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CASE

Depression and anxiety: Distinguishing unipolar and bipolar disorders

Presented by
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The use of steroids and supplements can complicate the clinical picture in a young man with mood swings, anxiety, and depression referred for psychiatric evaluation by his primary care clinician and psychologist.

Identifying information: A 20-year-old single man was referred by his primary care physician and a psychologist for medical management of mood swings, anxiety, and confusion.

Chief complaint: The patient reported unremitting sadness that had lasted more than a year, and said that he generally felt "dead inside" or "like a zombie." He was often ruminative and irritable, with difficulty concentrating.

History of present illness: The young man's sadness and disagreeable sensations were relieved only for periods of 3 to 4 days when he felt more worried than sad. It was during these intervals of worry that he grew more ruminative, tired, and irritable, and said he could not "sort out" his thoughts.

The patient could not recall when he last felt well enough to have fun with friends. He ruminated about the past, often trying to change it in his mind and thereby causing himself to become confused about what was real and what he might have imagined to be real. In particular, he was preoccupied with the recent loss of a relationship with a girl, which began in high school. He blamed the loss on his moodiness. However, he also acknowledged that he briefly dated her younger sister, a short time after which the girlfriend abruptly stopped returning his calls, telling him it was payback for dating her sister. The patient spent a great deal of time online looking at his ex-girlfriend's MySpace social-interaction page, which only caused him to feel worse.

He blamed himself for everything that was wrong in his life and struggled with thoughts that people were talking and thinking about him negatively. Because he believed he was physically too small, he exercised regularly to stay in good shape.

Medications and allergies: The referring primary care physician and psychologist had prescribed sertraline 100 mg/d for 3 weeks. They then switched him to venlafaxine 225 mg/d which he took for 4 to 5 weeks. However, the patient stopped taking both drugs on his own initiative because they made him feel numb, and he also thought they made him feel more depressed. In the week before the initial psychiatric evaluation, his father had given him some sleeping medications because he was often tense, keyed up, and unable to relax in the evenings and around bedtime. They did not help. Otherwise, this young man had not been taking any medications during the previous 6 months.

Psychiatric history: The patient had never been hospitalized and denied any suicidal or homicidal ideation. As mentioned, he sometimes thought he could undo the past by some ritualistic mental action.

The young man was an only child and spent a lot of time talking about this. He denied any history of childhood trauma. However, he held an unusual suspicion that his parents were hiding a birth defect from him, and that this defect was in some manner related to his current issues and difficulties. He did not give any more details about this suspicion, saying, "Every time I ask them about it, they tell me I'm crazy and just make a joke about it." His mother reported that it took about 10 years to conceive, but there were no complications with the pregnancy or delivery.

The patient received no intervention during the first 6 months of the current episode, when his family doctor was contacted. The doctor referred the patient to a psychologist for counseling, and the psychologist quickly referred him back to the doctor, believing that the young man needed a prescription for antidepressant medication.

His mother said he was drinking alcohol more regularly while on his medications, and that he was probably not fully compliant with the antidepressant regimens. He was never prescribed benzodiazepines for his anxiety and tension, apparently due to concern about abuse potential.

Medical history: The patient reported no medical problems connected with his mental symptoms, and he specifically denied any history of cardiovascular disease, seizures, or head injury.

Family history: The mother had been diagnosed with situational anxiety and depression and was taking fluoxetine. A paternal aunt was taking sertraline for a diagnosis of panic disorder. There was no known family history of schizophrenia, bipolar disorder, or suicide.

Social history: The patient had always been social, had no developmental delays, and did well academically until his senior year in high school when his grades declined. He withdrew from friends and began experiencing anxiety and periods of sadness. It was during this time that he was working out more vigorously and using dietary supplements.

The patient still lived at home with his parents. Although he finished high school, he did not enroll in college. He had no specific plans for the future and was working part-time at a fast food restaurant.

Review of systems: He had not experienced panic attacks, excessive physical rituals or compulsions, nightmares, or flashbacks. He worried chronically in the past year, experiencing poor sleep, restlessness, and muscle tension.

On direct questioning, the patient denied hallucinations, thought insertion, or broadcasting. However, referential thinking did seem to weave through some of his history.

There were no clear periods of euphoria or classic manic symptoms. He often had been irritable and had a difficult time separating the irritability from the depression. Periodically, his anxiety rose above the daily baseline of tension and on-edge feelings to include confused thinking, which he described not as racing thoughts but as having many simultaneous thoughts that aggravated the tension and interrupted sleep.

