Current PSYCHIATRY

CASES THAT TEST YOUR SKILLS

Ms. R is irritable, depressed, tired, and worries incessantly. Misdiagnosis has led to numerous failed drug regimens over 3 years. Can you pinpoint and treat her problem?

Is it anxiety, depression, or bipolar disorder?

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HISTORY 'A ZILLION RACING THOUGHTS'

Ms. R, age 44, is referred by her primary care physician. She complains of tenseness, irritability, avolition, and fatigue. She worries incessantly that her children will get sick, a catastrophe will befall her husband, or she'll do something wrong. She says she sometimes feels as if she's thinking "a zillion racing thoughts."

Once fun-loving, outgoing, and energetic, Ms. R says she began feeling unusually anxious 3 years ago. A psychiatrist diagnosed bipolar disorder type II based on her racing thoughts, irritability, low energy, and history of mood swings. Over 2 years, the psychiatrist tried combining valproic acid with bupropion, citalopram, or extended-release venlafaxine, then tried lithium monotherapy. Nothing worked.

Frustrated, Ms. R left the psychiatrist and consulted her primary care physician, who prescribed gabapentin, 200 mg each morning and 300 mg at night; fluoxetine, 50 mg/d; and quetiapine, 12.5 mg/d. Ms. R noticed no improvement and stopped the medications after 6 weeks. The physician urged her to see another psychiatrist, and she presented to us 2 weeks after stopping the medications.

Ms. R also has been feeling depressed and irritable the past 4 months and has trouble falling and staying asleep at night. She sleeps 4 to 5 hours nightly, constantly feels tired, cannot concentrate, and overeats to try to alleviate her stress. She has gained 6 pounds over 2 to 3 months and weighs 160 lb; her body mass index of 26 indicates she is overweight.

She says her worries overwhelm her and cause heart palpitations and muscle tension in her neck and shoulders. She admits to feeling "worthless," but denies suicidal thoughts.

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Table 1

Overlap among symptoms that suggest GAD, mania, or major depression

Symptom	GAD	Mania	MDD
Difficulty concentrating/ distractibility	X	X	X
Mood irritability	X	X	X
'Racing' thoughts	X	X	X
Sleep disturbance	X	X	X
Tiring easily/low energy	X		X
Excessive psychomotor activity/ restlessness	X	X	X

GAD: generalized anxiety disorder
MDD: major depressive disorder
Source: Reference 1

Ms. R describes her husband and two teenage daughters as "very supportive," but admits that her fatigue and irritability have strained these relationships; she says she snaps at them for minor things, such as coming to dinner 1 minute late. She misses her job, which she recently quit because of her decreasing ability to function.

At intake, Ms. R says she will not resume previous medications but will consider alternatives. She refuses psychotherapy because of time constraints and transportation problems but is willing to return every 2 weeks for medication checks. She says she adhered to every prescription over 3 years with no major side effects. She has never taken an antidepressant or anxiolytic without a mood stabilizer.

Ms. R reports no medical problems, past substance use, current or past psychotic symptoms, or psychiatric hospitalizations. Her family history shows depression in one first-degree relative and anxiety in others. Her Hamilton Anxiety Scale (HAM-A) score of 20 indicates moderate anxiety. Laboratory tests ordered by her primary care physician are normal.

At this point, I would diagnose:

a) generalized anxiety disorder (GAD)
b) bipolar disorder type I
b) bipolar disorder type II
d) GAD with comorbid depression

The authors' observations

Racing thoughts, irritable mood, decreased sleep, and concentration problems can point to GAD, mania associated with bipolar disorder type I, or hypomania suggesting bipolar disorder type I or II (*Table 1*).[1]

We suspect GAD because:

- Ms. R's thoughts "race" only when she worries
- her irritability and concentration problems seem more sustained than episodic
- she has difficulty falling and staying asleep, but her need for sleep has not decreased
- she complains of constant fatigue, whereas abnormally high energy characterizes bipolar disorder's manic or hypomanic phase.

Does Ms. R have depression? Determining if the patient's depressive symptoms are secondary to GAD or warrant a separate diagnosis can be difficult (*Table 1*). With Ms. R's permission, we talked to her family, because collateral information often helps clarify the diagnosis. Her husband and daughters offered no significant new insights, however.

