Clozapine-associated Pisa syndrome: A rare type of tardive dystonia

Sir,

Tardive dystonia are delayed-onset drug-induced movement disorders associated with traditional neuroleptic agents, characterized by involuntary muscle contraction, which may be tonic, spasmodic, patterned, or repetitive.[1] Pleurothotonus or Pisa syndrome is a rare type truncal dystonia, first described by Ekbom *et al*. in the 1970s.[2] Recent data show that factors such as female gender, old age, previous treatment with classical neuroleptics, the presence of an organic brain disorder, and a combination of pharmacologic treatment increase the risk of this condition.[3] In contrast to other atypicals, such as olanzapine,[4] which have been reported to cause tardive dystonia, clozapine has been used in treating tardive dystonia, including blepharospasm.[5]

A 52-year-old woman, with schizophrenia, was on regular treatment with clozapine monotherapy for the last 2 years. Past and family history revealed no psychiatric or neurological illness. She was initially treated with risperidone 8 mg/day and due to partial response switched to quetiapine 200 mg/day for 1 year which was replaced with clozapine due to partial response. The dose of clozapine was increased from 50 mg to 200 mg/day over 6 months and was maintained on the same for 1½ years.

In the past 6 months, she developed back pain and frequent, forceful bending of spine to the left along with difficulty to walk, and a leaning posture towards the left side which was gradual and progressive. Medical history was significant for adult onset diabetes. Orthopedic, ophthalmic, and neurological examinations were normal. Computed tomography scan of the brain and magnetic resonance imaging of both brain and spine were normal. Full biochemistry profile, liver function test, serum ceruloplasmin, and thyroid functions were normal.

The appearance of dystonia with monotherapy of clozapine for 2 years strongly implicates the role of clozapine. The diagnosis of tardive dystonia can be made based on the criteria by Burke *et al*. in 1982.[6] The fact that this patient was on clozapine monotherapy for 2 years clearly rules out the involvement of other antipsychotics. It is possible that previous antipsychotic exposure resulted in long-term functional dopamine receptor abnormalities through chronic dopamine receptor blockade. This could have created a sensitizing or priming effect on this patient's striatum.

Thus, clozapine exposure alone may not be sufficient to cause dystonia; it may be necessary for the substrate of an abnormal striatum to be already in place.[7]

While reviewing the literature, we found only few reports[7-11] of possible tardive dystonia associated with clozapine. Davé[8] reported a patient with the recurrent oculogyric crisis while on clozapine. Although this is considered to be a type of tardive dystonia, this patient had previously experienced this while taking perphenazine, calling into question the relationship of these symptoms to clozapine. In 1996, Peacock *et al*.[9] reported mild finger dystonia in one of 100 patients treated (>5 years) with clozapine. In 1999, Molho and Factor reported a case of cervical tardive dystonia in a patient while on clozapine monotherapy.[10]

With the increasing use of clozapine in treatment resistant schizophrenia, the issue of its potential association with tardive syndromes gathers importance. Reporting of similar cases will lead to a more accurate understanding of the incidence of this potential side effect of clozapine.

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Conflicts of interest

There are no conflicts of interest.

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