Bipolar II Disorder in a Primary Care Setting: Clinical Vignette

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Bipolar II disorders may be common in primary care settings, but most cases remain undiagnosed because hypomania is often difficult to recognize. Eliciting a history of recurrent periods of expanded mood interspersed with periods of major depression is important, since antidepressant monotherapy is often unproductive or even counterproductive. Once the diagnosis is made, appropriate medications to alleviate hypomanic episodes and depression should be initiated. These medications include mood stabilizers such as lithium and valproate, alone or in combination with antidepressants. Close monitoring of medication levels and patient response is essential in the ongoing treatment of this disorder. Psychotherapy is often an integral part of treatment.

(Primary Care Companion J Clin Psychiatry 1999;1:47–49)

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Bipolar spectrum illness may be more common in primary care settings than previously thought, with recent longitudinal investigations placing 30% of identified depressive illnesses into this category.[1,2] In these investigations, the bipolar illness resembled bipolar II disorder, but the hypomania documented in many individuals lasted less than the 4 days required by the DSM-IV.[3] However, there is good evidence that 1 to 3 days is the most common duration of hypomania, and periods of expanded mood lasting less than 4 days are equivalent to the DSM-IV criteria from the standpoint of diagnostic validity.[3–5] Such illness has been referred to in the psychiatric literature as "soft" bipolar, because of the absence of mania.[6]

Hypomanic episodes may be difficult to recognize because the predominant mood is elated and because the energy and productivity associated with hypomania are often adaptive. Although the mood elevations experienced by bipolar II patients do not reach manic levels (Table 1), individuals are typically able to recognize and describe these periods as being distinct from their usual mood. It is important to evaluate these illnesses from a longitudinal perspective, as patients typically do not seek treatment during hypomania and do not mention it in clinical histories. Only a careful discussion of symptom patterns and treatment history, close observation of treatment results, and corroborating information obtained from significant others will result in an accurate diagnosis. Focused clinician education may also be necessary to enhance diagnostic reliability.[7] Finally, treating "soft" bipolar patients can be challenging, since partial or total resistance to antidepressant monotherapy is common.[8]

We present the following clinical vignette as one that illustrates the presentation and clinical obstacles that are common in soft bipolar illness.

CLINICAL PRESENTATION

Ms. A, a moderately obese 32-year-old white woman, initially presented to our office in January 1997 for a refill of her estrogen replacement medication, which she had been taking since her hysterectomy for endometriosis after the birth of her fourth child in 1995. She complained of increasing problems with depressed mood, for which she had been treated by her previous physician with fluoxetine, 20 mg/day, for the past year. Although her current level of depressive symptomatology fell short of major depression, a careful history uncovered multiple past episodes that met those criteria. Ms. A related feeling "depressed and moody" since her teenage years. Paroxetine and other antidepressants administered for previous depressive exacerbations usually caused increased lethargy and little improvement in mood. While fluoxetine initially helped decrease her tearfulness and increase her energy and goal-directed behavior, the improvement had lasted only a few weeks. Her mood aberrations were not related merely to estrogen replacement or adherence problems. Ms. A denied current use of alcohol or illicit drugs and smoked cigarettes about 1 pack per day for 20 years. She also drank 1 or 2 servings of caffeinated beverages per day. A physical examination and routine laboratory work were unrevealing. Her TSH level was normal. She was advised to exercise, reduce her fast-food intake, consider psychotherapy, and increase her fluoxetine dose to 40 mg/day.

