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CASE REPORT

Mydriasis Associated with Atomoxetine Treatment in a Child with Attention-Deficit/Hyperactivity Disorder (ADHD) and Specific Learning Disorder (SLD)

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ABSTRACT
Attention-deficit/hyperactivity disorder (ADHD) is a chronic condition marked by persistent inattention, hyperactivity, and sometimes impulsivity, which begins in childhood and often lasts into adulthood. Here, we report a patient with ADHD and specific learning disorder (SLD) who had a mydriasis following atomoxetine treatment. The temporal relationship between the time of atomoxetine administration and development of mydriasis in the absence of an identifiable medical condition or confounding medications and the fact that there was no occurrence after atomoxetine discontinuation suggests that atomoxetine was responsible for mydriasis. Although mydriasis is a rare side effect, clinicians should be aware that atomoxetine may cause mydriasis and inform the patients about these potential side effects when prescribing.
Keywords: Attention-deficit/hyperactivity disorder, atomoxetine, mydriasis, specific learning disorder, Naranjo scale

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a chronic condition characterized by developmentally inappropriate inattention, hyperactivity, and impulsivity, resulting in maladaptive behaviors at home and school. The most prevalent neurodevelopmental disorder in childhood, ADHD, affects 12.7 % of children in Turkey (1). Worldwide approved effective medications used for ADHD are methylphenidate, as a stimulant, and atomoxetine, as a non-stimulant drug. Atomoxetine is generally safe and well tolerated for treatment of ADHD in school-aged children. Headaches, upper abdominal pain, decreased appetite, vomiting, nausea, irritability, dizziness, and somnolence are among the most common side effects. In addition to these common side effects, it has been reported that the use of atomoxetine can be associated with an increased risk of mydriasis (2–4). Here, we report a case of mydriasis associated with atomoxetine use in a child with ADHD and specific learning disorder (SLD) with impaired in reading.

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CASE PRESENTATION

A 13 year old boy who had no significant medical history, was referred to our outpatient clinic by his mother who complained of his hyperactivity, fidgetiness; being easily distracted; difficulties in paying attention to details; reading well below the expected level for age; and avoiding activities that involve reading. His symptoms caused problems at school and at home. The boy was diagnosed with ADHD combined presentation and SLD

with impaired in reading according to the Diagnostic and Statistical Manual of Mental Disorders-5 criteria (5). The patient was started on 25 mg of atomoxetine orally once daily for 7 days. The dose was then increased grudually to 60 mg orally once daily. After three weeks of atomoxetine treatment pupil dilatation was noticed by him and his mother. The patient denied any blurred visions, headaches, nausea, vomiting or pain in his eyes. The patient was informed about his dilated pupils as being a possible side effect of atomoxetine treatment. Patient was consulted to ophthalmology department two days after atomoxetine cessation for differential diagnosis and detecting possible effects of atomoxetine treatment on visual functions. In his ophthalmologic examination, his visual acuity was 20/20 in both eyes without any correction. Direct and indirect light reflexes were normal. His intraocular pressures were both within normal range. Other than mydriasis in his both eyes biomicroscopic and fundus examination revealed normal signs bilaterally. Pupil sizes were measured using a milimeter ruler while the patient was fixating on a distant, non-accomodative target. Under scotopic, mesopic and photopic conditions his pupil sizes of his right and left eye were 8.1 mm and 8.2 mm; 6.6 mm and 7 mm; 3 mm and 3.8 mm respectively. Atomoxetine treatment was stopped, and mydriasis resolved within five days.

DISCUSSION

In this report, we described a patient with ADHD and SLD who had a mydriasis following atomoxetine treatment. The chronological relationship between the time of atomoxetine administration and development of mydriasis in the absence of an identifiable medical condition or confounding medications and the fact that there was no occurrence after atomoxetine discontinuation suggests that atomoxetine was responsible for mydriasis. The probability of adverse event have calculated with the Naranjo Scale (6,7) and our patient was getting 6 points which refers to probable adverse effect of a drug.