The last 6 months were dominated by fragmented sleep, decreased appetite and libido, pervasive guilt with passive thoughts of death, but absolutely no suicidal ideation.

Substance use history: He rarely used alcohol, but admitted to drinking more heavily during his senior year of high school. He also denied any illicit substance abuse. He had used the supplements purchased over the counter and online; however, he denied using injectable steroids. He would also augment his workouts with large amounts of energy drinks.

Although he denied current use of dietary supplements, he admitted to having done so in the past. He had used several herbal preparations as well as creatinine, protein supplements, and androstenedione that he would buy at nutrition stores or on the Internet to increase his testosterone levels and promote muscle growth. He conceded that he might have been more irritable, aggressive, and volatile while taking the supplements for his workouts. Though he claimed not to be using these supplements at present, he still had them and refused to discard them, saying he did not want to waste more than $300.

Physical examination: The patient was in good general health, clearly well-developed with increased muscle mass. Neurologic exam was unremarkable.

Mental status examination: This was largely within normal limits, although the patient exhibited a restricted affect when discussing his ex-girlfriend, in contrast to expected sadness or tearfulness. His thought process was logical, linear, and goal-directed. Cognitive testing, while limited to a brief Mini Mental State Exam, detected only some difficulty doing the serial seven test, but his effort was poor.

Assessment: The initial psychiatric impression was that while there were a number of diagnostic considerations, this young man most likely suffered from a mood disorder. Although he was never clearly manic, the presence of significant irritability and "crowded" thoughts along with the cyclical nature of his symptoms suggested Bipolar II disorder.

Provisional diagnosis:

AXIS I: Bipolar disorder, mixed episode, with psychotic features
- R/O substance-induced mood disorder with psychotic features
- R/O paranoid schizophrenia
- R/O schizoaffective disorder, bipolar subtype

AXIS II: Deferred

AXIS III: None

AXIS IV: Problems with primary support group; problems with social environment; educational problems; problems with access to health care services

AXIS V: 21

Treatment: Baseline blood work, including thyroid function, heavy metals, metabolic panels, and toxicology screens were ordered. Although the patient's presentation and family history suggested mood disorder rather than thought disorder, an MRI of the brain and projective testing were obtained to better evaluate a potential first-break psychosis. All test results were within normal limits.

The patient was referred to a 5-week mood disorders intensive outpatient program. Given the acute severity of his condition and the suspicion that he would require longer-term maintenance therapy for bipolar disorder, combination treatment with quetiapine (dosed up to 300 mg at bedtime during the first week) and lamotrigine (gradually titrated up to 200 mg/d over 5 weeks) was initiated.

DR MUZINA: There are numerous clinical features and historical clues that may aid in the distinction of bipolar from unipolar depression in many patients (see Table). For this patient, the clinical presentation of depression with mood swings and anxiety, as well as a family history of mood disorder, early age of illness onset, presence of potential psychotic features, and irritability with crowded thoughts all pointed to the potential presence of bipolar disorder.

The initial treatments with the antidepressants sertraline and venlafaxine may have been reasonable options, given the consideration of unipolar depression and anxiety. However, if clinical suspicion of bipolar disorder exists in such a patient and psychiatric consultation is not available, the primary care clinician might consider quetiapine monotherapy (which has evidence to support its use for bipolar disorder, major depression, and generalized anxiety disorder) or combining the traditional antidepressant with any mood stabilizer, such as lithium or valproate.

DR. NASRALLAH: The sudden onset of depression and anxiety in a previously well-adjusted young person can suggest several diagnostic possibilities and present a complicated clinical puzzle demanding careful exploration. Are there any comments on the initial steps in evaluating a referred patient such as this one?

DR PARISER: Having patients complete the Mood Disorder Questionnaire (MDQ) can be quite helpful, but it is important that they understand you are assessing symptoms experienced *during* an episode.[1] You are not asking them to report symptoms experienced randomly at different points in their lives.

Sometimes I also ask family members to fill out the MDQ as a means of recounting their observations of the patient. As long as I get consent from a patient in refractory cases, I will do everything I can to talk with one or more family members to help fill out the patient's history. These cases are very challenging.

