

Patient Management Exercise

CHILD AND ADOLESCENT PSYCHIATRY:

LIFE CYCLE AND FAMILY

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This exercise is designed to test your comprehension of material presented in this issue of FOCUS as well as your ability to evaluate, diagnose, and manage clinical problems. Answer the questions below, to the best of your ability, on the information provided, making your decisions as you would with a real-life patient.

Questions are presented at “consideration points” that follow a section that gives information about the case. One or more choices may be correct for each question; make your choices on the basis of your clinical knowledge and the history provided. Read all of the options for each question before making any selections. You are given points on a graded scale for the best possible answer(s), and points are deducted for answers that would result in a poor outcome or delay your arriving at the right answer. Answers that have little or no impact receive zero points. At the end of the exercise, you will add up your points to obtain a total score.

CASE VIGNETTE

Samantha is a 29-year-old Caucasian female who came to see you with concerns about depression and dementia risk.

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When you inquired as to her chief complaint at the initial assessment, she reported that she has struggled with depressed mood for the past three years, but was now seeking care because she had read about research linking depression in adulthood to the later development of Alzheimer's dementia, a condition her mother was experiencing. She was enrolled in a Ph.D. program in political science at a nearby university, having completed her undergraduate degree in history at a top-flight college. She reported that she began to feel depressed about three years ago, after she found that her fiancé was romantically involved with another woman, and he broke off their engagement. When she first learned of this, she initially had reacted with great anger and volatility (“I was out of control”), and threw all the pictures she had of the ex-fiancé out the window of her apartment, into a dumpster below. She reported that this was rapidly followed by symptoms of sadness; fatigue; sleep disturbance with spending 12-14 hours/day in bed with interrupted sleep; ruminative thoughts around her ex-fiancé's affair with a mixture of anger, guilt, and dejection; increased appetite with 30 lbs of weight gain. She reported no periods without symptoms since this began after the break-up.

CONSIDERATION POINT A

At this point in your evaluation, the diagnosis which seems most appropriate for this patient would be

- A.1—— Major Depressive Disorder, single episode
- A.2—— Adjustment Disorder, related to learning of her ex-fiancé's infidelity
- A.3—— Substance induced mood disorder
- A.4—— Bipolar disorder, depressed phase

VIGNETTE CONTINUES

As you inquired more about the end of her engagement to her ex-fiancé, she reported that she engaged in brief counseling through student psychological services at her school, and was able to gain a better perspective on the events. The couple's mutual friends had rallied around her, and expressed a consensus that her ex-fiancé was "a jerk and a loser" for having cheated on her and breaking off the engagement. While all this had helped her "try to put this in the past," the feelings of pervasive sadness had continued to intensify over time. She reported that she had continued to find comfort and support with her circle of friends before, during, and after the break-up, and that she had actually tried dating six months ago, but couldn't find anyone suitable for a long-term relationship.

She denied any prior periods in which she experienced manic or hypomanic symptoms, obsessive thoughts or compulsive behaviors, hallucinatory experiences, or delusional thoughts.

As you inquired more about her early life history, you learn that the patient's childhood recollections of her mother revolve around her mother being "in bed, crying a lot, and being 'out of it' a bit," which in hindsight may have been depressive episodes. The patient was largely left to her own to set her schedule, and frequently would stay up late if she was reading something riveting. She did well academically, but did relate an instance in which she had to go to the junior high school principal because "I was too enthusiastic about a project and the teacher freaked out." She is the elder of two sisters; her sibling has had issues with cocaine use, but, as of this evaluation visit, the sister has been abstinent for nine months after spending time in a residential care facility in the midwest.

In other aspects of family history, the patient's 62-year-old mother has a history suggestive of past depressive episodes and more recently a diagnosis of Alzheimer's disease. The neurodegenerative disorder

came to light after she "got lost" driving in town, and called "911" in a panicky state; she was evaluated in an emergency room and then by a geriatric psychiatrist as an outpatient. Reportedly she had "some sort of radioactive brain scan" that showed "a 'classic' pattern for Alzheimer's." Her maternal grandparents died in a plane accident before the patient was born, and she knows little of their medical history; her paternal grandmother and grandfather are both in their 80s and are described as alive, well, and living independently in their own home.

In reviewing her medical history, the patient denied having any major medical conditions and reported one instance of a broken arm as a child when she fell from a tree she had been climbing. When you evaluated her, she reported taking no medications and that she had no drug allergies.

The patient reported never smoking tobacco or using drugs of abuse. She reported occasional consumption of wine, estimated as two or three glasses of wine on a weekend over dinner with friends.

