

can lead to significant positive effects on the lives of patients with schizophrenia.

AUTHOR DISCLOSURE INFORMATION

H.T. has received lecture honoraria from Sumitomo Dainippon Pharma Co, Ltd within the last 1 year. T.A. is currently receiving a grant from the company. T.O., Y.S., N.S., T.T., and T.H. declare no relevant conflicts of interest.

ARTICLE INFORMATION

Received February 1, 2021; accepted after revision April 25, 2021.

DOI: 10.1097/JCP.0000000000001453

Takafumi Ogawa, MD

Majors of Clinical Sciences, Graduate School of Comprehensive Human Sciences
University of Tsukuba
Tsukuba City, Ibaraki Prefecture, Japan

Hirokazu Tachikawa, MD, PhD

Department of Disaster and Community Psychiatry, Faculty of Medicine
University of Tsukuba
Tsukuba City, Ibaraki Prefecture, Japan
tachikawa@md.tsukuba.ac.jp

Yuki Shiratori, MD, PhD

Noriko Sodeyama, MD

Department of Psychiatry, Faculty of Medicine
University of Tsukuba
Tsukuba City, Ibaraki Prefecture, Japan

Takaya Taguchi, MD, PhD

Department of Disaster and Community Psychiatry, Faculty of Medicine
University of Tsukuba
Tsukuba City, Ibaraki Prefecture, Japan

Takafumi Hori, MD, PhD

Ibaraki Prefectural Medical Center of Psychiatry
Tsukuba City, Ibaraki Prefecture, Japan

Tetsuaki Arai, MD, PhD

Department of Psychiatry, Faculty of Medicine
University of Tsukuba
Tsukuba City, Ibaraki Prefecture, Japan

REFERENCES

- Catty J, Burns T, Knapp M, et al. Home treatment for mental health problems: a systematic review. *Psychol Med.* 2002;32:383–401.
- Aagaard J, Tuszewski B, Kølbaek P. Does assertive community treatment reduce the use of compulsory admissions? *Arch Psychiatr Nurs.* 2017;31:641–646.
- Luo X, Law SF, Wang X, et al. Effectiveness of an Assertive Community Treatment program for people with severe schizophrenia in mainland China — a 12-month randomized controlled trial. *Psychol Med.* 2019;49:969–979.
- Khawaled R, Bauer A, Rosea P, et al. Community emergency psychiatric service in Israel: a one-year experience. *Isr J Psychiatry Relat Sci.* 2009;46:207–212.
- Inoue Y, Tsuchimori K, Nakamura H. Safety and effectiveness of oral blonanserin for schizophrenia: a review of Japanese post-marketing surveillances. *J Pharmacol Sci.* 2021;145:42–51.
- Kishi T, Matsui Y, Matsuda Y, et al. Efficacy, tolerability, and safety of blonanserin in schizophrenia: an updated and extended systematic review and meta-analysis of randomized controlled trials. *Pharmacopsychiatry.* 2019;52:52–62.
- Kishi T, Yoshimura R, Matsuda Y, et al. Blonanserin patch vs. other antipsychotics for acute schizophrenia: a systematic review of double-blind, randomized, placebo-controlled, phase 3 trials in Japan. *Pharmacopsychiatry.* 2020;53:122–132.
- Isaac M, Holvey C. Transdermal patches: the emerging mode of drug delivery system in psychiatry. *Ther Adv Psychopharmacol.* 2012;2:255–263.
- Iwata N, Ishigooka J, Naoi I, et al. Long-term safety and efficacy of blonanserin transdermal patches in Japanese patients with schizophrenia: a 52-week open-label, multicenter study. *CNS Drugs.* 2020;34:103–116.
- Iwata N, Ishigooka J, Kim WH, et al. Efficacy and safety of blonanserin transdermal patch in patients with schizophrenia: a 6-week randomized, double-blind, placebo-controlled, multicenter study. *Schizophr Res.* 2020;215:408–415.
- Itoh H, Saito T, Nojiri S, et al. National burden of the pharmaceutical cost of wet compresses and its cost predictors: nationwide cross-sectional study in Japan. *Health Econ Rev.* 2019;9:20.

