Cases from the Psychiatry Letter - I

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Written by Nassir Ghaemi.

Edited by S. Nassir Ghaemi MD

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Case 1. A functional young adult with intrusive suicidal thoughts

A 23-year-old woman is admitted to the hospital with intermittent suicidal thoughts that come and go multiple times in the course of the day. She also has a current depressive episode with decreased interest, energy, appetite, and concentration. Duration of these symptoms is three months. When admitted to the hospital, the admitting psychiatric team prescribed fluoxetine. The patient denies prior depressive episodes, but describes depressive symptoms lasting up to two days but not longer in the past. During those two days of depressive symptoms though, she would experience the intrusive suicidal thoughts. These thoughts consisted of images of hanging herself, or of otherwise dying. These few day periods of depressive symptoms with suicidal thoughts began around age 15. She had never been diagnosed with or treated for any psychiatric condition, nor had she sought help for the symptoms until recently. She was able to function throughout high school and in college, with good academic achievement. After graduation from college, and beginning work for the first time, she felt unable to tolerate these symptoms and function in her employment in the medical field. Past medical history is negative. There is no history of substance abuse, and family history of psychiatric illness is unknown. She feels it is likely that she has relatives with psychiatric conditions, but due to stigma details are unknown. She has no history of trauma.

In PL evaluation, manic symptoms were explored. She denied manic or hypomanic episodes in the past, but she reported that her moods would fluctuate up and down in the course of the day many times. When asked about her baseline personality, she reported that she was an "always on

the go person." She was always very active, busy, and productive. After some reflection, she also reported that she would have 1 to 2 week periods of up-and-down moods, with the brief depressive days and suicidal impulsivity. And then she would have 2 to 3 weeks where she felt "normal like myself."

The PL diagnosis was recurrent mixed episodes, with possible cyclothymic temperament. The patient clearly does not have only "depression". The use of fluoxetine doubles the risk of suicidality in this age group, and that medication was discontinued. Low-dose lithium was recommended both for her mixed states and cyclothymia, as well as for direct suicidal benefit.

Case 2. Bipolar diagnosis or trauma?

A 21-year-old woman presented with a new diagnosis of bipolar disorder in the setting of a recent sexual trauma 2 months earlier. She had gone to the emergency room after the trauma, and had experienced anxiety and panic attacks in the week following it. She went back to the emergency room due to the latter symptoms, along with some suicidal ideation, which led to one-week psychiatric hospitalization.

In the psychiatric hospital, clinicians noted that the patient had a family history of bipolar illness in her maternal aunt and maternal grandmother. On history-taking from the patient as well as both of her parents, it was reported that the patient had not experienced past depressive episodes nor had she experienced past manic or hypomanic episodes. This denial was confirmed with multiple family members.

Until the recent event, she had never been treated with any psychotropic medications, nor had she ever received counseling. She had no prior psychiatric hospitalizations and no self-cutting or prior suicidality.

She and her family denied any prior physical or sexual abuse. Her medical history was normal; she took no medications and had no allergies.

She had many friends in college, and was sociable. She was sexually active, but interview with her and her family suggested that her sexual activity was within the normal range of her peers. She had prior sexual relationships which were not fleeting or inherently unstable, but lasted sometimes 6 months or longer.

In the psychiatric hospital, she was treated with lithium and risperidone. Upon discharge, she stopped risperidone. A few weeks later, her anxiety

symptoms had improved notably. She had avoidant behavior about the recent sexual trauma and was teary about it, but denied other depressive neurovegetative symptoms. She denied flashbacks or nightmares related to the trauma, but she reported being anxious when sleeping alone. She was still taking lithium 300 mg/d, reduced from higher doses due to cognitive side effects, but had not started psychotherapy. The family wanted to know if she had bipolar illness and what medication treatments were recommended.

On consultation, the diagnosis of bipolar illness was not confirmed, given the above history. It was recommended that lithium be stopped since she was not suicidal nor did she have any mood episodes currently or in the past. The bipolar genetics were noted, and the family was informed that if mood episodes should begin in the future, then the bipolar diagnosis may be valid at that time, and lithium treatment could be restarted.

Instead, the PL view was to recommend individual psychotherapy to help cope with the acute stress reaction of recent sexual trauma. The patient and family were informed that acute stress reactions to trauma occur in almost everyone, while post-traumatic stress disorder (PTSD) is defined as happening 6 months to a year after the traumatic episode. Further PTSD only occurs in about 10-20% of persons[1] who experience trauma. Thus, the importance of psychotherapy is to help cope with the natural acute stress reaction, as well as hopefully to decrease the likelihood of future PTSD. Further, if there are aspects of the history that are unclear, or mild manic symptoms that might be difficult to observe, ongoing psychotherapy may be a place to make such subtle diagnostic observations.

