**CASE STUDY**

**A 32-YEAR-OLD MALE WITH SUICIDE ATTEMPT**

Charles B. Nemeroff, MD, PhD

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**BACKGROUND**

A 32-year-old white male presented to the hospital reporting increasing depression. He has a history of attention-deficit hyperactivity disorder (ADHD) and chronic depression. Most recently, he has been treated with paroxetine, but he still notes an escalation in his symptoms to the point where he made a suicide attempt.

**HISTORY OF PRESENT ILLNESS**

This patient presented for treatment of increasing depression. No clear precipitant could be identified. He indicated that he had been depressed for several months with decreased sleep, fatigue, low self-esteem, and problems concentrating. He also indicated that his appetite had increased and that he had gained 10 pounds within this period. He had gone to his physician who subsequently prescribed paroxetine 20 mg in the morning, along with zolpidem 10 mg hs (hours of sleep) for sleep. Within 1 week, he felt "like his own self" with increased energy and he was much more optimistic about his future. This improvement lasted several more days until he became precipitously depressed again. The dose of paroxetine was increased to 30 mg; however, he remained depressed and started experiencing suicidal thoughts. He began to drink up to 3 to 4 glasses of wine a day to "calm his nerves" and help him sleep. He subsequently attempted to cut his wrists, requiring several stitches, and was hospitalized.

His examination on admission to the hospital indicated a depressed male looking his stated age. He was also anxious. Speech was fluent with normal rate and rhythm. His thought was goal directed and he denied paranoid ideation, auditory hallucinations, or other psychotic phenomena. He reported intense suicidal ideation, saying that there was no reason to live anymore. He was tearful and admitted to unexplained crying spells. Cognitive function was intact.

**PAST PSYCHIATRIC HISTORY**

There were no past hospitalizations reported. However, he indicated that he had problems with chronic depression since childhood. He dates the onset of his depression at age 9 years—likely secondary to the divorce of his parents. He was treated with a variety of antidepressants, including bupropion, venlafaxine, and citalopram, starting in his early 20s. None of these medications relieved his depression for a prolonged period of time. He denied prior suicide attempts. He reported chronic problems with low self-esteem and often was shy and withdrawn. He reported that on occasion for brief periods of time he would become sociable and outgoing and could be "the life of the party." Sometimes this was associated with drinking several shots of alcohol; however, they sometimes occurred by themselves without clear precipitants. At no time did these episodes last more than 2 to 3 days. There were no sustained manic or hypomanic symptoms or episodes reported.

**MEDICAL PROBLEMS**

There is a history of hypertension, which is currently under adequate control with enalapril. There is also a history of moderate obesity, which has persisted over the past 15 years, despite multiple attempts at dieting.

**CHILDHOOD AND SCHOOL HISTORY**

There is a history of problems with attention in grade school and difficulty sitting still. He also had a tendency to get into fights. He was diagnosed as having ADHD at 8 years of age. A trial of methylphenidate was not helpful. He was able to graduate high school with average grades.

**FAMILY HISTORY**

There is no reported formal history of any psychi-
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Psychiatric disorder in the family. His parents divorced after 11 years of marriage. His mother attributed this to his father's multiple extramarital affairs. His father precipitously left the area after the divorce and has had no further contact with his family. His paternal uncle was hospitalized on several occasions for schizophrenia; however, details of his history were sketchy.

SOCIAL HISTORY

The patient reported difficulty sustaining prolonged intimate relationships, which he attributed to his depression. However, he has had multiple brief affairs. He sometimes has had unprotected sexual contacts, although he recognized that this was not safe or advisable. He has maintained several close casual friendships primarily through work. He has been able to work at the same company and job as a data-entry technician in the accounting department.

SUBSTANCE ABUSE HISTORY

There is a history of episodic drinking and he sometimes drinks to intoxication. He finds that the alcohol helps him decrease his anxiety and shyness. He has never used alcohol daily; however, his alcohol use has interfered with his job performance at times. There was no history of other substance abuse.

CASE DISCUSSION

This case brings up many interesting points concerning the differential diagnosis of an affective syndrome. The individual presents with a major depressive episode superimposed on a chronic history of depression. However, a diagnosis of bipolar disorder should be strongly considered in such an individual, and there are many clues that this may be the primary Axis I diagnosis.