When seen next, Ms. A complained of continued hypersomnia and daytime lethargy, increased appetite, frequent crying, headaches, and memory problems. Increasing her fluoxetine dose from 20 mg to 40 mg seemed to help for a while, but then gradually stopped working—the

Table 1. Criteria for Hypomanic Episode[a]

A. A distinct period of persistently elevated, expansive, or irritable mood, lasting at least 4 days, that is clearly different from the usual nondepressed mood.
B. During the period of mood disturbance, 3 (or more) of the following symptoms have persisted (4 if the mood is only irritable) and have been present to a significant degree:
   1. inflated self-esteem or grandiosity
   2. decreased need for sleep (eg, feels rested after only 3 hours of sleep)
   3. more talkative than usual or pressure to keep talking
   4. flight of ideas or subjective experience that thoughts are racing
   5. distractibility (ie, attention too easily drawn to irrelevant external stimuli)
   6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
   7. excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, the person engages in unrestrained buying sprees, sexual indiscretions, or foolish business investments).
C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.
D. The disturbance in mood and the change in functioning are observable by others.
E. The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features.
F. The symptoms are not due to the direct physiologic effects of a substance (eg, a drug of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism).

[a]Adapted from reference 3, with permission.

same pattern of response noted on initiation of fluoxetine treatment. We asked her to describe the timing and quality of her initial improvement on the increased dose. After only 2 to 3 days on 40 mg of fluoxetine, she went from lying in bed much of the day to playing kickball in the backyard with her children. Her hypersomnia reversed abruptly to her needing only 3 to 4 hours of sleep per night. Ms. A described feelings of elation and of having her mind filled with ideas and activities, racing from one thought to another. She became markedly more talkative and social. Those around her noticed her behavior as distinctly different than usual. This sudden and dramatic response lasted about 1 week, ended suddenly, and was followed by a steady decline in energy and motivation over the next several weeks. When asked if these episodes had ever occurred in the past, Ms. A described experiencing similar brief periods of expanded mood that occurred every 2 to 3 weeks, typically lasting from 2 to 3 days, but occasionally as long as 5 days. She recognized these periods as being time limited and would try to make the best of them by shopping and doing housework, often late into the night. Her symptoms during spontaneous periods of expanded mood met the DSM-IV criteria for hypomania. When combined with her recurrent major depressive episodes, the presence of the hypomanic episodes confirmed the diagnosis of bipolar II disorder.

On closer examination, Ms. A's family history contained elements often seen in bipolar illness. She described her mother as an emotionally unpredictable individual who controlled much of Ms. A's life by being both her employer and her baby-sitter. Her father was an often depressed individual "who probably should have been on medicine." Both Ms. A and her mother have a pattern of divorce and remarriage to the same individual—her mother has been married 4 times to 2 different men, while Ms. A has been married 3 times to 2 different men.

Lithium carbonate was titrated to 300 mg t.i.d., while Ms. A continued her 40-mg dose of fluoxetine. Psychotherapy was encouraged to help her deal with parenting concerns, financial pressures, and ongoing relationship problems with her mother and ex-husbands. Two weeks later, she reported a decrease in lethargy and sadness and less pronounced mood swings. Early improvement was also evidenced by her initiation of psychotherapy and attempts to establish more structure at home and boundaries in her interactions with family members. After 1 month of combined lithium and fluoxetine, she was nearly asymptomatic. Her lithium dose was increased to 1200 mg daily to maintain a serum level of 0.7 mEq/L. After 4 months of treatment, Ms. A was essentially euthymic. However, she related to us a pattern of growing conflict with her mother regarding autonomy issues.

After numerous missed appointments, Ms. A returned 8 months later complaining of a sinus infection. She explained that shortly after her last visit her mother had convinced her to stop taking both the lithium and the fluoxetine. Ms. A stated that she was no longer interested in ongoing treatment for depression and was unwilling to discuss her decision. All subsequent efforts to reestablish a therapeutic relationship with her failed.