1. https://psycnet.apa.org/doiLanding?doi=10.1037/0003-066X.59.1.20

Case 3."PMDD" which isn't

This case came from one of our colleagues:

A 26 year-old female without prior psychiatric history presents for a consultation upon the recommendation of primary care. Both primary care and gynecology have diagnosed pre-menstrual dysphoric disorder (PMDD). In 2014, primary care prescribed Sarafem (fluoxetine) for several months, "but it didn't do anything." Primary care also recommended this consultation for an ADHD evaluation. The patient has taken a friend's ADHD medication (Adderall 5-10mg) and "it brings me up to par. It just really helps with the lows and the attention." The patient describes a long history, since teenage years, of alternating mood cycles. She only became aware of them in 2012 when she experienced several months of continuous depressive symptoms after a family death. She reports that about 14 days before menses she develops significant depressive symptoms, especially very low energy ("it just completely dives"), poor motivation ("don't even want to get out of bed"), no desire to socialize and very low mood. At the same time, attention and thinking are poor ("I feel like there is this film over my brain, a hard time thinking and articulating things"). In contrast, the other two weeks of the month (at menses and onward), she experiences the opposite: "I'm just motivated, doing a lot better. It's the way I should be feeling all month long." She reports being productive at work, bright and optimistic, "but I think my mood is usually optimistic." The patient reports chronic sleep impairment and racing thoughts since teenage years: "I have always been a night-owl... My brain is incredibly more active at night time. I have a hard time shutting my mind off in the evenings." There are periods where sleep is worse and she averages 6 hours at night, (1am-730am), but she still has good energy. She denies past manic episodes. In reference to

the 2 weeks of elevated mood, energy, and thinking, she denies these as above her baseline: “I feel like this is how I should be. I just feel more organized. I have more motivation to do the small things like working out or doing chores."

She recently had another consultation with a psychiatrist who agreed with the PMDD diagnosis but referred her back to her gynecologist. "He said there is nothing behaviorally he could do for me. He said what was happening was a chemical process and I should go back to gynecology." Past medical history is notable for past ovarian cysts s/p excision x 2 (emergency surgery after a rupture). She has taken several oral contraceptives but each caused various psychiatric side effects: "a few months where I felt depressed 24/7."

Family history is as follows: Maternal aunt: was "treated for some depression throughout her life." Father "is like me in a lot of ways, hyper focused sometimes and stays up late;" also a "procrastinator like me." Brother is diagnosed with ADHD and uses stimulants, "but I think he just uses it for a high stress job."

She had no behavioral or academic problems throughout schooling, with a high school GPA of 3.5. She was active with many hobbies including tennis, soccer, and softball. Mother has told patient that she has suspected patient was periodically depressed in high school.

She denies any physical symptoms associated with menses - no bowel changes, cramping, bloating, heavy bleeding, or headaches. Extensive laboratory testing for TSH, FSH, prolactin, and cortisol are all within normal limits.

During the consultation, her mental status examination was notable for: Hyperactivity (restless, fact and quick movements); pressured speech but interruptible; mood "pretty great!"; mildly euphoric affect - very animated, gregarious; and mild tangentiality requiring some redirection.

The colleague who sent this case had the following overall clinical impression:

The case reflects a long history of mood cycles, which likely have less to do with her menses than with bipolar illness. Pre-menstrual dysphoric disorder is unlikely here because of (1) severity of symptoms between pre- and post menses cycles (2) lack of any physiologic symptoms associated with menses (no bloating or cramping) (3) chronic symptoms of insomnia and racing thoughts (which have nothing to do with PMDD but are a frequent feature of untreated bipolar) (4) family history being suspicious for mood cycling, likely in father (5) lack of response to Prozac, and (6) oral contraceptives induced depression. Timing of cycles may not be as clear-cut around menses as the patient believes, but hormonal exacerbations are likely happening. There is no indication that ADHD is present.

Questions for PL:

(1) IS PMDD A VALID scientific construct? What about PMS?

(2) If this patient actually has underlying bipolar (type 2, rapid cycling?), what does the literature say about hormonal influences of mood cycles?

(3) What is the approach for medication management in this patient who disagrees that anything other than PMDD could be occurring?

(4) Is ADHD present?