On exam, she was pleasant and generally cooperative with the interview, casually attired in sweatpants, and wearing a baseball cap to conceal some what unkempt hair. There was mild psychomotor slowing noted. Eye contact was adequate. Speech was of slowed rate and volume, with slightly monotonous prosody. Affect was constricted, stable, and sad, with Veraguth's folds and Darwin's "omega sign." (1) Mood was endorsed as being "unhappy" most of the time. Thought process was linear and coherent. Thought content was without present or past suicidal or homicidal ideation or intent, delusions or hallucinations. Cognitively she was awake, alert, and oriented to self, place, date, and circumstances. Memory registration was intact with 3/3 stimuli, and recall after delay was 2/3 items spontaneously but with considerable mental effort. Presidents were recalled accurately for the past five office-holders. Similarities were abstract. Insight was good, in that she recognized being depressed. Judgment currently was good, as evidenced by her seeking care voluntarily.

CONSIDERATION POINT B

In light of the additional information gained in your evaluation, the diagnosis which seems most appropriate for this patient would be

- B.1—— Major Depressive Disorder, single episode
- B.2—— Adjustment Disorder, related to learning of her fiancé's infidelity
- B.3—— Substance induced mood disorder
- B.4—— Bipolar disorder, depressed phase

VIGNETTE CONTINUES

After discussion of the options for treatment for her depressive episode, the patient accepted your recommendation for treatment with an antidepressant agent. She voiced particular concerns about additional weight gain and sexual dysfunction, as “deal breaker” side effects. Although this would be her first time with a biological treatment for a psychiatric disorder, she has read a lot online and had some discussions with friends.

CONSIDERATION POINT C

In light of this discussion, which treatment recommendation(s) is/are both evidence-based and respectful of her expressed preferences and concerns about side effects?

- C.1—— Paroxetine
- C.2—— Mirtazepine
- C.3—— Bupropion
- C.4—— Transcranial Magnetic Stimulation (rTMS)

VIGNETTE CONTINUES

After you described the potential risks, anticipated benefits, and likely side effects of treatment options, the patient preferred bupropion, and so you initiated a treatment trial with that agent. Over the following 12 weeks, her mood improved along with her sleep, energy, and ruminations.

She continued on this medication for another four months under your direction, when she reported at a follow-up visit that her mental energy and motivation were not as good as they initially had been after starting treatment. While she expressed eagerness to try to address these symptoms with medication adjustments, she voiced concerns about acceptability of the side effects of several options you initially recommended as evidence-based practices (e.g. sexual dysfunction with SSRIs, metabolic syndrome and tardive dyskinesia with antipsychotic agents). She did not endorse anxiety or insomnia, but rather sought something more likely to be experienced as activating than sedating.

CONSIDERATION POINT D

Given these changes in clinical situation and the patient’s preferences, which medication(s) would you consider (for use within the labeled indications or for off-label use)?

- D.1—— Methylphenidate
- D.2—— Buspirone
- D.3—— Triiodothyronine
- D.4—— Electroconvulsive therapy

VIGNETTE CONCLUDES

The patient pointedly expressed her wish to try the use of a psychostimulant agent, like methylphenidate, because a cousin on her mother’s side who also struggled with depression had benefitted from the addition of that drug to an antidepressant.

After discussing the limitations of the research literature on psychostimulants as augmentation agents, and the risk-benefit profile of this off-label use of a medication, you and she agreed to a trial of methylphenidate.

She returned after two weeks, reporting that not only was her mental focus was better, but that she felt “calmer” and “more peaceful” internally. She denied any insomnia, anxiety, restlessness, or agitation. In revisiting her past history, she reported additional detail about how in college, she had selected classes that offered take-home tests without time constraints because “I never did all that well on timed tests.” When asked to expand on her remarks, she reported that, even as a child, she had “followed her bliss” as her mother put it, and was raised in a fairly undisciplined environment in which she would “multitask” on a number of different projects simultaneously, flitting from one to another “whenever I got bored.” She reported that procrastination was a chronic problem beginning in elementary school. She also reported sometimes she “forgot” to do her homework at home, but would “power through it” during study-hall breaks or before classes.

While this strategy had worked sufficiently well for her through high school, she “hit a wall” in college and had abandoned her pursuit of premed studies “when I couldn’t get through the whole test in time.” She also loved the social sciences and history, and so transitioned easily to classes where she could write essays “on my own timetable.” Because her grades had never flagged, she had never been referred for evaluation for attention deficit hyperactivity disorder (ADHD) at college.

This discussion brought to light a history consistent with ADHD starting in childhood and persisting to the present, with specific symptoms of a history of difficulty sustaining attention, difficulty organizing tasks, making careless mistakes in schoolwork, failing to finish schoolwork, reluctance to engage in tasks that require sustained mental effort, being easily distracted, and being forgetful in daily activities.

With additional titration of methylphenidate, the patient was able to complete her dissertation and its defense after being “stalled” for several years. She had also begun dating seriously.