TREATMENT: TARGETING THE ANXIETY

To address Ms. R's anxiety symptoms, we start buspirone, 5 mg tid, and titrate to 15 mg bid over 2 weeks. We choose buspirone—which is FDA-

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approved to treat GAD—because it is unlikely to cause a mood switch if bipolar disorder is causing Ms. R's depression. We discuss with her the drug's indications, benefits, and potential side effects (such as vertigo, headache, lightheadedness, and nausea).

At the first 2-week follow-up, Ms. R reports no side effects but little improvement. After another 2 weeks, she says she feels less anxiety, irritability, pain, and fewer racing thoughts. She reports less difficulty falling asleep, though she's still sleeping only about 6 hours nightly. Her HAM-A score falls to 12, indicating mild anxiety.

Ms. R, however, says she still feels depressed, tired, distracted, unmotivated, and worthless. Her Hamilton Rating Scale for Depression (HAM-D) score of 16 indicates moderate depression.

Ms. R's depressive symptoms:
a) are secondary to GAD
b) suggest a comorbid depressive disorder
c) suggest bipolar depression

The authors' observations

The persistence of Ms. R's depressive symptoms suggests comorbid major depressive disorder (MDD). In fact, MDD and GAD are considered the most common mood-anxiety comorbidities.[2]

Determining whether Ms. R has unipolar depression or bipolar disorder is extremely important,

For Your Patient

Depression, mania, or hypomania? Signs family, friends should not miss*

Patient could be depressed if he/she:

- is constantly sad or irritable
- seems lost, withdrawn, or isolated
- is preoccupied with negative ideas and concerns
- persistently feels guilty, hopeless, and helpless
- says he or she has considered suicide
- has not been showering regularly or is unkempt (indicates low mood)
- shows significant changes in sleep
- moves slowly or sparingly, as if "slowed down" (indicates depressed affect)
- is often restless (indicating agitated/anxious depression)
- talks in a low-tone or monotone voice
- no longer enjoys activities or hobbies he or she once found pleasurable
- shows significant changes in appetite
- no longer enjoys sex
- cannot concentrate or make decisions

Patient could be manic or hypomanic if he/she:

- seems abnormally hyperactive, restless, and energized, compared with normal self
- is inappropriately euphoric and jubilant or, on occasion, extremely irritable
- talks rapidly and excessively
- often wears clothes that are too bright or colorful
- seems unusually self-confident, grandiose, and highly distractible
- shows increased sexual desire
- is impulsive, increasingly daring, and shows seriously impaired judgment, such as by investing/spending large sums of money for ill-advised reasons
- seems energetic despite lack of sleep

*If a family member shows any of the above symptoms, get him or her to a mental health clinic as soon as possible. Take the family member to the nearest ER or call your local crisis unit or 911 if you suspect the family member might hurt him/herself or others.

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How would you handle this case?

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considering the treatment implications. In patients with bipolar disorder, any antidepressant can trigger mania or hypomania if used without a mood stabilizer. Some studies also have associated rare cases of suicidal behavior with antidepressant use.[3,4] Lifetime risk of suicide in bipolar disorder is approximately 20 times that in the general population.[5]

Although Ms. R's history does not reveal a previous manic episode, ruling out hypomania is difficult because it usually does not impair work or social functioning. Hypomania often goes unreported because others hardly notice it. Collateral history can uncover clues to hypomania (See *For Your Patient, page 98*), but Ms. R's husband and daughters say they have not seen such episodes.

An extroverted personality can be mistaken for hypomania between depressive episodes

On the other hand, normal behavior can be mistaken for hypomania. Ms. R's previous psychiatrist and primary care physician might have misinterpreted Ms. R's baseline extroverted personality as hypomanic behavior. Also, her overwhelming depressive and anxiety symptoms between depressive episodes made her normal moods appear hypomanic.

Compared with unipolar depression, bipolar depression is more frequently associated with psychomotor retardation, hypersomnia, early onset, and family history of bipolar disorder.[6] Ms. R, however, suffered low energy, terminal insomnia, and late onset, and had no known family history of bipolar disorder.

The Mood Disorder Questionnaire, a scale of self-administered questions, can help screen for symptoms that suggest bipolar disorder. A positive questionnaire result demands further clinical evaluation.[7]

CONTINUED TREATMENT: 'NORMAL' AGAIN

In addition to the HAM-D, we also administer the Mood Disorder Questionnaire. Results suggest Ms. R does not have bipolar illness.