PL commentary

The PL view is that PMDD may be a valid scientific construct, but we caution against the general process of adding the word "disorder" to a collection of symptoms and assuming that ipso facto it is valid. There certainly are premenstrual symptoms of mood/anxiety/hot flashes/bloating

and so on. These symptoms can be caused by other conditions - like manic-depressive illness - or they can occur by themselves as part of the normal process of menstruation. The key issue in our view is to differentiate those two circumstances. In other words, we need to apply the concept of diagnostic hierarchy: Does the patient have anything else that could cause premenstrual symptoms? (You could call "PMS" the presence of the symptoms; this doesn't answer the question of whether it is occurring by itself or caused by something else).

Mood cycles in bipolar illness often are triggered by stressors, not just psychosocial ones, but also biological ones, and hormonal changes around menstrual periods are common biological triggers of mood cycles in bipolar illness. Since they occur monthly, PMS-related mood episodes are rapid-cycling by definition (> 4 mood episodes yearly).

Again applying the diagnostic hierarchy concept, ADD isn't present since distractibility is a consequence of the mood episodes, not a separate "disorder," just as "fever disorder" isn't present during pneumonia. Benefit with Adderall isn't diagnostic of ADD because attention improves in everyone with amphetamines. This would be like saying decreased anxiety with benzodiazepines, which occurs in all human beings, means that everyone has an "anxiety disorder."

Regarding the diagnosis of bipolar illness, the question is whether her 2 non-depressed weeks per month represent normal happiness or hypomanic episodes. One hint is that hypomania is recurrent, happiness is not (a favorite quote of Dr Hagop Akiskal). 6 hours nightly of sleep with good energy is biologically abnormal (sleep studies indicate that about 9 hours of sleep is the biological norm, although culturally most of us don't get it). This is decreased need for sleep, a manic symptom; it is not normal. This symptom, along with increased activities and racing thoughts support the higher probability of hypomania rather than normal happi-

ness. The biology of this condition is supported further by her father's apparent similar symptoms.

If we can agree on the bipolar diagnosis, with a rapid cycling course and type II subtype, then the PL recommendation is straightforward, like any other person with bipolar illness: Use mood stabilizers. Since this is a rapid-cycling course, multiple mood stabilizers will likely be needed, and lamotrigine in particular has been shown to be ineffective in rapid-cycling. Since many patients are concerned about weight gain, PL might recommend carbamazepine first, because it doesn't have weight gain. If a second agent is needed, lithium at low doses may be sufficient. Dopamine blockers don't combine well with carbamazepine because the latter reduces blood levels of the former, rendering them less effective. Another approach would be to start with lamotrigine, see how much benefit is gained, and then add lithium or dopamine blockers which don't have weight gain, like aripiprazole or ziprasidone or lurasidone, at low doses preferably.

How could you convince this person to take this approach? Some people are beyond convincing. But here are some strategies: Tell her not to search this matter randomly on the Internet. The PL approach is not mainstream and if she goes by majority vote, she'll be directed against the recommendations made here. Recommend the PL website for a rationale for these ideas. Talk to the patient about the concept of a diagnostic hierarchy, using unimpeachable medical examples such as pneumonia and fever. Make it a pragmatic decision: If it doesn't work, she can see someone else to take other approaches. For many people, this rationale can be persuasive.

Case 4. Can bipolar illness go away?

A 45-year-old man presented with two past manic episodes, one of which led to hospitalization, as documented in discharge summaries which provided evidence for manic symptoms in those episodes as follows: 3 weeks of markedly increased energy, less sleep, rapid speech, grandiose thoughts that he would be a famous person in the next year (while a graduate student), and agitation and aggression leading his friends to call the police due to fear that he would get into fights and get hurt.

For the following 12 years, the patient was untreated and didn't have another manic episode. He never experienced depressive episodes. In application for work, he sought consultations from his psychotherapist and from two different psychiatrists. They all gave the opinion that the patient didn't have bipolar disorder since he hadn't experienced any further mood episodes despite absence of treatment.

PL's view is that these conclusions aren't valid scientifically. Bipolar illness is a historical diagnosis. It's defined as having a manic episode - at any point in life. In fact, DSM doesn't capture the range of manic-depressive conditions as PL has described previously. This patient is not "bi"-polar since he only has had manic episodes, not depressive episodes. But he doesn't have "unipolar" depression either, since he never has been depressed. Instead he has unipolar mania, a pre-DSM-III diagnosis ignored since 1980.

The concept of manic-depressive illness involved *recurrent* mood episodes, of either kind, depressive or manic. Recurrence was the central feature. Thus, if someone only had a single depressive episode or a single

manic episode, they didn't have manic-depressive illness. In fact, dating back to Kraepelin, single depressive episodes were identified, but there was no such thing as a single manic episode. If a manic episode occurred, future recurrent episodes occurred. That Kraepelinian concept has been confirmed by repeated studies over a century. For instance, a classic study[1] from the 1990s found that after a first manic episode, 90% of patients would have a second one within 5 years.

