Quetiapine-Induced Galactorrhea With Normal Prolactin Level in an Adult Female Patient

To the Editor: Quetiapine is an atypical antipsychotic agent with less propensity than other atypical antipsychotics to induce antipsychotic-associated hyperprolactinemia in standard recommended therapeutic dosages,[1,2] and when it does induce the condition at all, the rise in serum prolactin level is only transient.[3] Accordingly, quetiapine has been recommended as an alternative in patients who develop galactorrhea associated with other antipsychotics.[4–6] However, hyperprolactinemia with related side effects may rarely be encountered in a few susceptible individuals.[7] We describe a case of quetiapine-induced galactorrhea without an increase in blood prolactin level in an adult female patient. We then discuss the implications of quetiapine with respect to such an adverse effect.

Case report. Ms A, a 45-year-old white woman, was diagnosed with *DSM-IV-TR* bipolar disorder at the age of 23 years and experienced repeated episodes of both depression and mania over the years. Treatment with lithium carbonate and sodium valproate was tried without much success. She recently presented to the psychiatric emergency department with an acute manic episode (*DSM-IV-TR*). The patient was agitated and refused to sit during the interview. She paced back and forth, talked or mumbled incessantly, and occasionally busted into laughter and cursed during the interview. Around the time of admission, her symptoms comprised irritability, psychomotor agitation, pressured speech, flight of ideas, insomnia, grandiose and aggressive behavior, sexual disinhibition, and lack of insight. She denied any auditory and visual hallucinations.

Upon her admission to the hospital, a drug screen was negative. Findings of a head computed tomography scan were within normal limits. Results of other routine investigations including complete blood count, complete metabolic profile, thyroid function tests, liver function tests, and prolactin level were within normal limits. Treatment with quetiapine was initiated for both therapeutic as well as prophylactic purposes; she responded well, and her manic symptoms subsided. She was discharged from the hospital after 1 week.

After 2 months of continued treatment, she reported breast enlargement, "milk" discharge from her breast, and bilateral breast pain and amenorrhea. Galactorrhea was confirmed by physical examination. Surprisingly, her serum prolactin level at this stage was again found to be within normal range (13 ng/mL; normal range, 2.80–20 ng/mL) instead of being high. Pregnancy test was negative. Thyroid function tests revealed no abnormalities and excluded hypothyroidism from being the cause of galactorrhea. Physical examination revealed no other abnormality. She neither complained of visual disturbance nor described symptoms suggestive of raised intracranial pressure. A brain scan was not performed as the serum prolactin elevation was within normal limits. Since we assumed quetiapine was one of the possible causes of galactorrhea, quetiapine was stopped, which led to dramatic resolution of symptoms within 72 hours. Ms A, however, took another 2 months to resume her normal menstrual cycle.

A PubMed search for the years 1996 to 2011 with the keywords *antipsychotics*, *quetiapine*, and *galactorrhea* was performed; other articles were obtained via a Google Scholar search that included the same time span and keywords. To the best of our knowledge, this is the first case reporting galactorrhea without hyperprolactinemia in the medical literature. However, several studies have shown that quetiapine does not increase prolactin level to the same extent as do other antipsychotic medications. The newly accepted explanation for the prolactin-sparing property of quetiapine and other atypical antipsychotic agents is the poor occupancy of dopamine D_2 receptors on lactotrope cells in the anterior pituitary gland compared to striatal dopamine D_2 occupancy.[8] This contrasts with the property of all conventional antipsychotics and some atypical agents like risperidone in blocking dopamine D_2 receptors on prolactin-secreting cells in the pituitary gland, removing the main inhibitory effect on prolactin secretion.[9] A study on the incidence of hyperprolactinemia and prolactin-related side effects in children and adolescents treated with antipsychotics showed that there is no significant increase in prolactin level after the long-term use (2 years) of quetiapine.[10] In 2006, a 12-week randomized, double-blind study of quetiapine, risperidone, or fluphenazine on sexual functioning in people with schizophrenia showed that, overall, quetiapine was associated with normal prolactin levels.[11] Treatment with quetiapine and olanzapine caused prolactin levels to be elevated just temporarily. However, no correlation between prolactin levels and dosage could be found in these subjects under treatment.[12] Detailed endocrine-metabolic studies performed on 5 women showed isolated galactorrhea with normal serum prolactin levels.[13] To our knowledge, 2 case reports[7,14] have been published on subjects who developed hyperprolactinemic galactorrhea with quetiapine. However, no case reports have been published about quetiapine-induced galactorrhea with normal level of prolactin as was seen in our subject.

Although quetiapine is considered to be a prolactin-sparing atypical antipsychotic, quetiapine-induced galactorrhea may rarely be encountered as a side effect in susceptible individuals, and therefore physicians should routinely inquire about quetiapine as one of the possible causes of galactorrhea even when the prolactin level is within normal limits.

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