OPEN

Atomoxetine-Associated Eyebrow Alopecia in a Girl With Attention-Deficit/Hyperactivity Disorder

To the Editors:

Atomoxetine, a nonpsychostimulant agent used in the first-line treatment of attention-deficit/hyperactivity disorder (ADHD), increases extracellular synaptic levels of norepinephrine and dopamine by obstructing norepinephrine presynaptic reuptake.¹ It is generally considered to be safe, effective, and well tolerable.² Adverse effects may be seen with the clinical use of atomoxetine, including appetite decreased, headache, insomnia, abdominal pain, nausea, vomiting, constipation, dyspepsia, dizziness, somnolence, irritability, mood swings, etc.^{3–5} However, an association of eyebrow alopecia with atomoxetine has not been reported. In the present case, we report an 8-year-old

girl with ADHD who experienced bilateral eyebrow loss after atomoxetine treatment. To our knowledge, this is the first case of eyebrow alopecia associated with atomoxetine treatment in the literature. Informed consent was signed by parent before case presentation.

CASE REPORT

Because of focusing deficits, distractibility, hyperactivity, and low academic achievement, an 8-year-old girl was referred to our department. The patient was diagnosed with ADHD combined type based on *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, diagnostic criteria and was prescribed atomoxetine (Strattera; Eli Lilly and Company). The girl has a body weight of 22.5 kg. Atomoxetine therapy was initiated at a total daily dose of 12.5 mg for the first and second weeks. No adverse events were observed with atomoxetine at 12.5 mg/d. Then, as the dose increased to 25 mg/d, the symptoms of ADHD were improved. However, at the same time, she developed dizziness (the third week). A week later (the fourth week), her mother reported that she experienced eyebrow loss without observing behavior of hair pulling. Gradually, the eyebrows became increasingly sparse from their initial dense state, but no hair/eyelashes were lost (Fig. 1A). She had no history of alopecia, no dermatological disease, and no previous specific drug reactions. She was not exposed to any other medications, heavy metals, toxins, or stressors while taking atomoxetine. The girl also had no signs of depression or anxiety. Considering the adverse effect of eyebrow loss, the medicine was discontinued. She has done some blood tests, including blood cell count, general biochemistry, thyroid function test, sex hormone test, serum zinc/copper/iron/vitamin B level tests, and autoimmunity-related examination. They were all within the reference range. After 36 days of interruption, the eyebrows returned to their normal state, and no other medications or dietary supplements were given (Fig. 1B). Atomoxetine was reintroduced (25 mg/d) after 50 days of interruption because of ADHD problems. However, this time, no signs of eyebrow alopecia or hair loss were observed, and there was a marked improvement in the clinical symptoms of ADHD.

DISCUSSION

Eyebrow alopecia can occur as a complication of certain skin conditions, autoimmune disorders, malnutrition, and as an adverse effect of prescription drug use, chemotherapy, heavy metals, or other toxins exposure. The most common type caused by medication is telogen effluvium, which characterized by the thinning or shedding of hair

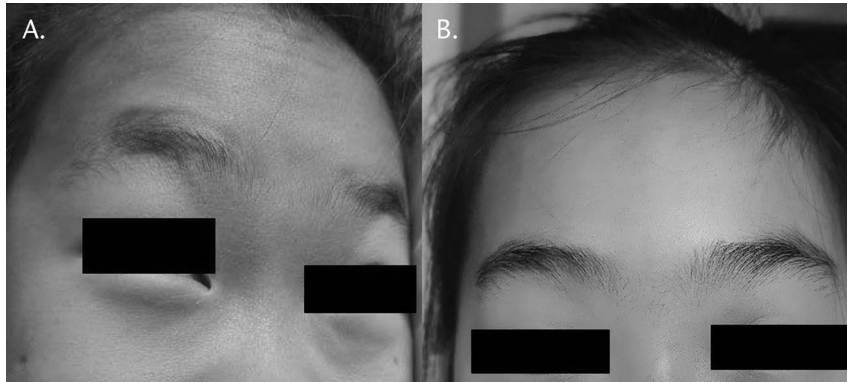


FIGURE 1. A, Bilateral eyebrow loss after atomoxetine treatment. B, Eyebrows returned to normal state after 36 days of interruption.