So why has this patient not had any other manic or other mood episodes for 12 years? This is uncommon, but it doesn't mean he never had those manic episodes. In other words, it doesn't mean that he doesn't have the diagnosis of unipolar mania. Another aspect to the case that PL considers important is whether or not the patient has any affective temperament. He had evidence for hyperthymia (generally high energy, low need for sleep, high activity levels, sociability, extraversion). PL has observed that patients with hyperthymic temperament often go for 40,50, 60 years before having their first full depressive or manic episode. The PL editor has consulted on a patient with life-long hyperthymia who experienced his first manic episode at age 84 (with negative medical work-up)!

In short, not only can 12 years pass without an episode, so can 80 years. So too one can have a heart attack, and not have another one, even if untreated, for decades. The course of an illness can be variable, but it doesn't change the diagnosis if the basic definition is met. If a manic episode ever occurs, then manic-depressive illness (or bipolar disorder, if you prefer) is the diagnosis, even if the future course is benign.

"The course of an illness can be variable, but it doesn't change the diagnosis if the basic definition is met."

1. http://jamanetwork.com/journals/jamapsychiatry/article-abstract/495169

Case 5. Childhood ADD worsened by stimulants

A 10 year-old male is brought by his mother for consultation. He has been treated with Focalin, Concerta, Adderall, methylphenidate, and Dexedrine. He also has received aripiprazole and olanzapine, added to the above agents. His main problems involved not being able to pay attention in school, and being aggressive and agitated toward other children. In two years of treatment, he had not improved, and was forced to change schools multiple times. At one point, while at a restaurant with his parents, he bolted out the door and tried to run down the street. On other occasions, he tried to open the car door on the highway. His parents were concerned about these impulsive behaviors, which had not improved with multiple amphetamines.

He was markedly anxious and had marked insomnia, but his family denied increased or a high level of energy. They also denied any observable depressive symptoms such as suicidality or noticeable sadness or anhedonia. He was adopted and biological family history was unknown. He lived in an intact and loving family with two parents and an older adopted sister, who had no psychiatric problems and was very successful in school and social life.

He was observed to be very short for his age, and very thin.

On mental status examination, he was polite but played mostly with a video game, answering questions briefly. He was frustrated about his poor social and academic skills and how it harmed his friendships with his peers. He expressed this frustration appropriately and rationally dur-

ing the interview. He said he wanted to come off his current medications of methylphenidate 60 mg/d and aripiprazole 5 mg/d.

PL diagnosis and approach

THE PL DIAGNOSIS WAS that anxiety symptoms were present, which could explain all of his attentional impairment, which could further explain his school-related agitation. The worsened impulsivity was attributed to the harmful manic-like effects of amphetamines. The recommendation made was to stop both methylphenidate and aripiprazole. Since the latter has some dopamine agonist effects, it could be contributing to the worsening impulsivity. Two treatment options were given for symptomatic purposes: very low dose SRI for anxiety, or low dose risperidone for pure anti-dopamine effects to target impulsivity. The diagnosis was unknown since family history was unknown and because of his young age. It is typical for anxiety symptoms to be the earliest manifestation of other psychopathology, such as later depressive or bipolar illness.

The PL approach in children is to use medications minimally for symptoms, provide as many behavioral interventions as possible at school and home to improve function, and then to observe the evolution of the illness until a more definitive diagnosis could be made.

Within weeks of stopping methylphenidate, his parents reported that he was much calmer, less anxious, and less agitated. He began to eat more and was putting on needed weight. A few months later, he became somewhat anxious, and the family chose to start SRI treatment. The PL recommendation was 10 mg fluoxetine given twice weekly. This is because fluoxetine has a very long half life of one week and thus it can be dosed weekly. This approach would give the lowest amount of SRI feasible, and also the child would not see himself as being medicated daily. Within weeks, his anxiety resolved and his behavior improved notably.

At one year follow-up, taking only fluoxetine 10 mg 1-2 times weekly and no other medications, he had grown a number of inches and was closer in stature to his peers, which markedly improved his self-esteem. He had gained weight and was normal in his body mass index. He was doing very well in a private school with sufficient attention to providing behavioral assistance for executive dysfunction. His peer and family relationships had improved markedly.

Case 6. A messy case

A 48-year-old woman presented in referral after failing to respond to many different antidepressants and amphetamines and benzodiazepines. She had been diagnosed with major depressive disorder (MDD), adult attention deficit disorder (ADD), and generalized anxiety disorder (GAD). She had been treated for about 20 years with one serotonin reuptake inhibitor (SRI) or another. She had some improvement at times, but then she would have anxiety and depressive symptoms again. She was functional, able to work, even somewhat successful in her profession, but with great struggle. She felt that she could achieve even more if she didn't have so much anxiety and depression.

