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Case Report

Psychiatry/Mental Health Section

Acute Dystonia Associated with Low-Dose Aripiprazole in a Male Child: A Case Report

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ABSTRACT

Aripiprazole is a newer anti-psychotic agent with low liability for Extrapyramidal Symptoms (EPS). Acute dystonia develops due to a lack of dopamine, resulting in a relative overactivity of cholinergic neurons. In the past, cases of Aripiprazole-induced acute dystonia have been reported more frequently among adults than children. Here, the authors present a case in which acute dystonia developed at a very low dose (2 mg) of Aripiprazole. The case involves a 10-year-old boy diagnosed with Oppositional Defiant Disorder (ODD) who exhibited aggressive behaviour and irritability. Aripiprazole (2 mg) was initiated for treatment, but after five days, the patient developed excessive sleepiness, slurred speech, oculogyric crisis, and torticollis, indicative of acute dystonia. To rule out any organic causes, a detailed assessment and investigations were conducted, including complete blood counts, liver and kidney function tests, serum calcium, electrolytes, ceruloplasmin, blood copper levels, slit-lamp examination for Kayser-Fleischer ring, and electroencephalography, which did not reveal any significant organic conditions. Aripiprazole was discontinued, and Promethazine was administered. The dystonia score on the Unified Dystonia Rating Scale (UDRS) decreased from 10 to 0 in 5 days, indicating complete resolution of dystonia. Naranjo's causality assessment score was seven, reflecting the probable association of aripiprazole with acute dystonia. This case emphasises the importance of monitoring for adverse reactions to anti-psychotic medications, particularly in paediatric patients, and the need for prompt recognition and management of adverse effects to ensure patient safety and treatment efficacy. To the best of our knowledge, this is the first case report of acute dystonia in a child at such a low dose of Aripiprazole. Clinicians should be vigilant for the emergence of such significant adverse effects of commonly used drugs.

Keywords: Anti-psychotic agent, Aggressive behaviour, Oppositional defiant disorder

CASE REPORT

A 10-year-old boy presented with complaints of aggressive behaviour for one year. Upon detailed assessment, the child appeared irritable and easily got annoyed over trivial issues. He would frequently argue with his parents and refuse to comply with their instructions. Deliberately annoying his parents and blaming them for his mistakes and behaviours were common occurrences. On a few occasions, he directed abusive language towards his mother and forcefully slammed doors without any major anticipatory reason. His early developmental history revealed nothing significant; he maintained a cordial relationship with his siblings and performed averagely in studies. There was no history of abuse, abnormal behaviour, low mood, seizures, or substance abuse either in the child or his family.

Following a detailed psychiatric evaluation and investigations, a diagnosis of ODD was made. He was started on tablet Aripiprazole 2 mg daily. The patient's father reported an improvement in the child's behaviour; however, on the sixth day of treatment, the patient started experiencing excessive sleepiness. He developed slurring of speech, abnormal eye movements (left eyeball would roll upwards), and left-side deviation of the neck. These movements occurred multiple times a day, lasting for five to six minutes each time, and the patient was unable to control them. Upon examination, it was found that the patient was experiencing oculogyric crisis, torticollis, and slurred speech. To rule out any organic cause, a detailed assessment and investigations (including complete blood counts, liver and kidney function tests, serum calcium, electrolytes, ceruloplasmin, blood copper levels; slit-lamp examination for Kayser-Fleischer ring; and electroencephalography) were conducted, but they did not reveal anything significant.

Finally, considering the temporal correlation of symptom onset, a diagnosis of Aripiprazole-associated acute dystonia was considered, and the score on UDRS was 10 [1]. In outpatient care, aripiprazole was immediately discontinued, and the patient was started on tablet Promethazine 25 mg orally. Over the next five days, the symptoms improved completely, and the UDRS score decreased to zero, indicating resolution of dystonia with promethazine administration. Naranjo's causality assessment score was 7 [2]. Written informed consent was obtained from the father.

