DOI: 10.14744/DAJPNS.2020.00111
Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2020;33:429-432

CASE REPORT

Risperidone-induced tardive dystonia in a 10 years old boy and the efficacy of aripiprazole: a case report

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ABSTRACT

Tardive dystonia (TDt) is one of the extrapyramidal syndromes caused primarily by long-term use of dopamine receptor antagonists such as antipsychotics. Although the risperidone-induced TDt cases have been reported in adults, there are few case reports and clinical anecdotes in children. The first step in treatment is the controlled withdrawal of the drug causing the TDt and, if necessary, a transition to a newer "atypical" antipsychotic class. In this article, we present a case of risperidone-induced tardive dystonia and the efficacy of aripiprazole in a 10-years-old boy with moderate mental retardation and conduct disorder referred to us due to restlessness, aggression, self-mutilation, and leg and hip spasms. The child's dystonic symptoms and challenging behaviors almost fully recovered 3 months of after the aripiprazole administration. Given that the long-term use of antipsychotics in children is increasingly widespread, TDt should be evaluated and monitored periodically. Furthermore, aripiprazole may be a suitable substitute in the TDt treatment in children.

Keywords: Aripiprazole, child, risperidone, tardive dystonia

INTRODUCTION

Tardive Dystonia (TDt) is a movement disorder that affects the extremities, trunk, neck, or face, and develops as a side effect of long-term antipsychotic treatment. Sustained muscle spasms caused abnormal postures, repetitive twisting or rotating movements, or both. Some potential risk factors for the development TDt are chronic use of antipsychotics, younger age, male sex, previous brain injury, early extrapyramidal symptoms (EPS), intellectual disability, and mood disorders. The prevalence of TDt is about 3% of patients receiving long-term antipsychotic treatment. Unlike tardive dyskinesia, TDt develops in a shorter period of time, following antipsychotic medication and with significantly less cumulative antipsychotic intake. The duration of exposure to antipsychotic medications required to precipitate tardive dystonia varies from months to years (1-3).

TDt can be overlooked in pediatric patients since atypical antipsychotics are less likely to cause tardive syndromes than typical antipsychotics (3) and there are few case reports in children compared to adults (4). In this report, we present a 10-year-old boy with risperidone-induced tardive dystonia. Our aim is to describe the characteristics, management, and treatment of TDt, and to demonstrate the therapeutic effects of aripiprazole on dystonic symptoms in this patient

How to cite this article: Uzun Cicek A, Hocaoglu C, Ozmen T. Risperidone-induced tardive dystonia in a 10 years old boy and the efficacy of aripiprazole: a case report. Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2020;33:429-432.

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Received: March 31, 2020; **Revised:** August 21, 2020; **Accepted:** September 26, 2020

example. Written informed consent was obtained from the parents of patient for the case presentation and publication.

CASE

The patient was admitted to our clinic with restlessness, aggression, self-mutilation, and leg and hip spasms. He had been diagnosed with a moderate intellectual disability, at the age of four. Risperidone 0.25 mg/day was started due to challenging behaviors and hyperactivity and was gradually increased to 1 mg/day, six years ago. The child had not been examined by a child and adolescent psychiatrist for three years, however, the mother had adjusted the risperidone dose according to the child's symptoms (doses ranging from 5 to 8 mg/day, and in the last year 6 mg/day). He had been using risperidone without interruption for 6 years, initially uneven, but regularly for the rest of the time.

He had abnormal twisting and rotational movements and contractions in his hips and legs, for 2 years, and thus he had unsteady gait, eventually losing his ability to walk 6 months ago. He was unable to stand up and walk due to twisting and hyperextension of his trunk and legs and hyperpronation of the arms were also observed. The physical examination revealed no tics, akathisia, or any other EPS. No other drug and alcohol-substance use was reported before and after the complaints, and there was had no history of involuntary or dystonic movements. His medical records showed abnormalities in his previous neurological examinations. There was nothing remarkable in his medical history. In his family history, his mother had a major depressive disorder diagnoses and she had used sertraline 3 years ago. A family history of movement disorder and/or EPS was detected. With suspected risperidone-induced tardive dystonia, a full diagnostic and differential diagnostic work-up was performed dystonic movements including neurological consultation, routine laboratory investigations, coagulation, and metabolic examinations, cranial computed tomography and magnetic resonance imaging, electroencephalography and electromyography. These investigations showed no abnormality. The child's score on the Abnormal Involuntary Movements Scale (AIMS) (5) was 16. The movement disorder severity score was four, and the loss of skill secondary to abnormal movements score was four on AIMS.

Based on the history and clinical examination findings, a diagnosis of risperidone-induced tardive dystonia was made. Risperidone was immediately stopped, and since antipsychotic therapy was required for the patient's disruptive behaviors, temper tantrums, and self-mutilation, aripiprazole 2.5 mg/day was started and gradually increased to 7.5 mg/day. We did prescribe other psychotropic agents during the follow-up period. Psychiatric examinations were performed at 2-weeks intervals. At the end of 3rd month the AIMS score was two (the severity of movement disorder score was one, and the skill loss score secondary to abnormal movements was 1). Clinical symptoms almost completely recovered within three months. Further, there was a noticeable improvement in his emotional and behavioral symptoms and outbursts of temper.

