**CASE REPORT**

Lithium - Induced Tardive Dystonia Treated with Clozapine

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**Summary**

Tardive dystonia is an uncommon form of chronic dystonia, which usually develops on exposure to neuroleptics. Tardive dystonia (Tdt) following lithium therapy has not been previously reported. The case of a 38 year old man with bipolar affective disorder who developed tardive dystonia while on maintenance lithium treatment is described. Presentation of Tdt in this patient was fairly characteristic although there was no suggestion of recent neuroleptic exposure. Tdt known to have poor treatment response, responded very well to clozapine, a novel anti-psychotic, in this case. To conclude, Tdt may develop on exposure to drugs other than neuroleptics. An adequate trial to clozapine can prove to be a useful treatment option.

**Key words** : Tardive dystonia, Lithium induced, Response to clozapine.

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**Introduction**

Tardive dystonia (Tdt) is a rare, persistent dystonia, associated with exposure to neuroleptics. It is unique in its presentation, attendant distress and disability, and refractoriness to different treatment modalities. It is characterized by development of twisting and sustained muscle spasms, usually involving the head and neck, producing torticollis, retrocollis or anterocollis. Back muscles can also be involved giving rise to opisthotonus, axial rotation and gait disturbance. Youth, male gender, mental retardation, previous head injury and convulsive therapy have been identified as specific risk factors. Apart from neuroleptic exposure, other medications associated with Tdt are anti-emetics such as prochlorperazine, promethazine and metoclopramide, antidepressants like amoxapine, and novel antipsychotics e.g. risperidone (focal Tdt). An effective cure remains elusive. A number of drugs such as tetrabenazine, reserpine, dopamine agonists as well as antagonists, beta-blockers, GABA agonists as well as antagonists,
calcium channel blockers etc. have been tried for treatment, with only modest benefits.2 There are isolated reports of treatment with electroconvulsive therapy, thalamotomy and botulinum toxin injections.2 More recently clozapine has been tried, but whether this drug has any special therapeutic effect, as claimed is debatable.2

Case Report

A 38 year old male presented to the hospital outpatient clinic with a history of bipolar disorder for 11 years and two episodes each of mania and depression. He had received neuroleptics and ECTs for his manic episodes. He had been stable on a combination of lithium (800 mg/day), carbamazepine (100 mg/day) and chlordiazepoxide (10 mg/day) for 3 years, when he first started experiencing twisting of head and neck to the left side, and arching of his back.

These painful movements progressed gradually over the next 6 months, and were associated with severe distress and discomfort. The movements were worse when he was tense, but disappeared during sleep. There were no perioral/tongue movements, facial grimacing, and difficulty in chewing, swallowing or breathing. He had sustained a minor head injury 10 years ago in an accident. No family history of psychiatric illness or movement disorder was reported.

All drugs were stopped on his first visit to the outpatient department. He had significant depressive symptoms, which remitted with 20 mg of fluoxetine daily for 8 weeks. Clonazepam upto 10 mg/day was then tried for the abnormal movements with little success. He subsequently developed a manic episode during which the dystonic movements actually got better. He was admitted during this episode. Apart from manic features (mania rating scale-MRS-score of 40), neurological examination confirmed the presence of torticollis, retrocollis, and opisthotonus, without any cranial nerve or sensorimotor deficits. Abnormal involuntary movement scale (AIMS) score at this point was 11. All investigations including EEG and CT head were normal. Sodium valproate upto 1800 mg/day was added with which manic symptoms started to improve (MRS fell to 20), but dystonia got worse (AIMS rose to 14). Clozapine was started and adjusted at 250 mg/day, the maximum he could tolerate. Clonazepam was tapered off and valproate reduced to 400 mg/day. At discharge, three weeks later he had no manic symptoms (MRS-1). Dystonic movements, pain and discomfort had also reduced (AIMS-10).

On follow-up 12 months later, he was on 150-200 mg of clozapine daily (valproate had been stopped), and showed remarkable improvement. He was euthymic, AIMS rating was down to 2, and disability was minimal. He was back at work and lead a more or less normal life.

Discussion

This patient had several features considered characteristic of drug induced Tdt. Young age, male sex, early onset of dystonia, receiving ECTs and head injury are documented risk factors of Tdt. Involvement of neck and back muscles is very common. Retrocollis, anterocollis, and torticollis (to the right) may be significantly more common in drug induced Tdt, than in primary (idiopathic) dystonias. Pain, emotional distress, physical disability, gait disturbance and social embarrassment are typical of Tdt. Dystonia can occur permanently, even at rest. All movements worsen with anxiety and cease during sleep.2 Spontaneous improvement in dystonia during manic phases has also been reported.3 Tdt differs from acute dystonia that usually occurs within two to five days of starting neuroleptics and disappears within 48 hours of reduction/discontinuation of neuroleptics. Oculogyric crisis, a common presentation in acute dystonia, rarely occurs in Tdt. Similarly, Tdt differs from idiopathic torsion dystonia on grounds of history of antipsychotic drug exposure, early involvement of face and neck, rarity of generalization, and chronic disabled bed ridden state.2 Tdt is also dissimilar to the more commonly occurring tardive dyskinesia. It usually occurs in young men, whereas dyskinesia is more common in older women. Involvement is more widespread in Tdt, and gait disturbance is more frequent. Significant disability, subjective discomfort and awareness of symptoms are much more characteristic of Tdt.2

The presentation also satisfied all the usual criteria for Tdt, i.e. chronic dystonia, exclusion of known causes of secondary dystonia and absence of family history of dystonia.1,4 As far as could be ascertained, he had not been exposed to neuroleptics for, at least, 3 years prior to onset of Tdt. Instead, he had been on lithium and small doses of carbamazepine. We could not come across any instances of lithium - induced Tdt, apart from a reference to onset of Tdt on adding lithium to neuroleptics in a single patient belonging to a large
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Response of Tdt to clozapine is not unusual. The pattern of response in this case with gradual improvement was similar to that reported earlier. However, it is possible that withdrawal of lithium, rather than institution of clozapine led to the improvement. A similar argument has been advanced for remission of Tdt following cessation of neuroleptics. The role of clozapine in treatment of Tdt is, thus, controversial. Some insist that it is the drug of choice, others find little evidence for its usefulness. Nevertheless, this case highlights two important aspects of drug-induced Tdt, the likelihood that drugs other than neuroleptics may cause this syndrome, and that an adequate trial of clozapine is always a worthwhile option in such cases.

References


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