resulting from the early entry of hair in the telogen phase.^{6–9} Methylphenidate is a stimulant drug used for the treatment of ADHD. A case of eyebrow loss caused by methylphenidate had been reported.¹⁰ Until now, atomoxetine-associated eyebrow alopecia has never been reported in literature. In our case, we excluded conditions and medications that can cause eyebrow alopecia. After the interruption of atomoxetine, the eyebrow loss event resolved without any other medicine or dietary supplements. Atomoxetine was then reintroduced during a second regular treatment period. However, no significant adverse effects, including eyebrow alopecia, were observed after continued use of atomoxetine. In the treatment period, as no other medicine or dietary supplements were given to the patient, drug tolerance was considered as the primary reason. The exact mechanisms of eyebrow alopecia and drug tolerance are still unknown, but studies showed that adverse effects were noted to be transient, occurring mainly early in atomoxetine treatment and then declining.¹¹ Clinicians should be aware that eyebrow alopecia is a possible but very rare adverse effect of atomoxetine treatment, and such adverse effects may be tolerable.

ACKNOWLEDGMENTS

The authors thank the patient and her family for participating in this study.

This work was carried out at the Children's Hospital of Fudan University. All authors have made substantive contributions to the study and endorse the data and conclusions.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

AUTHOR DISCLOSURE INFORMATION

The authors declare no conflicts of interest.

ARTICLE INFORMATION

Received January 23, 2021; accepted after revision May 18, 2021.

DOI: 10.1097/JCP.0000000000001454

**Ying Zhang, MMed
Xiu Xu, MD, PhD**

Department of Child Health Care and Developmental-Behavioral Pediatrics, Children's Hospital of Fudan University, National Children's Medical Center
Shanghai, China

Kaifeng Zhang, MMed

Department of Child Health Care and Developmental-Behavioral Pediatrics, Children's Hospital of Fudan University, National Children's Medical Center
Shanghai, China
liliezkhf@sina.com

REFERENCES

- Cortese S. Pharmacologic treatment of attention deficit-hyperactivity disorder. *N Engl J Med.* 2020;383:1050–1056.
- Mohammadi MR, Akhondzadeh S. Pharmacotherapy of attention-deficit/hyper-activity disorder: nonstimulant medication approaches. *Expert Rev Neurother.* 2007;7:195–201.
- MacKenzie KR, Zhao M, Barzi M, et al. Metabolic profiling of norepinephrine reuptake inhibitor atomoxetine. *Eur J Pharm Sci.* 2020; 153:105488.
- Akaltun İ, Kara T. Atomoxetine-related trichotillomania in a boy with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol.* 2017;27:923.
- Ledbetter M. Atomoxetine: a novel treatment for child and adult ADHD. *Neuropsychiatr Dis Treat.* 2006;4:455–466.
- Kumar A, Karthikeyan K. Madarosis: a marker of many maladies. *Int J Trichology.* 2012;4:3–18.

- Iorizzo M, Oranje AP. Current and future treatments of alopecia areata and trichotillomania in children. *Expert Opin Pharmacother.* 2016;17:1767–1773.
- Tosti A, Pazzaglia M. Drug reactions affecting hair: diagnosis. *Dermatol Clin.* 2007; 25:223–231.
- Mercke Y, Sheng H, Khan Tet al. Hair loss in psychopharmacology. *Ann Clin Psychiatry.* 2000;12:35–42.
- Yektaş Ç, Samurcu ND, Tufan AE. Loss of eyebrows (madarosis) after use of long-acting methylphenidate: case report. *J Clin Psychopharmacol.* 2017;37:485–486.
- Wernicke JF, Kratochvil CJ. Safety profile of atomoxetine in the treatment of children and adolescents with ADHD. *J Clin Psychiatry.* 2002;63(suppl 12):50–55.

Perphenazine-Associated Nausea A Case of Protracted Withdrawal

To the Editors:

Child and adolescent aggression is associated with a complex combination of genetic, neurobiological, and social factors.¹ Although psychosocial interventions are the first-line treatment for aggression, pharmacologic treatments, such as psychostimulants, α -2 agonists, atomoxetine, and risperidone, are beneficial.¹ Yet, there is no algorithm for the pharmacologic management of children and adolescents with aggression.² As a result, physicians must rely on limited literature and use medications without FDA indications for pediatric use.³

In this case report, we examine the course of an adolescent patient who was prescribed perphenazine to manage aggressive and poor impulse control behaviors. Perphenazine is a first-generation antipsychotic used for the management of psychotic disorders and severe nausea and vomiting.