• There is a history of depression dating since childhood, and early-onset depression is more typical of bipolar disorder than unipolar depression.
• There is a history of ADHD. A significant proportion of children with ADHD actually suffer from bipolar disorder. In a study by Biederman et al, 11% of children were diagnosed with bipolar disorder at initial evaluation. An additional 12% of the cohort was diagnosed with bipolar disorder at the 4-year follow-up period. Furthermore, there is a history of aggressive behavior as evidenced by the tendency to engage in fights, indicating an early onset of problems with anger and impulsivity. These behaviors have been associated with the later development of a bipolar disorder. The poor response to methylphenidate indicates that a diagnosis other than ADHD may be appropriate.
• Several trials of antidepressants were not successful or helpful for only brief periods of time. Although the doses or length of treatment of the prior agents used were not mentioned, the fact that none of them appeared to be helpful may be an indication that antidepressants alone were not adequate in this individual.
• The current treatment with paroxetine resulted in a relatively rapid relief of symptoms followed by a worsening of depression. Increasing the dose to 30 mg may have resulted in worsening of depression, as evidenced by increased suicidal ideation and hospitalization. This type of rapid yet unsustained response is not uncommon in bipolar disorder. Antidepressant treatment may be associated with increased cycling, and stopping the antidepressant and starting a trial of a mood stabilizer or antipsychotic drug may alleviate the depression.
• There is a history of brief periods of increased social behavior characterized by the patient as becoming the “life of the party.” Although these do not occur frequently and they are associated at times with alcohol use, they do appear spontaneously and are not consistent with the patient’s depressed mood. Therefore, they may be a “soft sign” of bipolar disorder.
• There is some suggestion of impulsive behavior and impaired judgment in adulthood. He reports that despite the inability to maintain sustained intimate relationships, he has engaged in several brief affairs. These may be impulsive, as evidenced by the tendency to engage in unprotected sexual encounters.
• There is evidence of psychiatric difficulties in the family that may be related to the bipolar spectrum disorders. The father had multiple extramarital affairs that reportedly resulted in the breakup of the marriage. Although many factors and conditions could help to explain and contribute to this behavioral pattern, it may indicate problems with impaired impulse control and sexual preoccupation. That the father left the family precipitously without further contact also suggests the presence of impulsive behavior.
The paternal uncle has a history of a psychotic disorder termed “schizophrenia.” The fact that a serious psychiatric disorder, most likely with psychotic features, is present on the father’s side reinforces the possibility of a paternal genetic inheritance. In the absence of a clear history of symptoms and course, a diagnosis of schizophrenia should not be accepted at face value. This diagnosis is often used as a generic term for serious mental illness, especially by the lay public. As our diagnostic system has become more developed and systemized, more accurate diagnoses are being made. Furthermore, there appears to be a genetic link between schizophrenia and bipolar disorder in some families.

TREATMENT OPTIONS

The treatment algorithm in this particular patient is made more complex by the lack of diagnostic clarity. One may view the therapeutic course as indicative of treatment-resistant unipolar depression. Alternatively, there are multiple lines of evidence suggesting the presence of a “soft” bipolar spectrum disorder, and this may lead the clinician to entertain different forms of interventions. Whatever the formal diagnosis, the failure to respond to previous antidepressant trials and the apparent worsening of course with new-onset suicidal behavior in the midst of an antidepressant trial indicate the need for new therapeutic interventions. In the acutely suicidal hospitalized patient, the clinician should use interventions with a high likelihood of success and that are most likely to lead to rapid stabilization of symptoms. An intervention that is helpful in refractory depression and bipolar disorder would provide for the broadest spectrum of coverage and intervention.

Some of the pros and cons of treatment options are as follows:

- **Increase paroxetine dose.** This would probably not be advisable as a first intervention considering the apparent worsening of depression as the dose was increased previously.
- **A trial of another antidepressant agent.** Switching to another antidepressant, possibly with a novel therapeutic action (eg, mirtazapine), may be one approach. However change of antidepressants would not address a possible underlying bipolar disorder and may result in poor efficacy of the agent or increased cycling. However, if this intervention is used, the patient should be watched closely for deterioration.
- **Augmentation of the antidepressant.** There are several possible augmenting agents that have been used, including thyroidine, inositol, and pin dolol. Although there have been some positive studies with these and other agents, many of the trials are uncontrolled, small in size, or offer conflicting evidence of effectiveness. Therefore, there is a paucity of controlled clinical trials to guide the clinician with these interventions. Furthermore, the possibility of a bipolar spectrum disorder is not addressed with this approach. Lithium has also been studied as an augmenting agent to antidepressants.
- **Addition of an atypical antipsychotic.** There is increasing evidence that the atypical antipsychotics are effective as adjunctive agents added to antidepressants (selective serotonin reuptake inhibitors [SSRIs]) in treatment-resistant depression. An antidepressant that is associated with a low likelihood of switching into mania, such as an SSRI or bupropion, is advisable. Just because the patient failed treatment with paroxetine does not mean that he would not respond to another SSRI, such as sertraline or escitalopram. Olanzapine was the first of the atypical agents to be approved in the treatment of bipolar disorder. In a trial by Zajecka et al, monotherapy with olanzapine was found to be equally efficacious to treatment with divalproex, and a similar study by Tohen et al confirmed this finding. Olanzapine is also effective in the treatment of bipolar depression. However, olanzapine and clozapine have the greatest potential for weight gain among all the atypical agents and may exacerbate the weight gain in this already obese individual.