There has been no detailed investigation of atomoxetine-induced mydriasis. To our knowledge, there is only three case report describing atomoxetine-induced mydriasis in a patient with ADHD in the scientific literatüre. The first case report clearly stated that a 15-year-old adolescent developed mydriasis after treatment of ADHD with atomoxetine (3). The second case report concerns an 8-year old boy with ADHD who developed mydriasis after prescribing 25 mg of atomoxetine orally once daily (2). In the third case report, while the 9-year-old boy with ADHD was using 18 mg atomoxetine, bilateral mydriasis was developed at any time of the day (4). The mechanisms that underpin atomoxetine-induced mydriasis are not fully understood. Mydriasis results when stimulation of the sympathetic nerves excites the radial fibers of the iris causing dilation of the pupils. An increase in norepinephrine (NE) caused by NE reuptake transporter inhibition has been shown to induce mydriasis in healthy volunteers (8). Atomoxetine is a highly selective and potent inhibitor of the presynaptic NE transporter, acting both centrally and peripherally. Atomoxetine increases both NE and dopamine levels, especially in the prefrontal cortex. Atomoxetine also increases the effect of norepinephrine in various regions (9). It is possible that atomoxetine may induce mydriasis via indirect a-1 adrenoceptor activation, mediated in turn via NE reuptake inhibitor effects (9) and a direct noradrenergic effect on the iris may result in an increase in the dilator muscle activation that leads to increased pupil diamater (3).

Mydriasis is a risk factor for narrow angle glaucoma. Acute angle-closure glaucoma (AACG) is probably the best known type of glaucoma. Glaucoma, a major cause of impaired vision and blindness. Although it has not been previously reported, AACG may develop after mydriasis induced by atomoxetine and clinicians should be aware of the possibility of atomoxetine induced acute angle closure due to devastating outcomes (10).

Our case suggests an association between atomoxetine and mydriasis. Although mydriasis is a rare side effect, clinicians should be aware that atomoxetine may cause mydriasis and inform the patients about these potential side effects when prescribing. Further research is required to determine the frequency and clarify the mechanism of this side effect.

Patient Informed Consent: Written informed consent was obtained from the patient for the publication of the case report.

Conflict of Interest: Authors do not have any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations that could inappropriately influence or be perceived to influence.

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REFERENCES

1. Ercan ES, Bilac O, Uysal Ozaslan T, Rohde LA. Is the prevalence of ADHD in Turkish elementary school children really high? Social Psychiatry and Psychiatric Epidemiology 2015;50(7):1145–52.
2. Bahali K, Ipek H, Yalcin O, Orum O. Atomoxetine-induced mydriasis in a child patient. Eur Child Adolesc Psychiatry 2014;23(12):1231–2.
3. Alhatem FJ, Decker DH. Atomoxetine-Induced Mydriasis. J Child Adolesc Psychopharmacol 2008;18(5):539–41.
4. Haefliger IO, Herz MJ. Transient Mydriasis under Atomoxetine Treatment: Case Report and Brief Overview of the Literature. Klin Monbl Augenheilkd 2018;235(4):469–70.
5. Diagnostic and Statistical Manual of Mental Disorders. 5th edition American Psychiatric Publishing Arlington, VA; 2013.
6. Kose S, Akin E, Cetin M. Letter to the editor: Adverse drug reactions and causality: The Turkish version of Naranjo adverse drug reactions probability scale. Psychiatry and Clinical Psychopharmacology 2017;27(2):205–6.
7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30(2):239–45.
8. Kreuser S, Riley J, Kolbasa K, Keerl A, Yappa U, Khan A, et al. A novel method to analyze atomoxetine-induced mydriasis in Sprague Dawley rats. J AALAM 2006;45(4).
9. Dadashova R, Silverstone P. Off-label use of atomoxetine in adults: is it safe? Ment Illn 2012;4(2):e19.
10. Lachkar Y, Bouassida W. Drug-induced acute angle closure glaucoma. Curr Opin Ophthalmol 2007;18(2):129–33.