A 35-Year-Old Man with Depressed Mood, Insomnia, and Suicidal Ideation

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A 35-year-old man presented to the outpatient clinic with a history of depressive symptoms for the past 18 months. The symptoms had come on gradually, and approximately 12 months prior he sought treatment from his primary care physician (PCP) because of depressed mood most of the day almost every day, fatigue, and initial and middle insomnia. He had lost weight because of poor appetite and he felt listless. Immediately prior to beginning treatment, he began to have worsening suicidal ideation that started out as fleeting thoughts of wanting to be dead but increased steadily until he began to fantasize about crashing his car on the highway or jumping off the roof of the high-rise office building where he had worked for 5 years.

When he began treatment with his PCP approximately 1 year prior to presentation at our clinic, he was prescribed 20 mg/day of citalopram along with 10 mg of zolpidem at bedtime for sleep. He took the citalopram faithfully for about 1 month despite persistent nausea and a distressing loss of libido, but he experienced only partial improvement in his depressive symptoms, with ongoing fatigue, depressed mood, and suicidal ideation that was less intense but still present. At his follow-up visit with his PCP 1 week prior to his presentation at our outpatient clinic, he was referred for a psychiatric evaluation.

We reviewed the patient’s history in detail. There was nothing to suggest that he had any features of bipolar illness, psychosis, or substance abuse. He had no history of any ongoing medical problems, and laboratory tests, including complete blood count, complete serum chemistries, urinalysis, and thyroid function tests, were normal. We confirmed with the patient that in his previous medication trials he had indeed taken the medicine every day exactly as prescribed in spite of some distressing side effects, and he was also completely compliant with his current antidepressant medication (sertraline), which he had been taking for approximately 6 weeks. His sleep had improved some since the addition of clonazepam, although he complained of some early
morning sedation. Because he had been taking the clonazepam for about 2 weeks, we recommended a taper of this medicine. In its place, we recommended some simple sleep hygiene measures (eg, reducing caffeine intake in the evening, reducing time in bed while awake, regular aerobic exercise) and 5 to 10 mg of zolpidem at bedtime only as needed. After a detailed discussion of the pros and cons of his condition and its treatment, we recommended the addition of 5 mg of aripiprazole to his medication regimen, and he was also referred for cognitive-behavioral therapy in our clinic to address both his sleep complaints and his depression. Sertraline was continued at 200 mg/day.

The patient’s diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition was major depressive episode (MDE). Because he has never had a symptom-free period of at least 2 months, his MDE would be classified as a single episode, moderate to severe, without psychotic features, with melancholic features. Two weeks later, he returned to the clinic with ongoing improvement in his depressive symptoms. His sleep was also improved, with less middle insomnia, and his suicidal ideation had decreased to the point where he could ignore it. At his second follow-up visit after 2 more weeks, he reported some residual symptoms such as fatigue during the day, minimal to moderate depressive mood, and occasional initial and middle insomnia. After another thorough discussion of the pros and cons of his condition and its treatment, we recommended a rapid taper and discontinuation of the sertraline and we prescribed the patient 75 mg/day of extended-release venlafaxine to be increased to 150 mg/day after 1 week. A week later, his depressive symptoms were significantly improved but he had completely lost his appetite and his sleep remained disturbed with both initial and middle insomnia. We discontinued the zolpidem and added 30 mg of mirtazapine to be taken at bedtime. He continued taking 5 mg/day of aripiprazole. His sleep and appetite began to improve immediately after addition of the mirtazapine, and at his next visit 2 weeks later his symptoms appeared to be in remission. He maintained good medication compliance over the next few months, and during his monthly visits to our clinic appeared to be free of depression. He was educated at each visit about the importance of medication compliance and the length of treatment required to maintain remission and prevent relapse.

DISCUSSION

Approximately 30% to 40% of patients with major depressive disorder fail to respond adequately to treatment and are labeled “treatment resistant” (or treatment refractory), which is usually taken to mean failure to respond to two or more trials of antidepressant medication of adequate dose and duration. The goal of antidepressant treatment is remission of symptoms, which is usually taken to mean complete resolution of symptoms as signified by a Hamilton Depression Rating Scale score of 7 or less, as unremitting patients report poorer quality of life and are at higher risk of relapse and recurrence. Current guidelines suggest a step-wise approach to patients with treatment-resistant depression (TRD). Although there are no straightforward algorithms or charts and treatment must be individually tailored, current options suggest four main strategies, which can be remembered with the mnemonic: “SACO” (Switching, Augmentation, Combination, and Optimization).

Of these, the first and safest is optimization of the dose and duration of existing antidepressant medication. Adequate doses must be continued for at least 6 weeks and sometimes up to 12 weeks for optimal response.

There are multiple augmentation strategies available. First-line options with the strongest supporting evidence include low-dose second-generation antipsychotics, lithium, and triiodothyronine.
Data also exist for the use of the anti-inflammatory agents celecoxib and infliximab, L-methylfolate (a derivative of the amino acid folate) as well as its metabolite S-adenosyl methionine. Benzodiazepines (especially for “anxious” depression) and the novel stimulant-like drug modafinil (as well as its R-enantiomer armodafinil) are also options. Other augmentation strategies such as folate, buspirone, lamotrigine, omega-3 fatty acids, amphetamines, and others do not qualify because of lack of robust evidence supporting their use in TRD.\textsuperscript{4}

Switching between different classes of antidepressants is another strategy, although lack of head-to-head trials between switch techniques means there is little guidance available to clinicians on whether to switch within class (ie, one selective serotonin reuptake inhibitor [SSRI] to another) or to another class of medicines (eg, SSRI to selective norepinephrine reuptake inhibitor/tricyclic antidepressant [TCA] or other).

Similarly, the evidence base for combination therapy (ie, combining two different classes of antidepressants for broader antidepressant spectrum effect) is limited, although there is at least one positive meta-analysis for use of combination therapy (mirtazapine/SSRI, mirtazapine/bupropion, mirtazapine/venlafaxine, SSRI/TCA).\textsuperscript{8} Two pharmacologic agents, the N-methyl-D-aspartate receptor antagonist ketamine and the muscarinic acetylcholine receptor antagonist scopolamine, hold promise for patients with both uncomplicated depression and TRD. Evidence is also available for augmenting pharmacologic treatment of TRD with psychotherapy,\textsuperscript{6} somatic therapies (electroconvulsive therapy, repetitive transcranial magnetic stimulation, deep brain stimulation, vagus nerve stimulation),\textsuperscript{10} and alternative therapies (yoga, exercise, acupuncture, and light-based therapies).\textsuperscript{11}

REFERENCES