DR BLACK: He has also been in therapy for 6 months. My experience in such cases is that it is hard for patients to describe the nature of the therapy, so I seldom know exactly what the therapist has been doing with them. After 6 months, it is either time to get a new therapist or to stop it altogether.

DR PARISER: That is a good point. How many obsessive-compulsive disorder patients have you discovered who are in dynamic therapy?

DR BLACK: Quite a few.

DR PARISER: Another important point this raises is that we should do our own therapy. Issues such as the ones in this case can overlap, and it takes time to tease them apart. Unfortunately, even when talking to a therapist about prior counseling, it is often difficult to get a firm idea about what has been happening. For one thing, the therapist may be a little defensive.

DR MUZINA: All of these points are valid. The therapy, as best I could tell, focused chiefly on the patient's soured relationship with the former girlfriend. His mother was involved with 1 or 2 of those sessions at the outset. One of the therapist's principal concerns was that the patient was depressed and anxious—and perhaps even bipolar—because he had taken a couple of antidepressant medications without benefit.

Also, there was some concern that he might have a predilection for stalking. There was no evidence that he was stalking the ex-girlfriend, except perhaps the frequency of going online to visit her MySpace page.

DR BLACK: Because the patient did not tolerate the antidepressants and stopped taking them on his own, it is hard to know whether he is truly treatment-refractory or if something else is going on. He has never been adequately medicated. It also sounds like sertraline was administered at a dose too low to have an impact.

I wonder, too, if he may have some kind of body dysmorphic disorder—a feeling that his muscles are too small. I believe Pope, Hudson, and colleagues called it *bigorexia*.[2] Or does the patient have some other kind of personality disturbance? He was preoccupied with the young woman; checking her out online. I have certainly seen that sort of thing in individuals with personality disorders.

DR MUZINA: Yes, I had the same thoughts about personality disorder. From what I was able to gather in the first 90-minute visit, nothing he or his mother said strongly suggested a primary personality disorder diagnosis.

DR BLACK: I have one other comment. He was taking power drinks to help with exercise and muscle building. These products contain stimulants. I wonder if he might be a stimulant abuser, even though he may not see it that way.

DR MUZINA: I agree. There is a reason why locker rooms for competitive athletes have tubs of these energy drinks

TABLE Distinguishing bipolar from unipolar depression

Symptom	Bipolar	Unipolar
Substance abuse	Very high	Moderate
Family history	Almost uniform	Sometimes
Seasonality	Common	Occasional
First episode <25 years	Very common	Sometimes
Psychotic features <35 years	Highly predictive	Uncommon
Rapid on/off pattern	Typical	Unusual
>3 recurrent major depressive episodes	Common	Unusual
Antidepressant-induced mania/hypomania	Predictive	Uncommon
Mixed depressions (presence of hypomanic features within the depressive episode)	Predictive	Rare

Kaye NS. Is your depressed patient bipolar? *J Am Board Fam Pract.* 2005;18(4):271-281. Reproduced by permission of the American Board of Family Practice. © 2005 American Board of Family Practice.

available before and during games. It is not just to boost energy but to increase the desire to go out and play hard. The drinks claim to improve performance, especially during times of increased stress or strain, to increase concentration and improve reaction speed, and to stimulate the metabolism. The ingredients almost always include caffeine; they will throw in amino acids and things like taurine and pyridoxine, ostensibly to help with performance and concentration.

DR NASRALLAH: Could he have been taking the anabolic and herbal preparations before he broke up with his girlfriend? Is it possible his depression, irritability, and volatility could have been instigated by anabolic steroid use?

DR MUZINA: Yes. The timeline, as I was able to put it together, was that midway through his senior year of high school he was working out heavily and using these supplements along with friends. And he was dating the young woman. All of this continued the first 6 months after graduation. So the complaint of having felt sad over 14 months before I saw him certainly suggests that the substances could have been affecting him before any relationship problems developed with the girlfriend.

DR NASRALLAH: Then it is possible this patient could have a bipolar spectrum disorder exacerbated by steroid use (**TABLE**).[3]

DR BLACK: A toxicology screen would be appropriate, and not only for steroids. In a patient like this, you wonder what else he was putting into his body.

DR PARISER: And what about duty to warn? He was getting into e-mail, is that correct? Cocaine could even be an issue, in addition to steroids—that would be worrisome.

DR MUZINA: He was blocked from the e-mailing functionality on the social network. But that does not stop one from posing as someone else and being assigned a friend in one of these social networks. So, he could still be finding a way to track what another person is doing and still be looking at the pictures and blogs.