In prior evaluations, doctors had noticed some mood lability, but no definable hypomanic or manic episodes. She had refused to consider lithium due to its weight gain and stigma.

She had marked inattention, which led to the diagnosis of adult ADD and long-term treatment with a range of amphetamines, which helped her function at work. Anxiety was also treated with long-term clonazepam, which had mild benefit.

She also had been diagnosed with narcolepsy because she had periods where she would go for one week with much less sleep than usual, but then would fall asleep suddenly during the daytime. She denied manic symptoms during those one-week periods. She had severe insomnia most of the time, and had taken many sedating medications, with little benefit.

In her family history, she reported a lot of anxiety and depression but denied bipolar illness or schizophrenia.

She had occasional suicidal ideation (SI) but never had made an attempt. On evaluation, she was treated with oxcarbazepine 600 mg/d, fluoxetine 5 mg/d, Adderall (amphetamine/dextroamphetamine mixture) 20 mg/d, clonazepam 2 mg/d, and mirtazapine 10 mg at night.

On evaluation, the patient was very anxious, agitated, nervous, labile, worried, and had a number of depressive neurovegetative symptoms (low energy, interest, sad mood, poor concentration, and occasional SI). These symptoms had been present for months in a worsened state, and were present at least to a mild degree most of the time in the past year.

The entire history was based on the patient's self-report.

The PL consultant made the following observations: The patient's self-report is not sufficient for a dependable denial of past hypomanic or manic episodes, due to the problem of lack of insight, as described in the last PL issue. Thus, there was doubt whether the patient indeed did not have bipolar illness. It could be that what was called narcolepsy reflected cyclic manic/hypomanic episodes, which the patient couldn't describe in DSM-level detail. The recurrent decreased need for sleep that was described only occurs in manic/hypomanic episodes, not in narcolepsy, which is not a condition with weekly cyclic episodes, separated by periods of absence of narcolepsy symptoms.

The PL consultant raised the idea that the patient has "manic" symptoms, defined in the pre-DSM manner as "psychomotor excitation." Clearly, this patient is highly psychomotor excited, with marked agitation and lability, at the same time as she has clinical depression. This is the classic presentation for "mixed depression" as defined by Koukopoulos. As discussed on the PL website[1], mixed depression is treated by stopping all antidepressants and amphetamines, and using dopamine blockers and/or second messenger modifiers (mood stabilizers).

1. http://www.psychiatryletter.com/Mixeddepressionspectrum.html

"...the patient has 'manic' symptoms, defined in the pre-DSM manner as 'psychomotor excitation'..."

In other words, the PL consultant argued that the diagnoses of MDD, GAD, and ADD had been tried for 20 years, and had failed. It was time to have a different working diagnosis, and then to test it. The most likely working diagnosis, on the rationale given above, was "manic-depressive illness," meaning recurrent mixed depressive episodes. Using DSM terminology, the diagnosis would still be MDD. Using non-DSM terminology, it would be manic-depressive illness.

In this case, the implication of that approach to mixed depression would be to taper the patient off fluoxetine, Adderall and mirtazapine. Clonazepam is neutral in its effect, probably not helping or hurting at this time.

Oxcarbazepine would be stopped and replaced with an effective second messenger modifier, on the grounds that oxcarbazepine likely is ineffective as described in this issue of PL. Such scientific evidence of inefficacy is supported by the patient's limited benefit with the agent.

As the patient is taken off the three antidepressants/amphetamines, the PL consultant recommended adding a dopamine blocker like aripiprazole or ziprasidone or asenapine or lurasidone (all do not have metabolic syndrome or cardiac risks or weight gain). If the patient improved, then the question of lithium or valproate could be considered for long-term of prevention of mixed states.

"... the diagnoses of MDD, GAD, and ADD had been tried for 20 years, and had failed...."

Another option would be to add low-dose lithium or valproate at present, holding off on the dopamine blockers. In the opinion of the PL consultant low dose valproate (about 500-750 mg/d) might be the most

effective single treatment, with lower dose limiting weight gain. "Therapeutic" blood levels are irrelevant because we are not treating mania.

All these recommendations are made not because the patient has "bipolar" illness, as a DSM term, but because the patient has mixed depressive states. As noted on the PL website[2], mixed states are equally common in "unipolar" and "bipolar" illness, both of which can be seen as variations on the same disease: manic-depressive illness. This perspective is the original Kraepelinian view.