DISCUSSION

Ms. A's treatment history highlights the atypical response patterns that may occur when bipolar patients are treated with antidepressants alone. Her response to a single agent (fluoxetine), while initially positive, was sudden, dramatic, and short-lived. Efforts to replicate earlier improvements with dose increases were only marginally and temporarily effective. Antidepressant exacerbations of hypomania are common, but their clinical significance is still under investigation. However, treatment-emergent hypomania should arouse suspicion, as there is substantial clinical evidence that ties it to bipolar illness.[9,10]

Specific questioning documented distinct periods of hypomanic behavior, which were labile, recurrent, and disproportionate to current events. Her episodes of depression often manifested an atypical symptom pattern. This pattern of depressive symptoms is characterized by hypersomnia, hyperphagia, a tendency for mood to brighten in response to or anticipation of pleasurable events, and sensitivity to rejection by others. Atypical symptoms are more common in women, younger patients, and, possibly, individuals with bipolar depression, although the scientific lit-

erature is difficult to interpret in this regard. However, when combined with an early age at onset and positive family history, atypical symptom patterns may be a clue to the possibility of bipolar depression and due caution is advisable.[11] Although Ms. A had no other psychiatric disorders, conditions such as substance abuse, eating disorders, and anxiety disorders (e.g., panic disorder, social phobia, and obsessive-compulsive disorder) are often present.[12] Medical comorbidities such as thyroid disorders, history of stroke or heart attack, and the concurrent use of medications (prescription as well as nonprescription) may affect the course and treatment of mood disorders.[8]

While mood stabilizers are recommended as first-line treatment for individuals with bipolar disorder, the addition of a mood stabilizer to a partially effective antidepressant already in place, as in Ms. A's case, can also be an effective strategy. Although several options are available (e.g., lithium, valproate, carbamazepine), lithium is considered to be somewhat more effective than other mood stabilizers in treating depressive symptoms.[13] Initial lithium administration to otherwise healthy adults usually starts at 300 mg daily and is followed by dose titration. Therapeutic doses range from 600 to 2100 mg/day and are associated with serum levels of 0.4 to 1.4 mEq/L.[9] Lithium levels in the lower therapeutic range are often associated with good clinical results and tolerability. The workup prior to initiation of lithium therapy should include a complete physical examination, basic metabolic profile, thyroid function tests, complete blood count, and, in select situations, pregnancy testing and an ECG.[9]

As mood stabilizers often require several weeks to take effect, short-term use of benzodiazepines may be helpful in managing symptoms of agitation and/or insomnia. Psychotherapy can be a powerful adjunctive treatment option, particularly after somatic treatment results in improved sleep, improved memory and concentration, and enhanced decision-making ability. Interpersonal psychotherapy may be necessary to protect treatment gains that threaten the equilibrium of dysfunctional relationships with friends and family members. Adjunctive treatment includes maintaining a regular sleep pattern and schedule of daily activities. "Early to bed, early to rise" is best. Patients should avoid alcohol and all illicit drugs and limit the use of caffeine and over-the-counter medications used for colds, allergies, or pain. Support from significant others and lifestyle changes to reduce stress will be helpful in maintaining euthymic mood.

A supportive therapeutic alliance is critical to the treatment process. It is also important to discuss the initial delay in treatment response common to both antidepressants and mood stabilizers so treatment failure from poor adherence does not result in loss to follow-up. Health beliefs and the advice of significant others may also be critical to treatment adherence. This vignette highlights these difficulties. The Expert Consensus Treatment Guide for Bipolar Disorder[13] is available in a format written specifically for patients and families and can be obtained, along with physician treatment guidelines, on the Internet at www.psychguides.com.

The goal of treatment is consistent and complete response. As this may require adjustments to treatment, frequent visits are necessary, at least initially. Regular contact is also important to encourage compliance, monitor progress and side effects, and check laboratory values. Once a successful treatment regimen is established, strong consideration should be given to maintenance therapy.[13] Consultation or referral is advisable for diagnostic dilemmas, refractory illness, and mismatches in clinician experience or clinical resources. Patients considered a danger to self or others should be referred immediately to appropriate care settings.

Drug names: carbamazepine (Tegretol and others), fluoxetine (Prozac), lithium carbonate (Eskalith and others), paroxetine (Paxil).

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