

Kayhan Bahali¹
Ozden Sükran Uneri¹
Hamiyet Ipek¹

Atomoxetine-induced mania-like symptoms in an adolescent patient

¹Department of Child and Adolescent Psychiatry
Bakirkoy Research and Training Hospital for Psychiatry
Neurology and Neurosurgery
Istanbul, Turkey

To the Editor.

Attention-deficit hyperactivity disorder (ADHD) is one of the most common mental disorders with a worldwide prevalence of around 5% in children¹. Pharmacotherapy is the most commonly recommended intervention for ADHD. Methylphenidate, dexamphetamine and atomoxetine are widely used in European countries and North America for the pharmacological treatment of ADHD². Atomoxetine, a selective inhibitor of norepinephrine reuptake is the first non-stimulant drug approved by the Food and Drug Administration for the treatment of ADHD³. The efficiency of atomoxetine has been documented in short and long-term studies⁴. We report a case of mania-like symptoms induced by atomoxetine, which was observed in an adolescent with ADHD and oppositional defiant disorder (ODD).

A 12-year-old girl was diagnosed with ADHD, combined type and ODD according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, in our hospital. She showed inattention, hyperactivity and oppositional symptoms such as problems with inattention to detail, distractibility, forgetfulness, impulsiveness and anger regulation. She did not have a history of bipolar disorder and depression. There was no family history suggestive of bipolar disorder. Only her mother had a history of depression. The patient had not been treated previously with any medications for ADHD. Her body weight was 35 kg and physical examination did not reveal any abnormality. She

was started on atomoxetine 0.5 mg/kg/d, which she tolerated well. After 1 week, the dose of atomoxetine was increased to 1.2 mg/kg/d. However, on the 4th day of the increase in the dose, she demonstrated a marked increase in distractibility, hyperactivity, talkativeness, hostility and self-esteem at school and at home. She became more irritable. She had a decreased need for sleep (3 or 4 hours of sleep per night) than usual (5 or 6 hours of sleep per night). The patient threatened to kill the grandson of her aunt. She did not show grandiosity, delusions, hallucinations, flight of ideas, increased goal-directed behavior or hypersexuality. These symptoms were thought to be an activation similar to the one produced by SSRI-activation and this condition was evaluated as mania-like symptoms induced by atomoxetine. The dose of atomoxetine was decreased and stopped within three days. No medication was started. The mania-like symptoms improved within 1 week. The patient returned to her baseline behaviors both at home and at school. The patient was observed up to two months without medication and she did not have spontaneous episodes of mania or hypomania, but continued to have baseline problems such as inattention, hyperactivity and oppositional symptoms. Therefore, methylphenidate was started at a dose of 5 mg/d, and it was gradually increased up to a dose of 20 mg/d within 1 month. Her symptoms improved significantly with this medication. The mania-like symptoms did not occur while on methylphenidate.

The illustrated case has no confounding medications and shows clear onset and resolution of manic symptoms with the introduction and subsequent removal of atomoxetine. Although the other cases of mania induced by methylphenidate in children with ADHD^{5,6}, or worsening of the bipolar illness with stimulants have been reported in the literature⁷, in our case the child well tolerated methylphenidate. There is only one a case report of mania induced by atomoxetine in an adolescent patient with ADHD in the literature. This case had a personal history of drug-induced mania and had a family history suggestive for bipolar disorder⁸. Moreover, Henderson and Hartman (2004), in a study of 153 patient taking

This paper will presented to be a poster presentation in the 20th World IACAPAP Congress

Correspondence:

Kayhan Bahali

M.D. Department of Child and Adolescent Psychiatry, Bakirkoy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery
Istanbul, Turkey, 34147.

Phone: 00 90 212 5715730

Fax: 00 90 212 5719595

E-mail: mkbahali@yahoo.com

atomoxetine reported extreme irritability, aggression, mania, or hypomania induction in 51 cases (33%). While most of the 51 cases had a personal and family history of mood disorders, only six patients (11%) had neither personal nor family history of mood disorders⁹. According to the piece of literature above, a personal and/or family history of bipolar disorder is significantly a risk factor for mania/hypomania induced by atomoxetine. On the other hand, rarely, mania/hypomania that is induced by atomoxetine also can occur in patients with no personal or family risk factors of bipolar disorder. Our case suggests that the clinicians who choose atomoxetine for the treatment of ADHD should be careful for the mania/hypomania even in patients with no family or personal risk factors of bipolar disorder. As a result, all patients who are treated with atomoxetine should be closely monitored for mania-like symptoms that are induced by this medication.

REFERENCES

1. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry*. 2007;164:942–8.
2. Graham J, Banaschewski T, Buitelaar J, Coghill D, Danckaerts M, Dittmann RW, et al. European Guidelines Group. European guidelines on managing adverse effects of medication for ADHD. *Eur Child Adolesc Psychiatry*. 2011;20:17–37.
3. Kaplan G, Newcorn JH. Pharmacotherapy for child and adolescent attention-deficit hyperactivity disorder. *Pediatr Clin N Am*. 2011;58:99–120.
4. Pliszka S. AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2007;46:894–921.
5. Chakraborty K, Grover S. Methylphenidate-induced mania-like symptoms. *Indian J Pharmacol*. 2011;43:80–1.
6. Koehler-Troy C, Strober M, Malenbaum R. Methylphenidate-induced mania in a prepubertal child. *J Clin Psychiatry*. 1986;47:566–7.
7. Soutullo CA, DelBello MP, Ochsner JE, McElroy SL, Taylor SA, Strakowski SM, et al. Severity of bipolarity in hospitalized manic adolescents with and without a history of stimulant or antidepressant treatment. *J Affect Disord*. 2002;70:323–7.
8. Henderson TA. Mania induction associated with atomoxetine. *J Clin Psychopharmacol*. 2004;24:567–8.
9. Henderson TA, Hartman K. Aggression, mania, and hypomania induction associated with atomoxetine. *Pediatrics*. 2004;114:895–6.