Letter to the Editor

Ziprasidone-Induced Galactorrhea in an Adolescent Female: A Case Report

To the Editor: Prolactin is a lactogenic hormone, and its release is tonically inhibited by hypothalamic dopamine. Dopamine-2 (D₂) receptor blockage in the tuberoinfundibular pathway releases prolactin.1 Second-generation neuroleptics are not particularly associated with hyperprolactinemia. With the exception of risperidone,² it is assumed that hyperprolactinemia with second-generation antipsychotics (SGAs) is rare and transient.³⁻⁵ The rise in serum prolactin is directly associated with the degree of dopamine receptor blockage.⁶ Ziprasidone is considered to be a weak blocker of the D₂ receptor.⁷ Significant prolactin elevation was not reported as being associated with ziprasidone use.8 To our knowledge, there are at least 5 case reports of ziprasidone-induced galactorrhea in the literature.⁹⁻¹³ Chronic elevation in prolactin in females can lead to loss of libido, galactorrhea, gynecomastia, amenorrhea, oligomenorrhea, hirsutism, disturbance of normal ovarian cycle, or increased risk of chronic osteoporosis.

Case report. Ms A, a 16-year-old African American girl, has a history of neglect; sexual, physical, and emotional abuse; and multiple losses. She presented in 2009 with multidimensional symptomatology, which included attention-deficit/hyperactivity disorder (ADHD)–like symptoms (hyperactivity, impulsivity, and inattention); posttraumatic stress disorder–like symptoms (nightmares, flashbacks, numbing, avoidance, and sexually acting out behavior); psychotic symptoms (auditory hallucinations, eg, "voices asking me to do bad stuff"; paranoia, ie, "people are gossiping about me"); bipolar spectrum symptoms (eg, rapid mood swings, anger control issues, impulsivity, and decreased sleep); and oppositional defiant behavior.

There was no past history of illicit substance abuse or alcohol drinking. She has a longstanding history of self-mutilating behavior (cutting her wrists) and overdosing on pills, which required multiple psychiatric hospitalizations, including longterm placement in a residential treatment facility. Prior to her current hospitalization, she had been treated with divalproex, quetiapine, and fluoxetine. During the hospitalization, she was started on ziprasidone 80 mg bid and divalproex 500 mg po twice daily was continued. Two weeks after ziprasidone treatment began, she developed galactorrhea and her blood prolactin level was 68.6 ng/mL (laboratory reference value, 1.40-24.20 ng/mL). Ziprasidone was discontinued and aripiprazole 2 mg/d was started. Three weeks later, galactorrhea had stopped and her serum prolactin level was within the normal range. She had no medical condition that could explain the elevated prolactin and galactorrhea levels. Some other known causes of galactorrhea were excluded, eg, chronic renal failure, pregnancy and lactation, and primary hypothyroidism. On a mental status examination, she reported a dysphoric mood and her affect was mood congruent. She had clear speech and had no suicidal or homicidal ideation. There were no hallucinations, but she reported paranoid ideations.

Among atypical antipsychotics, ziprasidone has the highest serotonin (5-HT) receptor–dopamine receptor (5-HT_{2A}/D₂, 5-HT_{2C}/D₂, and 5-HT_{1A}/D₂) affinity ratios. Although ziprasidone is a weaker blocker of D₂ receptors than conventional antipsychotics, ziprasidone-induced symptomatic hyperprolactinemia has been reported in literature.⁹⁻¹³ At a dose of 120 mg/d, 60% D₂ receptor occupancy was obtained.¹⁴

Patients with the DRD2A1 allele had a 40% higher level of prolactin as compared to patients without this allele.¹⁵

Antipsychotic-induced hyperprolactinemia is not an uncommon condition, but it remains underdiagnosed and undertreated. In conclusion, physicians should routinely inquire about symptoms of hyperprolactinemia, eg, galactorrhea, gynecomastia, menstrual irregularities, and sexual dysfunction, in patients taking neuroleptics. If not treated, these symptoms could lead to noncompliance. Prolactin level can be elevated even in the absence of galactorrhea.

REFERENCES

- Petty RG. Prolactin and antipsychotic medications: mechanism of action. Schizophr Res. 1999;35(suppl):S67–S73.
- Kleinberg DL, Davis JM, de Coster R, et al. Prolactin levels and adverse events in patients treated with risperidone. *J Clin Psychopharmacol.* 1999;19(1):57–61.
- Maguire GA. Prolactin elevation with antipsychotic medications: mechanisms of action and clinical consequences. *J Clin Psychiatry*. 2002;63(suppl 4):56–62.
- Bench CJ, Lammertsma AA, Grasby PM, et al. The time course of binding to striatal dopamine D2 receptors by the neuroleptic ziprasidone (CP-88,059-01) determined by positron emission tomography. *Psychopharmacology (Berl)*. 1996;124(1–2):141–147.
- Miceli JJ, Wilner KD, Hansen RA, et al. Single- and multiple-dose pharmacokinetics of ziprasidone under non-fasting conditions in healthy male volunteers. Br J Clin Pharmacol. 2000;49(suppl 1):5S–13S.
- Smith S. Effects of antipsychotics on sexual and endocrine function in women: implications for clinical practice. J Clin Psychopharmacol. 2003;23(suppl 1):S27–S32.
- Seeman P. Atypical antipsychotics: mechanism of action. Can J Psychiatry. 2002;47(1):27–38.
- Addington DE, Pantelis C, Dineen M, et al. Efficacy and tolerability of ziprasidone versus risperidone in patients with acute exacerbation of schizophrenia or schizoaffective disorder: an 8-week, doubleblind, multicenter trial. J Clin Psychiatry. 2004;65(12):1624–1633.
- 9. Saldaña SN, Delgado SV. Ziprasidone-associated galactorrhea in an adolescent female. *J Child Adolesc Psychopharmacol.* 2007;17(2):259–260.
- Ramadan M, Khan A, Preskorn S. D2-blockade and possible ziprasidone-induced galactorrhea. *Int Clin Psychopharmacol.* 2005;20(2):113–114.
- Kopecek M, Bares M, Mohr P. Ziprasidone-induced galactorrhea: a case report. *Neuroendocrinol Lett.* 2005;26(1):69–70.
- 12. Lusskin SI, Cancro R, Chuang L, et al. Prolactin elevation with ziprasidone. *Am J Psychiatry*. 2004;161(10):1925.
- Jordan MP. Ziprasidone-associated galactorrhea in a female teenager. J Am Acad Child Adolesc Psychiatry. 2003;42(1):4–5.
- Young RM, Lawford BR, Barnes M, et al. Prolactin levels in antipsychotic treatment of patients with schizophrenia carrying the DRD2*A1 allele. *Br J Psychiatry*. 2004;185(2):147–151.
- Roose SP, Pollock BG, Devanand DP. Treatment during late life. In: Schatzberg AF, Nemeroff CB, eds. *Essentials* of *Clinical Psychopharmacology*. 2nd ed. Arlington, VA: American Psychiatric Publishing, Inc; 2007.

Shakeel Raza, MD shakeeldr@yahoo.com Fasiha Haq, MD

Author affiliations: Department of Psychiatry, University of South Alabama, Mobile.

Potential conflicts of interest: None reported.

Funding/support: None reported.

Published online: June 3, 2010 (doi:10.4088/PCC.09100855gry). Prim Care Companion J Clin Psychiatry 2010;12(3):e1 © Copyright 2010 Physicians Postgraduate Press, Inc.