DISCUSSION

Aripiprazole is a newer anti-psychotic with partial agonist activity at dopamine (D2, D3) and serotonin (5-HT1A) receptors and antagonist activity at serotonin (5-HT2A) and dopamine (D2 receptors) [3]. Among children and adolescents without definitive diagnoses or with more than one spectrum disorder, aripiprazole helps in achieving rapid stabilisation [4,5]. Acute Dystonia is characterised by muscle spasms in any part of the body [6]. Aripiprazole has a low liability for EPS [5]. Though rare, aripiprazole-induced dystonia has been reported in paediatric patients following overdose [6]. Aripiprazole-associated acute dystonia has been reported more commonly among adults than children. The majority of reported cases were taking a combination of medications, and the dose of aripiprazole was 2.5 mg/day or above [Table/Fig-1] [7-13].

In contrast to all reported cases, the male child in the index case developed acute dystonia with monotherapy of aripiprazole at a dose of 2 mg/day. To the best of our knowledge, this is the first case report where dystonia developed at a very low dose of aripiprazole. Dystonia resolved with promethazine administration. Naranjo's causality assessment score was 7, reflecting the probable association of aripiprazole with acute dystonia [2].

Acute dystonia is caused by a lack of dopamine, resulting in a relative overactivity of cholinergic mechanisms. The action of aripiprazole on the D3 receptor and its antagonism of 5-HT6 and

Authors	Sex/Age	Diagnosis	Medications
Singh MK et al., 2007 [8]	Male, 10 years	Bipolar disorder	Aripiprazole (10 mg/day) & Guanfacine combination
McLaren JL et al., 2010 [9]	Male, 11 years	Bipolar disorder & ADHD*	Aripiprazole (30 mg/day), here co-prescribed Methylphenidate was stopped before onset of dystonia
Huang YH and Lee CS, 2010 [12]	Male, 10 years	ADHD*	Aripiprazole (2.5 mg/day) & Methylphenidate (36+5 mg/day)
Basay O et al., 2016 [10]	Male, 17 years	ADHD* & Conduct disorder	Acute Dystonia following a switch from atomoxetine to Aripiprazole (5 mg/day)
Kubota K et al., 2017 [7]	Male, 14 years	Autism spectrum disorder	Acute overdose of 30 mg of Aripiprazole
Isik CM et al., 2020 [11]	Female, 11 years	Mild intellectual disability & ADHD	Aripiprazole (2.5 mg/day) & Methylphenidate (36 mg/day)
Hadler NL et al., 2023 [13]	Male, 19 years	Schizophrenia	Aripiprazole (5 mg/day)
Present case	Male, 10 years	Oppositional Defiant Disorder	Aripiprazole (2 mg/day)

[Table/Fig-1]: Comparative study of the case with past literature [7-13].
*ADHD: Attention deficit hyperactivity disorder

5-HT7 receptors are still unknown, and hence it may play a role in oculogyric crisis [14]. Aripiprazole lacks protective anti-cholinergic action, which is supported by the fact that acute dystonia resolved after the administration of promethazine, an anti-histaminic drug with anti-cholinergic activity as well [15].

The peak incidence of acute dystonia is usually seen within 24-48 hours of the initiation of therapy [16]. However, in the index case, dystonia developed after 6 days of aripiprazole, which is a new finding to report. Although the authors tried to rule out other possible causes of late onset of dystonia, there might still be some unknown contributing factors that need to be explored in the future.

CONCLUSION(S)

The index case highlights a less common but significant side effect of aripiprazole at a very low dose, especially in the paediatric age group. A thorough work-up and vigilance are required before the initiation of aripiprazole in children. Clinicians should be watchful for the emergence of such significant adverse effects of a commonly used drug, and family members should also be counselled to be vigilant during the initial week of therapy.

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