There was some resistance on the part of the treating clinicians to the PL consultation. It was argued that a very rapid diagnosis of bipolar illness had been made, and that the PL consultant wanted to treat everyone with mood stabilizers.

The PL consultant responded that bipolar illness was not being diagnosed, but rather manic-depressive illness, which is a larger and broader construct, as discussed above and in the PL website.

Further, the PL consultant suggested that there are more drugs in psychopharmacology than only antidepressants and amphetamines. This patient had been treated for two decades with only those two main classes of drugs (plus benzodiazepines). Why not try the two main drug classes - dopamine blockers and second messenger modifiers- that had not been used, at least on pragmatic grounds? While doing so, it makes sense not to just add one drug after another, but to stop some of the drug classes that had not helped much, especially since those agents can worsen some of her symptoms (amphetamines worsen anxiety, SRIs cause mania/agitation).

This case is not presented with follow-up, but it is described here so that PL readers can think themselves about such complex mixtures of symptoms. It also is presented as a common scenario where patients are not

2. http://www.psychiatryletter.com/Mixeddepressionspectrum.html

exposed to standard second messenger modifiers, but only receive disproven ones, like oxcarbazepine. The case also highlights importance of stopping symptomatic treatments, like amphetamines, in patients with marked anxiety and depressive symptoms, which cause inattention.

Case 7. Not ADD, not chronic fatigue, not "depression"

A 23 year-old female seeks consultation for unremitting depression and ADD. She had been first diagnosed at age 15 with chronic fatigue syndrome. A medical workup for possible causes of exhaustion was negative. Eventually her doctors decided to treat her with amphetamine stimulants to give her energy. Since age 16, she has taken one amphetamine or another, beginning with methylphenidate, later Concerta, and later Adderall.

In the past year, she began to see psychiatrists, who changed her diagnosis from chronic fatigue syndrome to major depressive disorder. They continued Adderall and added various serotonin reuptake inhibitors (duloxetine, fluoxetine, sertraline) without success. She was changed eventually to bupropion.

On evaluation, she was taking Adderall 20 mg twice daily plus bupropion SR 150 mg twice daily.

Besides exhaustion, her parents report that she has marked insomnia and notable cognitive impairment. Her sleep is quite poor: she stays up very late, and has multiple awakenings in the night, followed by tiredness during the day. Her cognition is poor also, with very impaired working and verbal and short term memory. She has been slowed down in her college studies to the point that despite 5 years of college, she has only completed her sophomore year. She has a great deal of trouble organizing herself for her college work and paying attention in class and in memorizing material for tests.

Adderall gives her "30 minutes glimpses of normality". After she takes the medication, she reports that she feels "like myself" for about half an hour, with improved concentration and energy and mood, but then she goes back into her usual depressed, low energy, poor concentration state.

She has these depressive symptoms continually, but 2-3 times per week, she has about 1-2 hours of spontaneous high energy states: "I feel elated, happy, like I can convince anyone to do anything. I try to do things, but it doesn't last long enough for me to do anything. My thoughts go fast, I talk a lot, I feel super smart briefly, and then I'm back to my usual unhappy slowed down state."

She reports repeated suicidal thoughts and wishes she was dead, but she has not tried to harm herself.

She and her family deny past manic or hypomanic episodes lasting 4 days or longer.

One psychiatrist suggested that she had type II bipolar illness, but he continued Adderall and added lithium 900 mg/d immediately. She stopped lithium after two days due to heart palpitations.

Family history provides evidence for a paternal aunt with severe depression that required ECT. All other illness is denied.

Medical history is otherwise normal and she has no drug allergies, nor does she abuse alcohol or drugs. She has no trauma history. She has had no psychiatric hospitalizations or suicide attempts or self-harm or dissociative or psychotic states, and no eating disorder symptoms.

PL diagnosis and recommendation

THE PL DIAGNOSIS IS that she is experiencing current mixed depressive states, as described in the PL February 2015 issue[1]. The broader diag-

nosis is manic-depressive illness, or one might use the term bipolar spectrum illness[2]. These diagnoses reflect brief manic states that occur as part of recurrent depressive episodes. The illness is not pure depression, since manic symptoms are present, nor does it represent classic bipolar illness, since full manic or hypomanic episodes are not present. Hence the concept of bipolar spectrum illness can be used to reflect being in the middle of the spectrum between pure depression and full manic or hypomanic episodes.

