A Case of Successful Treatment of Comorbid Obesity and Polycystic Ovarian Disease With Add-On Metformin in Bipolar Disorder

To the Editor: The association between bipolar disorder and polycystic ovarian disease has been a matter of considerable debate.[1] It has been hypothesized that a genetic overlay may explain co-occurrence of both disorders.[2] Treatment of bipolar disorder with valproate has also been described to be associated with increased incidence of polycystic ovarian disease.[3] The co-occurrence of both disorders significantly enhances risk of associated metabolic complications, especially since bipolar disorder, by itself, has been reported to be associated with increased risk of obesity.[4] In this report, we describe successful treatment of polycystic ovarian disease and obesity with add-on metformin in a female patient with *DSM-IV* bipolar disorder.

Case report. Ms A, a 29-year-old woman, presented to our hospital in the mid-summer of 2009 with her first manic episode with psychotic symptoms. There was no family history of psychiatric or medical illness. Personal history revealed irregular menstrual cycles occurring once in 3 or 4 months over the last year. At presentation, her weight was 83 kg and her body mass index (BMI) was 36.9 kg/m^2. Further investigations showed a lipid profile, fasting blood sugar level, and renal and liver functions within normal limits; however, her thyroid-stimulating hormone levels were elevated at 11.4 mIU/L. Treatment with risperidone up to 4 mg/d and thyroxine supplementation at 100 μg/d was initiated, to which she responded favorably.

Five months later, she subsequently had a depressive episode. Her weight at this point was 88.6 kg and her BMI was 39.4 kg/m^2. Oligomenorrhea and weight gain persisted despite normalization of TSH levels and a serum prolactin level (9.72 ng/mL) that was within normal limits. Polycystic ovarian disease was clinically suspected and confirmed by abdominal ultrasound, which showed polycystic ovarian changes. A diagnosis of polycystic ovarian disease was made per the Rotterdam criteria.[5] She was started on carbamazepine up to 600 mg/d, quetiapine up to 300 mg/d, and metformin up to 1,500 mg/d, and lifestyle modifications were advised.

On subsequent follow-up, she had reached euthymia. Progressive loss of weight of 12.4 kg was observed over a period of 7 months. Her weight was 76.2 kg and her BMI was 33.8 kg/m^2 after 7 months of metformin treatment. Her menstrual cycles had also become regular for the previous 6 months. There was no change in the patient's food habits or physical exercise as assessed with the brief physical activity questionnaire.[6]

The prevalence of coexisting polycystic ovarian disease and bipolar disorder is reported variously as 11.1%[7] and 28%.[8] Polycystic ovarian disease is known to be associated with metabolic abnormalities and weight gain.[9] Atypical antipsychotic treatment can further enhance the risk of metabolic abnormalities.[10] In the case described, Ms A had a BMI in the class II obesity range (36.9 kg/m^2) at baseline, possibly due to already existing polycystic ovarian disease; her BMI further increased to 39.4 kg/m^2 after atypical antipsychotic treatment. Metformin treatment improved menstrual irregularities as well as reduced BMI from the class II to the class I range of obesity.

Metformin has been evaluated in the treatment of obesity and is one of the first-line agents in polycystic ovarian disease.[11] Metformin has also been evaluated in a randomized controlled trial for its effectiveness in countering antipsychotic-related weight gain in schizophrenia patients.[12] However, the treatment of metabolic complications in bipolar disorder[13] has not been well studied. Metformin could be a useful agent in treatment of weight gain and menstrual abnormalities associated with polycystic ovarian disease and bipolar disorder and needs to be systematically examined.

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