Ziprasidone has been shown to possess antidepressant activity and has been used to augment treatment with SSRIs in an open study. Ziprasidone has been also shown to be effective in the treatment of acute mania and is one of the most recently Food and Drug Administration (FDA)-approved atypical agents for this indication. Keck et al found ziprasidone to be effective in acute mania and to separate from placebo at 2 days and its efficacy to persist throughout the 3 weeks of the study. This rapid onset of action would be advantageous in this acutely suicidal patient, but in the absence of any manic symp-
toms, ziprasidone should be added to an antidepressant. Furthermore, ziprasidone has little or no weight gain or tendency to cause metabolic disturbances, such as hyperglycemia or hyperlipidemia. This is advantageous in an individual who has had long-standing problems with obesity and is already at increased risk for diabetes and other chronic medical illnesses. A recent ruling by the FDA modified the language for ziprasidone and aripiprazole on the metabolic warning now required for all of the atypical agents, reflecting this benign side-effect profile.

Quetiapine\(^1\) and risperidone\(^19,20\) have also been shown to be effective in mania and risperidone has been shown to be effective in resistant depression\(^10\) when added to an SSRI. Quetiapine also has demonstrated efficacy in bipolar depression.\(^21\) Aripiprazole, the latest of the atypical agents to be introduced, has also been shown to be effective in acute mania.\(^22\) Weight gain with quetiapine and risperidone tends to be more modest compared to with olanzapine or clozapine\(^23\) but greater than that observed with ziprasidone\(^24\) or aripiprazole.\(^25\) Risperidone may induce hyperprolactinemia, which may be related to the reportedly higher rates of sexual disturbances that have been noted with this agent.\(^26\) In an open-label study by Knuepfer et al, the rate of sexual dysfunction in patients receiving risperidone was 50% compared to 16% of patients receiving quetiapine.\(^27\) Prolactin levels were increased in the risperidone-treated cohort (mean = 57.7 ± 39.7) compared to patients receiving quetiapine (13.8 ± 17.9). The mean standard deviation dose was 3.2 ± 1.3 mg/d for risperidone and 580 ± 224 mg/d for quetiapine.

- **Addition of lithium.** The evidence for lithium indicates its clear effectiveness in “classic” bipolar disorder.\(^28\) Lithium has also been used extensively to augment the effect of antidepressants in treatment-resistant depression.\(^10\) This dual role makes lithium a rational intervention for this patient. However, there is a need for blood-level monitoring of this agent. In addition, there are multiple undesirable side effects, including impaired cognition,\(^19\) tremor, and hypothryroidism.

- **Addition of an antiepileptic mood stabilizer.** The addition of an antiepileptic mood stabilizer also may be an effective intervention. The data regarding the use of these agents in patients with bipolar II are much less extensive than data guiding the treatment of bipolar I disorder.\(^29,31\) The greatest clinical experience exists for valproate. Valproate may have some antidepressant effects, in addition to its well-established antimanic properties,\(^32\) although the antidepressant effects tend to be much more modest. Weight gain is frequently associated with valproate and, as with several of the atypical agents, is an undesirable side effect in this already overweight individual.\(^33\) The need for blood-level monitoring also complicates the use of this medication.

Lamotrigine would be a very viable choice in this patient considering the established antidepressant and antimanic effects of this agent\(^34\) in bipolar disorder. Lamotrigine has been used as an effective adjunctive agent to antidepressant therapy in unipolar patients.\(^36,37\) The need for slow titration owing to the possibility of Stevens-Johnson syndrome may limit the use of this agent somewhat in an acutely suicidal hospitalized patient. There is some evidence that topiramate may be effective as an adjunctive agent in bipolar disorder;\(^36,37\) however, controlled data for this agent are limited. Topiramate may induce weight loss in some individuals and this makes this agent potentially beneficial in this patient.\(^38\) However, topiramate has several undesirable side effects, including cognitive impairment\(^39\) and the possibility of metabolic acidosis and renal calculi.\(^40\)

**CONCLUSIONS**

This patient is a diagnostically complex individual with treatment-resistant depression and possible bipolar II spectrum disorder. The broad number of interventions now available allows the clinician to tailor the interventions for maximum therapeutic impact with a minimum of side effects. The clinician should try to use agents with the broadest potential for therapeutic effectiveness, covering for the possibility of a bipolar disorder and treatment-resistant depression. A rapid onset of action is also desirable because the patient is hospitalized and presented with a serious suicide attempt.