The PL recommendation was to taper off Adderall and bupropion and to resume lithium again, this time in slow titration and in the absence of any antidepressants/amphetamines. This recommendation is explained below:

Readers should keep in mind that all amphetamines are antidepressants. They were introduced as the first class of antidepressants in the 1930s. Thus, like all antidepressants, they can have negative effects in bipolar illness of causing/worsening mania, or causing/worsening long-term rapid-cycling. In the case of mixed depression, as discussed on here[3] and in the February 2015 issue[4], antidepressants seem to worsen mixed states, thus causing more depressive and manic symptoms. They especially seem to worsen suicidality and impulsivity. In an analysis of mixed depression as described by Koukopoulos, antidepressants caused three times more suicide attempts in person with mixed depression when compared with those treated without antidepressants.

Further, as mood-destabilizing agents, amphetamines and antidepressants counteract the benefits of mood stabilizers[5], like lithium. Thus, it

1. http://www.psychiatryletter.com/psychopathology-mixed-depression.html

2. http://www.psychiatryletter.com/MDIspectrum.html

3. http://www.psychiatryletter.com/Mixeddepressionspectrum.html

4. http://www.psychiatryletter.com/psychopathology-mixed-depression.html

5. http://www.psychiatryletter.com/mood-stabilizers-bipolar-spectrum.html

is not enough to just add lithium. Adderall and bupropion need to be stopped also. Further, readers will recall that bupropion is an amphetamine in its pharmacological structure[6] - all the more reason to stop it.

This patient's apparent "adult ADD" had not improved with amphetamines because it was driven by her mixed depression. Until the mixed depression improves, the "ADD" will not improve. Since amphetamines worsen mixed depression, cognitive ADD-like symptoms persist.

Lithium is the best agent to choose partly because of its direct suicide prevention benefit, given that this patient has clear suicidal ideation and notable risk for suicide.

Specific PL recommendations were as follows:

- Reduce Adderall to 20 mg daily for 2 weeks, then 20 mg every other day for 2 weeks, then stopped.
- Reduce bupropion to 150 mg daily for 2 weeks, then stopped.
- At the same time, begin lithium at 300 mg at night for 1 week, then 600 mg at night for one week, then 900 mg at night, seeking a level close to 0.8 mmol/L.

The PL expectation would be that the patient would get worse before getting better, with amphetamine withdrawal leading to worsened energy and concentration and possible clinical depression. This could be the course for a few months, but then the patient would be expected to improve gradually on lithium alone, possibly with later combination with dopamine blockers and/or other mood-stabilizing anticonvulsants such as lamotrigine.

6. https://www.psychiatryletter.com/drug-bupropion-jan-2015.html

Case 8. A first depressive episode at age 18

An 18-year-old male has a first depressive episode. For the last two months, he reports decreased interest, energy, concentration, and appetite. Two weeks ago, his parents took him to his primary care doctor, who diagnosed depression, and began treatment with fluoxetine. The patient had no prior psychological problems or treatment, and has done quite well in school. A few days after starting fluoxetine, the patient reported some suicidal ideation, but denied any intent or plan. He also admitted to drinking some alcohol with friends. He has no other medical problems, no allergies, and is taking no other medications. There is no history of trauma, and he was raised in an intact and supportive family. He has multiple family members with depression, and one aunt diagnosed and treated for bipolar illness.

PL consultation was obtained. The observation was made that the course of illness and genetics of this case are more consistent with bipolar illness than major depressive disorder (MDD). The occurrence of suicidal ideation after treatment with fluoxetine was noted and a causal relationship implied. It was observed (as discussed on the PL website[1]) that the whole concept of MDD was associated with a lack of bipolar genetics and an age of onset around 30, as opposed to bipolar illness which began around age 19 and had bipolar genetics. The concern was raised that this depression may be the first episode of bipolar illness (with future mania), or at least cannot be the first depressive episode of MDD, given bipolar genetics and course of illness. The PL recommendation was to discontinue fluoxetine and begin lithium.

1. https://www.psychiatryletter.com/MDIspectrum.html

The patient saw a psychiatric nurse practitioner who concurred with the diagnostic and historical assessment, but concluded that lithium was a "third line" treatment for more severe illness than this patient possesses. In contrast, fluoxetine was a less intensive and more conservative treatment. Fluoxetine treatment was continued, with a plan to consider lithium later.