DISCUSSION

In this case presentation, we report the treatment of risperidone-induced TDt with the use of aripiprazole in a 10-year old intellectually disabled patient. Recognized risk factors for the development of TDt include chronic and uneven use of antipsychotics, (occasional discontinuation of antipsychotic treatment), young age, male sex, intellectual disability, and mood disorders (1,2). In our case there have been some risk factors for TDt such as pediatric age, male sex, intellectual disability, long-term and uneven antipsychotic use.

The pathophysiology of TDt is not fully understood yet. The most emphasized mechanism is the hypersensitivity of the dopamine receptor system following exposure to a dopamine receptor blocking agent (1). The risk of EPS with risperidone is higher, particularly at higher doses, due to high dopamine D2 antagonism (75-80%). Moreover, the risk of EPS may be higher in childhood, since the density of dopamine D2 receptors is high (6).

Although tardive movement syndromes such as TDt are more frequently associated with first-generation antipsychotics than second-generation antipsychotics, the latter has been shown not as safe as expected and the risk for tardive syndromes still exists (7). It has been demonstrated that second-generation antipsychotic agents such as olanzapine (8,9), risperidone (4,10), aripiprazole (11-15), and ziprasidone (16) may cause tardive dystonia or dyskinesia. In the literature, risperidone-induced tardive dystonia cases have been reported in children (4). However, little is known about its treatment and there is no definite consensus. TDt can be difficult to manage. If antipsychotic treatment is required to continue, clinicians should switch to

clozapine or a newer antipsychotic. Although there are no controlled studies, dopamine-depleting agents, anticholinergic agents, GABAergic drugs, serotonin agonists, botulinum toxin injections, and deep brain stimulation (DBS) therapy are also tried as a treatment option (17). Aripiprazole is an atypical antipsychotic with partial agonistic activity to dopamine D2 and serotonin 5HT1A receptors and full antagonistic activity to the 5HT2A receptor. The occupancy of D2 receptors occurs without inducing EPS in the majority of subjects since partial agonism induces a lower functional antagonism of D2 receptor-mediated neurotransmission, rather than full antagonists (18). Due to this property, there is a low risk of tardive dyskinesia (18), and has been found successful in treating TDt in several reports (19) as well as treatment with aripiprazole has shown considerable improvement in tardive dyskinesia caused by typical and atypical antipsychotics (20). On the other hand, there are also publications reporting aripiprazole-induced TDt and tardive dyskinesia (11-15).

In our case, we could not start clozapine since there were no Food and Drug Administration indications for the pediatric population or manufacturer guidelines for use in children in the absence of psychotic or schizoaffective symptoms, accompanied by persistent suicidal or self-injurious behavior (21). Thus, we preferred aripiprazole which is reported to be effective in TDt. We did not need to use any other treatment options, because the dystonic reactions almost completely disappeared, and AIMS scores decreased significantly with the cessation of risperidone treatment and switching to aripiprazole. However, we cannot make inferences about whether the improvement of tardive dystonia was a result of the stopping of risperidone treatment or the success of aripiprazole since aripiprazole was started immediately after the cessation of risperidone. If the improvement is due to cessation of risperidone treatment, we can suggest that the success of aripiprazole does not cure dystonia, but instead of this, not precipitating the dystonia again.

In summary, TDt can also be seen in children treated with atypical antipsychotics and TDt should be kept in mind especially in the presence of risk factors. Aripiprazole may be an option in the treatment of TDt in children, without loss of antipsychotic efficacy.

The best strategy against TDt is prevention. Therefore, clinicians should prescribe the lowes possible dose of antipsychotic drugs, when there is a definite indication. Also, clinicians are responsible for informing the patients and their parents about the side effects. For this purpose, it is recommended to have repeated interviews with the patient's parents regarding the side-effect profile of the antipsychotic drugs. To improve treatment outcomes and monitor drug compliance and side effects, pediatric patients using antipsychotic drugs should be supervised repeatedly as a baseline and continuous monitoring.

Contribution Categories		Author Initials
Category 1	Concept/Design	A.U.C., C.H.
	Literature review	A.U.C.
	Data analysis/Interpretation	A.U.C, C.H., T.O.
	Case follow-up (if applicable)	A.U.C, T.O.
Category 2	Drafting manuscript	A.U.C, C.H., T.O.
	Critical revision of manuscript	A.U.C, C.H., T.O.
Category 3	Final approval and accountability	A.U.C., C.H., T.O.
Other	Technical or material support	C.H.
	Supervision	C.H.

Acknowledgments: Authors would like to thank the patient and his family for their collaboration to the study.

Disclaimer: This manuscript has not been previously presented or published in any conference.

Informed Consent: Written informed consent for case presentation and publication was obtained from the patient's parents.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors reported no conflict of interest related to this article.

Financial Disclosure: There are no funders to report for this submission.

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