

Tardive Dyskinesia arising with Contemporaneous use of Aripiprazole and Quetiapine in an Adolescent with Intellectual Disability and its Spontaneous Remission with Treatment Cessation: Case Report

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INTRODUCTION

Tardive Dyskinesia (TD) due to antipsychotic use is characterized by involuntary, stereotypical, choreiform or athetoid movements affecting especially the mouth, tongue, and face which arise usually after at least three months of treatment, usually with typical antipsychotics (TAPs). The movements may also arise within the first month after cessation of treatment, last at least four weeks and may also be observed in the extremities and/ or trunk [1,2]. The rate of TD may vary widely (i.e. 0.5- 62.0 %, 3). TD, in classical form, is characterized by stereotypical movements of oral-facial-lingual-masticatory muscles [4]. Those may be expressed as protrusion or retrusion of the tongue, pursing/ smacking lips, sucking, chewing and other stereotypies. Emotional factors typically worsen symptoms while sleep causes cessation of movements [5]. Atypical Antipsychotics (AAPs) may have lower risks of TD compared to TAPs and some may even be used for its management. However, chronic use of AAPs at elevated doses are also known to lead to TD [2,6,7].

Here, we report a male adolescent who used aripiprazole and quetiapine, contemporaneously for approximately a year and who developed TD two months after an increase in quetiapine dose. The symptoms remitted spontaneously after cessation of treatment.

CASE

The patient was a 14-years old male who was brought to our department with complaints of "irritability, aggression, insomnia, self-harm and harming others". The symptoms had been present since early childhood, were non-episodic and not related to any stressors. He was diagnosed with moderate intellectual disability, Attention deficit/ Hyperactivity Disorder and Conduct Disorder while he was six years old and received methylphenidate, atomoxetine, valproate and risperidone in various

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durations and doses without benefit. Congenital, bilateral deafness was also present and necessitated use of hearing aids. A trial of methylphenidate (up to 72 mg/ day) led to development of tics and reduced symptoms only partially. Therefore, aripiprazole 5 mg/ day was added and titrated to 20 mg/ day. Due to continuing insomnia and behavioral problems quetiapine 25 mg/ day was added and titrated upwards to 300 mg/ day in three months. Involuntary movements including grimacing, lip smacking, tongue protrusion and movement of arms and hands arose two months after the last titration of quetiapine. Neurological evaluations revealed chorea-athetoid, dyskinetic movements affecting the oral-pharyngeal area and upper extremities. The movements started a month before and increased in severity in the last two weeks. Laboratory evaluations, magnetic resonance imaging, electroencephalography were all normal. An evaluation with the Abnormal Involuntary Movements Scale led to a score of 19 and a general movement disorder severity of 4. Different drugs have been reported to induce TD formation. In the last edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), it is described as a movement disorder developed by the use of a neuroleptic drug for at least a few months. According to history and evaluations, the patient was diagnosed with TD due to antipsychotic use. An evaluation with Naranjo Adverse Drug Reaction Probability Scale yielded a score of 7 (probably adverse drug reaction). Aripiprazole and quetiapine were tapered gradually and treatment with methylphenidate was continued. AIMS score at the first week of follow-up was 7 with a significant reduction in symptoms. Baseline psychiatric evaluation with the Clinical Global Impression Scale, Severity of illness (CGI-S) was 6 (severely ill), Global Improvement (CGI-I) was 2, and Efficacy Index was 2. Symptoms of TD were completely resolved at the second week. Clozapine 25 mg/ day was started at the first month of follow-up and titrated to 100 mg/ day due to his ongoing clinical symptoms. Behavioral symptoms and insomnia were significantly reduced during clozapine treatment while no symptoms of TD emerged in follow-up.

DISCUSSION

Here, TD arising in a patient treated simultaneously with aripiprazole and quetiapine and its spontaneous resolution with cessation of AAPs was presented. Incidence of TD developing after use of AAPs was reported to be 13.0 % [8]. The incidence was previously reported to rise 3.0- 5.0 % / year in the initial years of treatment and culminate in a yearly

rate of 20.0- 25.0 % with longer treatment durations [9].

The exact pathophysiology of TD is still not clarified. Proposed mechanisms include; hypersensitivity of striatal dopaminergic receptors, reduction in gamma-amino-butyric acid (GABA) turnover leading to up-regulation of GABA receptors in basal ganglia, neuro-toxicity probably mediated by free radicals, striatal injury probably related with change in ratio of D1 and D2 receptors, noradrenergic hyperactivity, cholinergic hypo-activity and changes in serotonin and/ or neuropeptides [10].

Quetiapine, an AAP, along with clozapine was listed among agents that may be used for management of TD, although reports also exist of TD arising due to its use [11-14]. The beneficial effects of quetiapine in TD may be due lower post-synaptic D2 affinity along with rapid receptor dissociation or a relative increase in dopamine at the striatum due to elevated 5-HT₂ and H1 affinities. The latter may compensate for D2 receptor hypersensitivity [11,12].

Aripiprazole, an AAP, acts as a partial agonist of presynaptic D2 auto-receptors and an agonist of post-synaptic D2 receptors. This action causes an agonist-like effect in cases of lack of dopamine while excess dopamine leads to an antagonist-like effect (i.e. "dopaminergic stabilizer", [15]). Some reports suggest that it may help in management of TD [16] while cases of TD arising due to aripiprazole were also reported [17,18].

Spontaneous remission of TD was rarely reported while previous reports of its resolution after changing AAP treatment exist [19].

This case was deemed worthy of reporting due to spontaneous and rapid resolution of TD after cessation of AAPs as well as its onset with quetiapine and aripiprazole treatment. Increased use of antipsychotics among children and adolescents may elevate the risk for extrapyramidal adverse effects such as TD. Those symptoms cause concern for parents, relatives and clinicians and youth with intellectual disability may be under elevated risk. Evaluation of involuntary movements in regular, follow-up visits, even for patients using relatively safe agents (e.g. quetiapine, aripiprazole) may be suggested.

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