due to a change in behaviour for several months when she was noted to be muttering to herself and incoherent in her speech. In addition, she felt that her neighbours were disturbing her and she kept knocking on their doors. She was started on chlorpromazine 100 mg daily and responded well initially. Over time, she had multiple re-hospitalisations for relapse of schizophrenia with similar clinical presentation often related to her non-adherence with her psychotropic medications. Her chlorpromazine was gradually increased to 600 mg a day and an intramuscular injection of 30 mg of fluphenazine decanoate administered once

every 2–4 weekly was added. She was maintained well with combination of oral and depot neuroleptic medications. In 2009, after more than three decades of treatment with neuroleptic combination, she was noted to have emergence of unusual behaviour for a week that was never observed previously, comprising sneezing and loud shouting many times a day. Her behaviour subsequently led to complaints by her neighbours to the housing authorities. There was no antecedent change in the type and dosage of her neuroleptic medications and she had no past history of tic disorder, other psychiatric comorbidities such as obsessive compulsive disorder, anxiety or mood disorder, substance abuse, surgical or medical illnesses. She related that she would feel a warm sensation on her chest, which was relieved by loud shouting and sneezing. In addition, she would often utter profanities, which she claimed were beyond her control, and frequently embarrassed herself as well. She also developed involuntary sudden repetitive stereotyped jerky movements involving bilateral shoulders. Physical examination did not reveal any choreo-athetoid movements typical of Tardive dyskinesia. She shared that any attempt to hold back the motor movements and vocal utterances would result in greater inner tension, which can end up with explosive yelling. During her admission, the ward nurses observed that her motor and vocal tics were in abeyance whenever she was engaged in ward-based activities but were exacerbated whenever she appeared anxious, excited or frustrated. Mental state examination during the admission did not reveal any significant or enduring psychopathology such as depressive, anxiety, obsessional or psychotic symptoms. She was aware about her discomfort, but said that she was unable to control the vocal, motor tics and coprolalia. Consultations with her neurologist ruled out other medical causes for her condition and neuroimaging investigations (magnetic resonance imaging of her brain) were normal. Other laboratory investigations including full blood count, liver, thyroid, renal function tests, serum copper levels, immune markers and infective screen were normal. Her depot neuroleptic was discontinued, the chlorpromazine was switched to risperidone up to 4 mg daily, and clonazepam 0.5 mg given up till thrice a day was subsequently added. Her vocal and motor tics improved over the next 6 months. A year after the change in medication regime, her motor tics and coprolalia completely resolved but she experienced infrequent vocal tics in the form of less intense sneezing.

Discussion

This case is unique in its onset of Tardive Tourette-like syndrome comprising vocal, motor tics and coprolalia after more than three decades of treatment with combination depot and oral neuroleptics, which was partially reversed with termination of previous medications, and initiation of risperidone and clonazepam. Use of the Naranjo Adverse Drug Reaction Probability Scale (13) indicates a probable relationship between the onset of Tardive Tourettism and the antipsychotic therapy in this patient. Earlier reports of Tardive Tourette-like syndrome in patients with schizophrenia typically occur within a few years of treatment and can happen as early as within 1–3 months of treatment with neuroleptics (10,11).

In terms of psychotropic agents associated with its onset in schizophrenia, implicated medications include both first-generation [haloperidol (9), thioridazine and perphanazine (14)] and second-generation [olanzapine (15), ziprasidone (10) and paliperidone (11)] neuroleptic medications. Our patient was receiving both oral and depot forms of first-generation neuroleptics, which may predispose towards the manifestation of Tardive Tourettism over time. The onset of Tardive Tourette-like syndrome usually occurs within weeks of medication dose adjustment or discontinuation but was not apparent in our case (16).

The pathogenetic mechanisms underlying Tardive Tourette-like syndrome are still unclear especially in relationship to the psychotropic medications as Tardive Tourettism has been associated with the use of first-and second-generation neuroleptics and yet are also relieved by these medications including haloperidol (17), clozapine (9), aripiprazole (11) and amisulpride (15). Postulated neural substrates involve mainly disrupted cerebral dopaminergic neurotransmission such as overexpression of D2 and enhanced release in the prefrontal cortex (18), relative super sensitivity of dopaminergic neurons in fronto-striatal circuitries (19). Treatment of Tardive Tourette-like syndrome can be challenging and without complete remission as illustrated in this case at this point. Options suggested from earlier reports include cessation of suspected offending agents, switching to atypical neuroleptics such as risperidone, aripiprazole, amisulpride, clozapine, use of benzodiazepine such as clonazepam and even typical agent such as haloperidol (9,11,15,17,20). In summary, clinicians need to be pay heed to the possible emergence of Tourette disorder-like symptoms in order to better manage its manifestation and prevent its worsening in the context of holistic care for patients with neuropsychiatric conditions including schizophrenia.

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