To address Ms. R's depressive symptoms, we start the selective serotonin reuptake inhibitor escitalopram at a low dosage (5 mg/d) to avoid exacerbating her anxiety. We discuss the drug's potential to induce mania, hypomania, or other adverse effects such as nausea, anxiety, sleep disturbance, headache, and sexual dysfunction. Buspirone is maintained at 15 mg bid.

Two weeks later, Ms. R reports some increase in energy and motivation. After another 2 weeks, she reports significantly improved mood and concentration. She consistently falls asleep at 10 PM and sleeps 8 hours each night. She also finds time to read and go out with her friends and she gets along more amicably with her daughters and husband.

One month later, we increase escitalopram to 10 mg/d, a normal therapeutic dosage. Ms. R continues to respond positively and reports no side effects. Two months after starting the antidepressant, her HAM-D score of 8 suggests normal mood. We decrease follow-up visits to once monthly.

At a subsequent visit, Ms. R tells us she wants to find a job. A month later, she says she is enjoying her new job in a department store. Over the next 6 months, she remains free of anxiety, depressive symptoms, hypomanic behavior, and

Table 2

Differentiating symptoms common to GAD, major depression, and mania

Symptom	GAD	Major depression	Mania
Concentration	Difficulty concentrating (mind goes blank)	Diminished ability to concentrate or think (indecisiveness)	Easily distracted (difficulty focusing on one task)
Energy	Tires easily	Constant fatigue or loss of energy	Subjective feeling of increased energy
Mood	Can be irritable	Irritable, though more depressed	Euphoric or extremely irritable
Behavior	Seems more keyed up	More withdrawn	Increase in risky behavior with potential for painful consequences
Sleep	Disturbed (mostly difficulty going to sleep)	Disturbed (hypersomnia or insomnia, more likely terminal insomnia)	Decreased need for sleep (energetic after sleeping 2 to 4 hours)

side effects. She tells us it's nice to feel "normal" again.

We reduce Ms. R's appointments to every 3 months. After another year, we refer her back to her primary care physician at her request.

The authors' observations

DSM-IV-TR[1] divides bipolar disorder into three categories:

- **type I,** in which the patient has had at least one manic episode with or without major depression
- **type II,** characterized by one or more major depressive episodes and at least one hypomanic episode
- **cyclothymia,** which is defined as fluctuation between hypomanic and minor depressive episodes.

Much is said about how underdiagnosis of bipolar disorder[8] delays or prevents proper therapy with mood stabilizers, leading to suboptimal symptom resolution. As with Ms. R, however, an incorrect bipolar disorder diagnosis can be just as harmful. Three years of unnecessary and ineffective treatment worsened her anxiety and depressive symptoms and quality of life.

A comprehensive clinical interview supplemented with insights from family and friends can minimize the risk of misdiagnosis when patients present with symptoms that suggest bipolar disorder, depression, or GAD.

Differentiating between the following clinical features can also help you reach a diagnosis:

Bottom Line

Generalized anxiety disorder, bipolar disorder, and depression share many symptoms. Differentiating how these disorders affect concentration, sleep, energy level, behavior, and mood can help narrow the diagnosis. Interview family and friends if possible, and educate them on recognizing signs of depression and hypomania.

Related resources

- Depression and Bipolar Support Alliance. www.dbsalliance.org.
- Anxiety Disorders Association of America. www.adaa.org.

DRUG BRAND NAMES

Bupropion • Wellbutrin
Buspirone • BuSpar
Escitalopram • Lexapro
Fluoxetine • Prozac
Gabapentin • Neurontin
Quetiapine • Seroquel
Valproic acid • Depakene
Venlafaxine • Effexor

DISCLOSURES

Dr. Williams is a speaker for Wyeth.

Dr. Singh reports no financial relationship with any company whose products are mentioned in this article, or with manufacturers of competing products.

Sleep/energy level. Mania/hypomania is characterized by decreased need for sleep; patients often feel energetic even after 2 to 4 hours of sleep. Both depression and GAD diminish energy level, although mood is more depressed in depression. Patients with GAD have trouble falling asleep, while those with depression awaken early or have hypersomnia.

Behavior. Patients in the manic phase of bipolar disorder engage in risky, pleasurable activities with high potential for painful consequences. This drastic behavior change is not seen in depression or GAD (*Table 2, page 103*).

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