The PL perspective is that fluoxetine is not a more conservative treatment than lithium in this case. Fluoxetine increases suicidal ideation and suicide attempts by about 70%, whereas lithium reduces completed suicides by about 90%, as discussed in the April 2015 PL issue[2]. Thus lithium is a more conservative treatment than fluoxetine from the perspective of suicide risk. Since this patient has suicidality, this issue is important. Further, the increased risk of suicidality with fluoxetine specifically occurs in patients in this young adult age group. Finally, the bipolar genetics of this patient raises the possibility that the patient may have bipolar illness, or at least does not have straightforward "MDD". Lithium is proven effective for both unipolar depression and bipolar illness, and is the only drug proven to reduce suicide risk. The psychiatric nurse practitioner's concern may have had to do with the perception that there are many more side effects with lithium than with fluoxetine, especially medical risks like kidney impairment. But, as discussed previously, lithium's kidney risk occurs in a 20-year time frame[3], and is irrelevant to treatment for an acute depressive episode. Also, even though lithium has a long list of side effects, most patients don't experience any of them, and they are dose related. Fluoxetine has its own list of concerning side effects as well, besides suicidality (which is bad enough), including severe sexual dysfunction and serious long-term serotonin withdrawal syndrome risk.

2. https://www.psychiatryletter.com/april-2015-PL-entrance.html

3. http://www.ncbi.nlm.nih.gov/pubmed/4003100

Case 9. Depression in heart disease

A 65 year-old man with coronary artery disease s/p bypass grafts 3 years ago presents with marked depression along with new-onset nonspecific homicidal ideation. He had been taking SRIs for years, most recently paroxetine 40 mg/d, which had been stopped three months earlier and switched to bupropion. His depressive periods had begun 30 years previously, and responded partially to SRIs, but had worsened in the past three years in association with worsening heart disease. He and his wife deny past manic/hypomanic episodes, and he denied any known psychiatric illness in first or second degree relatives. He had long standing diabetes since his early twenties, but not hypertension.

PL recommendation

THE PL RECOMMENDATION was to begin sertraline in place of bupropion, since the former is more proven safe in cardiovascular disease than the latter. Further, the patient's new and unusual homicidal ideas likely reflect serotonin withdrawal syndrome since stopping paroxetine abruptly three months earlier. PL also recommends brain MRI to assess possible white matter infarcts, associated with diabetes, which may explain recent worsening of unipolar depressive illness.

The prognosis of the patient's depressive illness is not good, but at least sertraline will be safer than other options and will mitigate serotonin withdrawal symptoms.

Case 10. "Narcissistic" personality that isn't

A 45-year-old male is diagnosed with narcissistic personality disorder (NPD) comorbid with generalized anxiety disorder (GAD) and major depressive disorder (MDD). He has been treated with long-term psychodynamic psychotherapy on multiple occasions for 6 months to two years at a time. He has taken escitalopram 20 mg/d for 10 years. Sometimes, he has brief periods of depression lasting a few weeks at a time.

He has occasional suicidal ideation for the past 10 years. He has abused alcohol in the past, but has been sober for 5 years. He has never been hospitalized, overdosed, nor engaged in cutting behavior. His first cousin was diagnosed with bipolar disorder and did well on lithium. He was raised by an intact supportive family, became a lawyer, divorced twice, now lives alone, and never had childhood trauma.

He was seen as narcissistic because he has very high self-confidence, generally thinks he is smarter than others, and devalued his ex-wives. When asked about his failed marriages, he says: "They didn't appreciate me enough." At work, colleagues see him as arrogant, and although he is productive, interpersonal tensions and disrespect for authority have limited his promotion in a corporate law firm.

On evaluation, when asked about his energy, sleep, mood, and activities, he reports constant mood swings, on an hourly basis, sometimes very happy for hours and sometimes irritable and down for hours. He usually only needs 4 hours of sleep nightly, and has a high energy and activity level compared to peers, and a very high libido all the time. He reports

feeling anxious and having "nervous energy" most of the time. He is an active rock climber, bikes 20 miles each morning before going to work, and sees himself as a "workaholic."

The PL diagnosis and clinical impression

The PL diagnosis is cyclothymic temperament. He also is high on the personality trait of neuroticism. The constant shifting his moods, with frequent manic symptoms, was misinterpreted as "narcissism" because the grandiosity of manic symptoms was interpreted in the psychoanalytic paradigm of narcissism, within the DSM categorization of personality disorders.

The patient was treated with low dose Depakote, 250 mg/d for 1 month, then increased to 500 mg/d. Cyclothymic mood symptoms improved moderately, including inflated self-esteem as part of the manic component. His co-workers noticed that he seemed more responsive to interpersonal cues, interpreted as being less "arrogant." His libido and energy was lower, but still higher than most people. He remained productive, but had improved interpersonal relations at work.

The PL Bottom Line

- Manic symptoms of inflated self-esteem were misdiagnosed as narcissistic personality disorder.
- Low dose divalproex was more effective than long-term psychodynamic psychotherapy.

Clinical Tip

Don't diagnose borderline personality in the midst of a depressive episode. Don't diagnose narcissistic personality if someone has manic symptoms. There are many more persons with personality "disorders" when they are in mood states than not.

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