

## Clozapine-induced Tardive Dyskinesia

Sir,

Tardive dyskinesia (TD) is an agonizing side effect of long-term use of antipsychotics, mainly convention but also atypical which is often found to be irreversible. It is characterized by involuntary, repetitive, purposeless movements that vary in localization and form and occur in eight main areas such as tongue, jaw, lips, face, trunk, upper extremities, lower extremities, and respiratory system which can lead to unintelligible speech, respiratory distress with diaphragmatic involvement, falls, shame, guilt, anger, and depression.<sup>[1,2]</sup> Pathophysiology of TD is complex and still remains elusive with proposed theories such as postsynaptic dopamine receptor hypersensitivity, abnormalities in the striatal GABAergic neurons and degeneration of cholinergic medium spiny interneurons in the striatum, and neurotoxic effects of the free radicals produced by excessive metabolism of dopamine. Clozapine due to its unique low affinity for striatal D2 receptors is relatively free from TD, and due to its anti-serotonergic (5HT<sub>2</sub>, 5HT<sub>1C</sub>) and anticholinergic properties, it is often found to be therapeutic in drug-induced, even drug naïve patients with TD. However, it is also found to be associated with the development of TD in patients with different psychiatric disorders.<sup>[3]</sup> Here, we present a case of clozapine-induced TD following the long use of clozapine monotherapy.

### CASE REPORT

A 30-year-old male has been suffering from schizophrenia for 8 years. He was treated with risperidone 6 mg for 1 month followed by aripiprazole 30 mg for 40 days earlier with minimal improvement 7 years ago. Later, he was started on clozapine and gradually hiked to

300 mg. He was stabilized with 300 mg for the past 7 years. The patient developed involuntary tongue movement which was like movement of a little snake for the past 6 months. Earlier, the patient did not bother as it was mild and not disturbing at all. For the last 2 months, it was exaggerated so much that he had difficulties in swallowing food particles. On inquiry, the patient did not have any psychotropic drug other than clozapine. He did not have any neurological event such as stroke or head trauma. He did not have any involuntary movement before 6 months. There was no family history of movement disorders. His blood investigations, magnetic resonance imaging brain, and electroencephalogram were within normal limits. Detailed neurological examination did not reveal any focal neurological deficit. Hence, we came to a conclusion that clozapine was the culprit drug for the causation of TD. The patient did not want to stop or reduce the dose of clozapine as he was stabilized with it for long 7 years. He opted for tetrabenazine (25–50 mg) which showed gradual improvement nearly after 6 months of continuous use.

### DISCUSSION

Few patients on clozapine also develop TD. It imposes a clinical dilemma when clozapine is a safer option in TD or the only option in some cases of resistant schizophrenia. A study conducted at Yanbian Socio-Mental Hospital and Yanbian Brain Hospital in China found that the prevalence of TD was 3.96% and of mild variety.<sup>[4]</sup> Clinicians will have to decide whether to continue clozapine in clinically settled patients or to stop it in view of TD. Knowledge about clozapine-induced TD is mainly from case reports and series. One might develop new-onset TD or have

worsening of TD while receiving clozapine. Most patients were on 300–500 mg/day with duration of clozapine use prior to the onset of movement disorder ranged from 1.5 months to 10.5 years.<sup>[3]</sup> Here, in our case, the symptoms of TD developed after approximately 6.5 years of use and while on 300 mg/day. It is unlikely that risperidone or aripiprazole would have caused TD in this case as he was exposed to these two drugs only for 70 days which was 7 years ago, with no movement-related side effects. Here, the patient was ready to bear TD as he was afraid to stop the drug which helped him for the past 7 years. We respected the view of the patient and started him of tetrabenazine which helped him slowly to a level which was not disabling or distressful.<sup>[5]</sup> It was found that few got resolved or reduction of symptoms from TD following stoppage or decrease of dose of clozapine where few did not get any help. Hence, the point of stopping of reducing the dose itself is not evidence based. There is definitely more data to indicate the beneficial effect of clozapine in patients with TD than clozapine leading to worsening of TD.<sup>[3]</sup> However, we need to be cautious while prescribing and should not invalidate the point that clozapine also can cause TD in few cases. In this respect, our case is a valuable add to the existing small literature on “clozapine-induced TD.”

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**Conflicts of interest**

There are no conflicts of interest.

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