ARIPIPRAZOLE ASSOCIATED RABBIT'S SYNDROME: A RARE CASE REPORT

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Abstract-

Rabbit syndrome (RS) is a rhythmic movement of the mouth and lips caused by antipsychotics that resembles rabbit munching. There is no tongue involved in the movement, which is solely vertical and has a frequency of about 5 Hz. Long-term use of first-generation neuroleptics has been proven to cause RS, but nothing is known regarding the risk of RS from newer atypical antipsychotics. Aripiprazole is a new dopaminergic drug that has been demonstrated to be clinically effective as an antipsychotic with little extrapyramidal motor adverse effects. We describe the case of a 47-year-old male patient who got RS while being managed with aripiprazole for delirious mania. The current case emphasizes the importance of being cautious while administering aripiprazole to patients.

Index Terms- Aripiprazole, Rabbits syndrome, extrapyramidal side effects, Young's Mania Rating Scale, Delirious Mania

I. INTRODUCTION

Antipsychotic-induced Rabbit syndrome (RS) is an uncommon kind of extrapyramidal syndrome (EPS) characterized by fast, subtle, rhythmic perioral muscle movements on a vertical axis with a frequency of around 5 Hz with no tongue involvement, resembling rabbit chewing and puckering movements[1] . Despite its rarity, the presence of RS has significant clinical implications.

Aripiprazole is a novel antipsychotic that is gaining in popularity among clinicians. Because of its unique mode of action as a dopamine-system stabilizer, aripiprazole is thought to be among the next generation of antipsychotics [2]. We describe a case on RS observed in a delirious maniac patient managed with Aripiprazole.

II. CASE HISTORY:

A 47-year-old male presented to the outpatient department with the complaints of tremulousness of hands, involuntary perioral movements, with slurred speech since past 1 week. The patient was on follow up with us on a regular basis for six months. when he brought up his complaints of hyper-religiosity, easy distractibility, suppressed need for sleep, over talkativeness, over familiarity, easy irritability, uncontrollable emotional outbursts, destructive acts, and exhibiting erratic behavior, such as remaining naked for an inappropriately extended period after bathing 10 days prior to the visit. The patient was tentatively diagnosed with a delirious manic episode based on the symptoms, and a score of 46 was recorded on the Young's Mania Rating Scale (YMRS). He was treated with Sodium valproate 600 mg/day, Olanzapine 10 mg at night, and Aripiprazole 20 mg/day, as well as Lithium carbonate 600 mg/day in divided doses. After 18 days, The patient got discharged with the YMRS score of 12 after full recovery. The patient was advised to continue with Aripiprazole 20 mg/day and Sodium valproate 400 mg/day, and asked to follow-up every 15 days. Subsequently, the patient's symptoms did improve upon regular follow-up, except irritability. Around 8 days prior to the current visit, the patient started experiencing involuntary movements of the lips and atypical trembling perioral movements. The tremors were modest, with a frequency of 4 to 5 Hz in the vertical axis. The patient claimed that the movements were frequent whenever he was under any kind of stress and persisted throughout the day intensifying during work. A comprehensive evaluation at the time revealed aberrant perioral movements that worsened when completing tasks requiring motor skills or attention. There were no out-of-the-ordinary tongue movements. There were no signs of Parkinson's disease nor dystonia was observed. All routine tests, including an ophthalmological examination and a computed tomography of the head were performed and found to be within the normal limits. His mental state examination revealed no psychopathology other than apprehension over his movements.

The conclusive diagnosis of Aripiprazole-induced Rabbit Syndrome was made after all other possible conditions were ruled out. Based on which Aripiprazole was discontinued and tablet lorazepam and trihexyphenidyl (THP) 2mg/day was started. After

a 5-day follow-up, the patient reported improvement in RS, and after a 20-day follow-up, the patient reported that the symptoms had completely subsided with the combination therapy. THP was stopped after 20 days. However, for a 5-month follow-up period, the patient was maintained on sodium valproate 400 mg per day and clonazepam 0.5 mg per day, with continuous improvement in his symptoms. The patient was recorded with a score of 1/4 on the Abnormal Involuntary Movement Scale (AIMS) of the 'lips and perioral' subcategory, compared to the previous score of 3/4 before the start of treatment with the combination medication. A score of 7 was recorded on the Naranjo adverse drug response (ADR) probability scale, suggesting a "probable" adverse drug reaction.

III. DISCUSSION:

Rabbit syndrome is a rare extrapyramidal antipsychotic side effect characterized by orofacial motions resembling rabbit gnawing and puckering. RS is one of four types of tardive dyskinesia (TD), which are all extrapyramidal adverse effects of long-term neuroleptic therapy [1,3]. The pattern of movement is not the same as tardive dyskinesia (TD), it's a type of oral dyskinesia that causes the tongue to move more slowly and erratically than usual. The tongue is not involved in the involuntary motions, which are restricted to oral and masticatory muscles.[1] The rabbit syndrome is categorized as an antipsychotic-induced EPS, although it varies from classical EPS in that it is more likely to develop later in the course of therapy and/or may appear without additional extrapyramidal adverse effects[4]. This particular syndrome is more common in mid-aged and older individuals, with women being more vulnerable than men. [5] The mechanisms that cause RS are thought to be comparable to those that cause neuroleptic-induced Parkinson's disease [1,5]. Long-term neuroleptic exposure has been associated to RS, although less is known regarding the risk of RS from newer atypical antipsychotics [6].

Aripiprazole is an atypical antipsychotic agent that acts as a partial agonist of the dopamine D2 receptor, as well as a 5HT 1A agonist and a 5HT 2A antagonist [7]. Aripiprazole is an antipsychotic drug classified under the chemical class of dihydroquinolinone. It has a unique mode of action that is dual in nature, exhibiting partial agonistic activity on dopamine D2, D3, and serotonin 5HT1a receptors. However, it antagonizes 5HT2a receptors [7,8]. Aripiprazole has a very high affinity and occupancy at striatal D2 receptors (average putamen- 87 percent; ventral striatum- 91 percent and caudate-93 percent). D2 occupancy levels were also found to be highly associated with plasma drug concentrations, with even the lowest dose (10 mg) resulting in 85 percent D2 occupancy. Thus, there is a more likelihood of developing EPS in a significant manner and it is reported that the D2 occupancy exceeded up to 78%, with atypical antipsychotics as well [9]. Furthermore, Aripiprazole has been found to have no anticholinergic action at any dose within its therapeutic range, which might excuse the development of antipsychotic-like effects because no muscarinic receptor blockage occurs [10]. Aripiprazole is considered as a viable antipsychotic medication, however, as in case of any other antipsychotic medication, careful considerations should be practiced while administering relatively high doses of Aripiprazole to the patients who have never had an exposure to psychiatric medication.

IV. CONCLUSION

The current case highlights the importance of exercising caution when prescribing aripiprazole to patients, as well as the importance of doing thorough EPS screening. Despite the fact that the risk of developing EPS and RS is lower, with novel antipsychotic agents like Aripiprazole, it is still recommended to the practitioners to be cautious while prescribing such medications, and moreover rapid titrating of Aripiprazole is advised, especially while co- prescribing with CYP26 inhibitors and in geriatric population. Furthermore, we believe that more research is needed to fully understand the hazards of EPS linked with partial dopamine agonists.

CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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