Tardive Dystonia Due to Aripiprazole Use in a Neuroleptic-Naive Patient

To the Editor: Lungu et al[1] published the first 2 cases of tardive dyskinesia due to aripiprazole in neuroleptic-naive subjects. Both of these subjects had tardive dystonia. One, a 19-year-old woman, had fragile X syndrome and developed her problem after 3 months of aripiprazole treatment. The other, a 56-year-old man, had no preexisting neurologic disorder and developed his movements after 18 months of aripiprazole treatment. Although other tardive syndromes have been ascribed to aripiprazole,[2–4] all of the individuals had prior exposure to dopamine receptor–blocking drugs.

The following is an additional case of tardive dystonia due to aripiprazole in a neuroleptic-naive woman with no history of neurologic problems.

Case report. Ms A, a 53-year-old woman seen in July 2009, reported a "lifelong" problem with depression but was first treated with psychotropic drugs starting 5 years before. The only neuroleptic she took was aripiprazole 5 mg/d, started in October 2007. In July 2009, she was taking aripiprazole 5 mg/d and also clonazepam 1 mg twice daily, escitalopram 20 mg/d, and propranolol 10 mg twice daily. She denied any use of prochlorperazine or metoclopramide.

She had been an intravenous heroin user in her 20s and had hepatitis C but was HIV negative. She denied use of any other drugs. Results of her neurologic examination were normal except for her involuntary continuous truncal spasms, mostly flexing of her trunk with occasional extension of her pelvis. These occurred when Ms A was sitting or standing but resolved when she lay down. She was also restless when the movements occurred but was relaxed and without movements when lying horizontally. She had mild facial masking and mild bradykinesia and walked without arm-swing. She displayed no choreiform movements.

Aripiprazole treatment was stopped, and Ms A was treated with tetrabenazine 25 mg bid. This caused a mild increase in her parkinsonism and significant benefit in a reduced level of dystonia. This benefit did not persist, however, and 2 months later she was taken off the tetrabenazine. Her dystonia was not signicantly different than at her initial visit.

While there is a general belief that the atypical antipsychotics are associated with fewer extrapyramidal disorders than first-generation neuroleptics, the data in support of this are not clear.[5–7] Parkinsonism has been associated with all of the atypical antipsychotics except quetiapine and clozapine,[8] but there are few data on how common the other disorders, akathisia, acute dystonia, and the tardive syndromes, are in patients not previously treated with neuroleptics.[9] There are few published reports of tardive syndromes occurring with atypical antipsychotics in neuroleptic-naive patients, possibly due to widespread first use of first-generation drugs, possibly due to a lower predisposition to develop a tardive syndrome without prior exposure to a first-generation neuroleptic, or possibly due to less interest by either authors or journals in publishing such cases.

Aripiprazole is a partial dopamine D_2 agonist as well as a serotonin 5-HT_{1A} agonist and 5-HT_{2A} antagonist.[10] Yet, it has been found, even at low doses, to worsen motor function in people with Parkinson's disease.[11]

The occurrence of a tardive syndrome in a neuroleptic-naive patient clearly implicates the single drug as the cause of the disorder. One possible explanation for the presumed lower incidence of tardive dyskinesia[12] with the second-generation drugs is that the syndrome simply takes longer to develop. These cases, although only 3,[1] argue against this explanation, as all occurred after relatively short exposure to the medication.

As aripiprazole has been approved for treatment of nonpsychotic major depression by the US Food and Drug Administration, and is being advertised for this purpose on television, we may see a marked increase in cases of tardive dyskinesia and parkinsonism. It should be noted that the neuroleptic syndrome has been reported with every atypical antipsychotic, including clozapine.[13]

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