DR PARISER: Dr Muzina, does the patient recognize anything strange in what he was doing, or is it egosyntonic? Has he admitted this is something he should not be doing, or does he see nothing wrong with looking the ex-girlfriend up on My Space and violating boundaries?

DR MUZINA: I do not know if he recognizes his behavior as strange. His own words were, "I know I shouldn't be doing this because she is no longer my girlfriend. She told me she doesn't want to talk with me or communicate with me anymore, and I've been told by my mom, my family doctor, and a psychologist that I should just let this all go." There was sort of an irresistible urge still to go online to check out those photos and see what she had been doing recently. Even though he knew he should not be doing it because he had been told it was not a good thing to do.

DR NASRALLAH: A bipolar patient of mine was jilted by a boyfriend. For several weeks, she would drive her car around his block as many as 50 times in a few hours just hoping to see him come out of his apartment. I have seen this kind of behavior in many bipolar patients who simply will not let go. Their manic energy and grief combine to

cause this kind of behavior. That is why it seemed to me this patient, in exhibiting what I call "mini-stalking," may not know how to let go of the object of his affection.[4,5]

DR BLACK: When you said that his father gave him sleeping pills, do we know if he was not sleeping because he was psychometrically active at night, or whether he was tired the next day?

DR MUZINA: No, he was not particularly tired the next day. He described what I thought was anxiety: lots of tension and being wound up. In some ways, it was almost an obsessive urge to log on and look at his ex-girlfriend's Web page. He knew he should not be doing that. These thoughts were coming to him in the evening and that prevented him from sleeping. One of the first things I discussed with his mother was limiting his Internet access or turning the wireless network off when everyone went to bed.

DR PARISER: He would meet most of the research diagnostic criteria for agitated depression, which does not exist in the DSM. The tension, the psychomotor agitation, the questions that are what are called "crowded thoughts."[6] Whether it is a variant of psychosis or of bipolar disorder, it is certainly not a simple unipolar presentation, and it is likely aggravated to some extent by substances. From a management standpoint, agitated depression warrants greater concern about the patient acting on impulses and calls for prescribing an antipsychotic.

DR NASRALLAH: I am wary of the term agitated depression. Any time a patient with presumed unipolar disorder is said to have agitated depression I want to rule out bipolar II disorder that has irritability, anger, and hostility as features. Using the MDQ and differentiating between agitated depression and bipolarity is useful for diagnostic accuracy. But in a sense, it is less useful for management because we have a treatment that addresses both situations.

A quandary for many practitioners is whether to use or avoid an antidepressant in bipolar disease. But the quetiapine-lamotrigine combination Dr Muzina is using with this patient would work in either case.

DR BLACK: Another aspect to this patient's case is the possibility of paranoia. I worry about the kind of intrusive behavior he has exhibited, and using an atypical antipsychotic may be appropriate.

DR PARISER: The psychological testing you have requested should yield answers about his potential for psychotic thinking, especially under stress, and as to whether any Cluster A personality disorder exists.

DR NASRALLAH: Dr Muzina, did you feel that this patient exhibited some psychotic or prepsychotic features?

DR MUZINA: Yes. He made me more uncomfortable than most patients do, and I supposed he was not giving me the whole story. He alluded to what could be psychotic or developing psychotic symptoms.

DR PARISER: What about traumatic brain injury? Any number of organic issues, including frontal lobe involvement, might be considered. You said there was no history of closed head trauma or anything like that?

DR MUZINA: None that he told me and none that his mother reported.

DR BLACK: Dr Nasrallah, I think you may have taught me that agitated depression in the late teens can often herald the onset of bipolar disorder. Nothing in this case absolutely indicates bipolar disorder, but there are clues suggesting it could evolve that way.

DR PARISER: That would be good news in terms of diminishing the possibility of Cluster A disturbance.

DR NASRALLAH: Yet, do not underestimate the potential for destructive behavior in this young man who had low self-esteem and was so worried about his dysmorphic features. He was obsessed about the lost girlfriend and was tracking her in what amounts to a mini-form of stalking. But I do not think that predicts psychosis as much as it does a bipolar-related stress. I think medication and psychotherapy will get him out of it. So, unless anyone has further comment, I think we're all agreed on the therapeutic approach Dr Muzina has chosen for this patient. ■

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