Pseudoresistant Bipolar Depression

To the Editor: Fekadu et al[1] are to be commended for their article on quantifying treatment-resistant depression (TRD). But while the authors note the importance of "paradigm failures"[2] in producing apparent TRD—for example, the failure to discern the type of depression showing "resistance"—I believe greater emphasis should be given to diagnosing what I call pseudoresistant bipolar depression (PBD). Parker et al[2] found that more than 30% of apparent TRD patients had undiagnosed and inappropriately managed bipolar disorder. In my own tertiary-level psychopharmacology consultation practice, I found that well over half of patients referred for TRD were actually bipolar spectrum patients. With the collaboration of Ghaemi and colleagues,[3] my findings led to the development of a screening instrument, the Bipolar Spectrum Diagnostic Scale, for the detection of bipolar II and other "softer" variants of bipolar spectrum disorder.

In general, I found that what referring doctors had called treatment resistance was actually a characteristic dysphoric response during multiple antidepressant trials. This was not the frequently reported "switch" into hypomania or mania; rather, patients almost always described feeling "antsy," "wired," irritable, aggressive, or insomniac while taking antidepressants. This is similar to what Phelps[4] called "agitated dysphoria," in a patient with apparent unipolar mood disorder who experienced this syndrome after

late-onset loss of antidepressant response. Similarly, Akiskal et al[5] have argued that "agitated, activated, or otherwise excited depressions (which we consider as depressive mixed states) overlap considerably with the so-called antidepressant 'activation syndrome.'"

Clinicians faced with apparent TRD should carefully assess the patient for covert bipolar spectrum disease, PBD, and antidepressant-induced agitated dysphoria.

References

1. Fekadu A, Wooderson S, Donaldson C, et al. A multidimensional tool to quantify treatment resistance in depression: the Maudsley Staging Method. *J Clin Psychiatry.* 2009;70(2):177–184.
2. Parker GB, Malhi GS, Crawford JG, et al. Identifying "paradigm failures" contributing to treatment-resistant depression. *J Affect Disord.* 2005;87(2–3):185–191.
3. Ghaemi SN, Miller CJ, Berv DA, et al. Sensitivity and specificity of a new bipolar spectrum diagnostic scale. *J Affect Disord.* 2005;84(2–3):273–277.
4. Phelps JR. Agitated dysphoria after late-onset loss of response to antidepressants: a case report. *J Affect Disord.* 2005;86(2–3):277–280.
5. Akiskal HS, Benazzi F, Perugi G, et al. Agitated "unipolar" depression re-conceptualized as a depressive mixed state: implications for the antidepressant-suicide controversy. *J Affect Disord.* 2005;85(3):245–258.

Ronald W. Pies, MD
ronpies@massmed.org

Author affiliations: Department of Psychiatry, SUNY Upstate Medical University, Syracuse, New York; and Tufts University School of Medicine, Boston, Massachusetts.

Financial disclosure: None reported. ***Funding/support:*** None reported.
doi:10.4088/JCP.09lr05181gre