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Case Report

TARDIVE DYSKINESIA WITH ARIPIPRAZOLE - – A CASE REPORT

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Abstract :

Aripiprazole,a novel antipsychotic agent is the latest addition to the class of atypical antipsychotics. It is a partial dopamine agonist and has been advocated for treatment of many psychiatric disorders including schizophrenia, bipolar affective disorder, irritability associated with autism and as an augmentation therapy for Major Depressive disorder. This drug is known for its minimal extrapyramidal side effects. Till now, aripiprazole has been regarded as a relatively safe agent when it comes to the risk of developing TD. Rather on the contrary, aripiprazole is known to have been used as a treatment of tardive dyskinesia. Here, in the case report that follows, we document a case of a 46 year old lady developing tardive dyskinesia manifesting as involuntary orofacial movements after continuous use of the drug in the dose of 15 mg once daily for 10 months.

Key words: Aripiprazole, Tardive Dyskinesia, Schizophrenia

INTRODUCTION

Tardive dyskinesia is a syndrome characterized by abnormal involuntary movements, typically involving the orofacial region, limbs, and trunk. Essential features of tardive dyskinesia include involuntary movements of the tongue, face, and jaw. Though most Tardive dyskinesia cases are mild, severe oral dyskinesia may result in dental and denture problems that can progress to ulceration and infection of the mouth as well as muffled or unintelligible speech. Also, gait disturbances due to limb dyskinesia may leave patients vulnerable to falls and injuries. Traditionally,first generation antipsychotics are considered to have higher risk of Tardive Dyskinesia when used in patients with schizophrenia, schizoaffective disorder, or bipolar disorder. Also,they occasionally occur in other patients,as people with fetal alcohol syndrome, developmental disabilities, and other brain disorders as well. Risk factors of TD include increasing age, preexisting parkinsonism, previous brain damage, antipsychotic treatment duration, and exposure to FGAs.

TD has been associated with polymorphisms of both the dopamine receptor D2 (DRD2) gene[1] , TaqI A and TaqI B and associated haplotypes[2], and of the dopamine receptor D3 (DRD3) gene[1,3] , the dopamine transporter(DAT) gene, and the manganese superoxide dismutase (MnSOD) gene. It was also proposed that a dysfunction of the dopamine transporter is responsible for causing tardive dyskinesia. However, no evidence of involvement of a polymorphism with a variable number of tandem repeats(VNTD) in the DAT gene (SLC6A3) in dyskinesias induced by antipsychotics could be associated by a

research done by Lafuente et al.[4] Thus, further research is needed to investigate the role of the dopamine transporter in the development and maintenance of TD.Galecki et al reported the possibility of a polymorphism of the manganese superoxide dismutase (MnSOD) gene behind causation of TD.[5]

With the advent of the second-generation (atypical) anti-psychotic agents (SGAs), all of which utilize a serotonin-2 receptor (5-HT2) blockade, the risk of TD has apparently decreased, thereby allowing clinicians to treat schizophrenia with less possibility of a side-effect burden. The off-label use of SGAs also continues to increase in the form of augmented therapies for resistant depression and anxiety[6,7]. In fact, the FDA recently approved aripiprazole as the first augmentation (add-on) strategy for the treatment of unipolar major depression. At a therapeutic dose, it is noteworthy that aripiprazole has one of the highest D2 receptor affinities; however, because of its partial agonist properties, it has a lower risk of causing acute EPS and, probably, TD.[8-11]

Till now, aripiprazole has been regarded as a relatively safe agent when it comes to the risk of developing TD. In fact few have reported aripiprazole to be therapeutic for TD. However, by contrast, there is slowly increasing published data which associates aripiprazole with TD.[12-14]

CASE

Mrs J. S.,a 46 yr old married female from Amolapatty ,Dibrugarh came to our hospital(ASSAM MEDICAL COLLEGE,DIBRUGARH),on 28/07/2012 with the chief complaints of disturbed sleep,suspiciousness,fearfulness and irrelevant talking for a duration of 6 months. She had history of similar illness in the past. The significant findings during her Mental Status Examination were delusion of reference,delusion of persecution, and auditory hallucinations. She was diagnosed as a case of schizophrenia paranoid type and so was prescribed TAB ARIPIPRAZOLE 15 mg once daily at bed time and TAB TRIHEXYPHENIDYL 2mg in the morning. In her next visit on 01/09/2012,her symptoms had improved and she was directed to continue the same treatment.Mrs sonowal was maintaining well on the same treatment until she came to our OPD having developed symptoms of chewing movements around the lips on 25/05/2013.She was complaining of orofacial involuntary movements for the past one month.she was prescribed tab vitamin E 800 mg after which she showed improvement.She maintained well for a year without reccurence of symptoms and revisited the OPD with complaints of the orofacial movements having started again for the past 2 weeks.She was prescribed tab Tetrabenzene 25 mg for two days and then subsequently increased to 50 mg in two divided doses as maintenance dose.When she was reviewed on 12/07/2014 ,she had improved much and was maintaining well.

DISCUSSION

The case that we discussed above is a clear example of new-onset oromandibular TD arising during the use of the atypical neuroleptic agent aripiprazole when used at the time for treating schizophrenia in this middle aged woman. A few important observations did not go unnoticed in the above described patient. First, above patient was antipsychotic medications naïve till she took aripiprazole although she had a similar type of illness in the past . Second, she developed classical TD like abnormal involuntary movements in the orofacial region within 10 months of starting therapy with aripiprazole 15 mg.The symptoms moreover could

not be attributed to the use of any other medications in the regime.Controversy does not cease to exist as regarding the use of aripiprazole both for and against as regards to treatment of tardive dyskinesia. Nearly all of the published data is in the form of case reports. We then conducted a literature review of aripiprazole-induced TD. Zacher and Hatchett (2006) used aripiprazole 20 mg to treat a case of bipolar illness. Pseudoparkinsonism ensued soon after starting the drug, and rabbit syndrome (characterized by rhythmic movements of the mouth) was considered to be a dystonic event but not necessarily TD[15]

Sajbel and Evcimen and their colleagues[16,17] reported two cases of aripiprazole-induced TD in two patients,both being cases of schizo -affective disorder. Both patients were receiving 20 mg/day. After 10 days of discontinuing aripiprazole in one of the patients,his abnormal tongue movements ceased.

In other case reports, aripiprazole was used to treat and alleviate TD induced by other neuroleptic agents in patients with bipolar and schizo-affective illnesses. It is difficult to determine whether aripiprazole acted as a treatment or whether stopping the previous higher-potency neuroleptic agent allowed the remission of TD[18-21] .

Risk of TD with aripiprazole can be explained by one probable mechanism as has been proposed by recent studies as regards to its 'functionally selective' action at the D2 receptors.It can act as an agonist or partial agonist or even an antagonist on the D2 receptors depending on the cellular milieu[22].This property of aripiprazole may result in it behaving as potent first generation antipsychotics with blockade of upto 90 percent of D2 receptors[23].But still though,which strata of the aripiprazole receiving patients are at a potential risk of developing TD is still a matter that can only be disclosed by further research.In our case of Mrs JS,she fulfils the aforementioned risk factors of developing TD i.e female gender and long antipsychotic treatment duration.This report suggests that physicians should be alert and observant enough when starting on Aripiprazole in a patient with stated risk factors.

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