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Diurnal Enuresis Secondary to Aripiprazole in a Child with Autistic Disorder: A Case Report

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Otizm Tanılı Bir Çocukta Aripiprazole İkincil Gelişen Diurnal Enürezis: Vaka Bildirimi

To the Editor;

Aripiprazole is a commonly used second-generation antipsychotic agent for the treatment of schizophrenia, bipolar disorder, and other mood disorders. The Food and Drug Administration (FDA) approved aripiprazole for autism spectrum disorder (ASD)-related irritability such as aggressive symptoms, temper tantrums, and deliberate self-injuriousness in children and adolescents aged 6-17 years. Frequently reported adverse effects of aripiprazole are extrapyramidal symptoms, akathisia and tremor. Diurnal enuresis exists in approximately 10% of children [1,2]. Although drug-induced urinary incontinence is noted as one of the substantial side effects of selective serotonin reuptake inhibitors (SSRIs); reports on antipsychotic-induced enuresis are available [2,3]. However, side effects of aripiprazole in children as urinary retention and enuresis has been rarely reported. In particular, there are very little information regarding aripiprazole-induced enuresis in ASD [4-6]. In this case presentation, we aimed to report diurnal enuresis developed secondary to aripiprazole treatment in a six-year-old boy with ASD.

CASE

A 6-year-old boy was referred to our outpatient clinic with complaints of aggressiveness, hyperactivity, repetitive and self-injurious behaviors. According to his developmental history, he was diagnosed with ASD because of verbal developmental delay, lack of eye contact, social-emotional reciprocity and stereotyped behaviors when he was four years old. The case was diagnosed with ASD according to DSM-5 criteria. Risperidone was prescribed at a dose of 0.25 mg/day; but discontinued because of the drug-related severe sedation. Thus, aripiprazole was started at the dose of 1 mg/day. On the fifth day of aripiprazole treatment, he developed new-onset diurnal enuresis recurring 5-6 times a day for 3 weeks until the medication was stopped.

His medical history, results of physical and neurological examinations and urinalysis were not remarkable. He had urinary bladder control at the age of 3 and had no history of urinary incontinence. Following discontinuation of aripiprazole, his enuresis ceased. After four weeks, due to re-exacerbation of behavioral symptoms, aripiprazole was restarted at a dose of 1 mg/day and then enuresis reappeared and recurred on the fifth day of treatment 5-6 times a day.

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Drug-induced adverse effects were measured with the Naranjo probability scale [7], which indicated a probable adverse effect associated with aripiprazole. Consequently, we could not maintain the treatment with aripiprazole due to the severity of enuresis. This case study demonstrates the development of diurnal enuresis in a child with ASD when aripiprazole was added to the pharmacological treatment. We also experienced that enuresis disappeared when aripiprazole was discontinued. Moreover, the reoccurrence of enuresis when aripiprazole was used for the second time indicates that the relationship between aripiprazole and enuresis may not be coincidental.

Consistent to our clinical experience, though rarely seen,there are some reports of aripiprazole-induced urinary retention and enuresis in children [2,4,5,8]. Although SSRIs cause enuresis in most of the cases [9,10] and aripiprazole is a treatment option for enuresis [3,11], sometimes aripiprazole might be the reason of nocturnal enuresis [2,5,6]. In this case, 5-HT2A antagonism of 5-HT2A receptors on detrusor muscle and the antagonism of alpha-1 receptors on internal sphincter might constitute the mechanisms of enuresis triggered by aripiprazole. In addition, aripiprazole with its serotonin reuptake effect might have another mediating role on enuresis due to cholinergic neuromuscular impact of serotonin on isolated detrusor muscle [10]. This is also an important reason of enuresis developing after SSRI use [12]. Another enuresis-enhancing effect of aripiprazole may occur through 5-HT1A system [4]. Antagonism of 5-HT1A inhibits bladder contractions [13]. Partial agonism of aripiprazole on 5-HT1A receptors may facilitate enuresis by increasing bladder contractions.

Herein, we are reporting a rarely seen case of aripiprazole-induced diurnal enuresis in autistic children. It is noteworthy that most of the case reports of aripiprazole-induced enuresis including the current study have come from Turkey. The etiopathogenesis of this condition is not clear . Frequent use of aripiprazole in ASD in Turkey or an unknown genetic background across Turkish population might be responsible for its more frequent occurrence in our country. Although aripiprazole has become widely common in treating behavioral problems associated with autistic disorder, this case report also highlights that development of enuresis with low doses of aripiprazole should be considered when using it in children with neurodevelopmental disorders such as ASD.

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