ANSWERS: SCORING, RELATIVE WEIGHTS, AND COMMENTS

CONSIDERATION POINT A

- A.1—— +3 *Major Depressive Disorder, single episode.* The patient has endorsed symptoms consistent with the DSM criteria for major depressive disorder (2).
- A.2—— +1 *Bipolar Disorder, depressed phase.* While current depressive symptoms can be part of the presentation of bipolar disorder, the patient's history does not contain elements of manic, or hypomanic episodes. Still, issues around accurate recall of subtle elevated mood are difficult to exclude without collateral history, so it may be worthwhile continue to consider this possibility (2).
- A.3—— 0 *Adjustment Disorder, related to relationship with the ex-fiancé.* This patient, like many, has experienced a set of stressful circumstances following the ending of a significant relationship, but after persisting for three years, major depression is probably a more parsimonious characterization (2).
- A.4—— +1 *Substance induced mood disorder.* Overt or covert substance use can lead to mood problems, either in intoxicated or withdrawal states (e.g. psychostimulants, alcohol), and there is a drug use problem in the family history. While the patient denied any personal history of substance misuse, there is a report of cocaine abuse in her sister, so it may be premature to rule this out (2).

CONSIDERATION POINT B

- B.1—— +3 *Major Depressive Disorder, single episode.* The symptoms are fully compatible with a prolonged episode of MDD (2).

- B.2—— 0 *Adjustment Disorder, related to relationship with the ex-fiancé.* With the additional data, major depression appears to be a more parsimonious characterization (2).
- B.3—— 0 *Substance induced mood disorder.* There continues to be no historical data consistent with substance induced disorders (2).
- B.4—— 0 *Bipolar Disorder, depressed phase.* The patient's history does not contain elements of depressive, manic, or hypomanic episodes characteristic of DSM criteria for a primary mood disorder (2).

CONSIDERATION POINT C

- C.1—— -2 *Paroxetine.* Though there is clear evidence to support efficacy of this agent, weight gain is common issue with its use (3), and so this choice is inconsistent with the patient's stated preferences.
- C.2—— -2 *Mirtazapine.* Though there is clear evidence to support efficacy of this agent, weight gain is common issue with its use (3), and so this choice is inconsistent with the patient's stated preferences.
- C.3—— +3 *Bupropion.* This agent has a low likelihood of inducing the “deal breaker” side effects this patient has identified, while it has evidence affirming its efficacy (3).
- C.4—— -2 *Transcranial magnetic stimulation (rTMS).* Although rTMS has shown effectiveness in the treatment of pharmacoresistant major depression and is unlikely to impact weight or sexual function (3, 4), data for using it as an initial treatment for someone who has never tried pharmacotherapy are both off-label and outside the current evidence base.

CONSIDERATION POINT D

- D.1—— +3 *Methylphenidate.* Data from randomized controlled trials have

offered support for the off-label use of this psychostimulant medication as an augmenting agent in major depressive disorder (3, 5, 6).

- D.2—— +1 *Buspirone*. While this agent was studied as an augmenting agent in the STAR*D trial, it was added to an SSRI (citalopram) rather than to bupropion (7), and the evidence base for off-label use of buspirone with bupropion is not as extensive as with other agents (8).
- D.3—— +1 *Triiodothyronine (T3)*. Thyroid hormone preparations have a long history as off-label augmenting agents in unipolar depression, including in the STAR*D trial (7), but effects on energy and cognition are less reliably present than with some of the other options.
- D.4—— -1 *Electroconvulsive Therapy*. While ECT has evidence to support its use in treatment resistant depression (3), it is usually considered for use later in the algorithm than after an incomplete response to the first antidepressant agent tried. The potential for cognitive side effects also suggests this may not have the best effect profile for this stage of treatment.

YOUR TOTAL

Decision Point	Score	Ideal Score
A		5
B		3
C		3
D		5
Total		16

REFERENCES

- Greden JF, Genero N, Price HL: Agitation-increased electromyogram activity in the corrugator muscle region: a possible explanation of the "Omega sign"? *Am J Psychiatry* 1985; 142:348–351
- American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed., text revision. Washington, DC, American Psychiatric Publishing, 2000
- American Psychiatric Association: *Practice Guideline for the Treatment of Patients With Major Depressive Disorder*, 3rd ed. Washington, DC, American Psychiatric Publishing, 2010
- Gaynes BN, Lux L, Lloyd S, Hansen RA, Gartlehner G, Thieda P, Brode S, Swinson Evans T, Jonas D, Crotty K, Viswanathan M, Lohr KN: Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults. Comparative Effectiveness Review No. 33. (Prepared by RTI International-University of North Carolina (RTI-UNC) Evidence-based Practice Center under Contract No. 290-02-0016L.) AHRQ Publication No. 11-EHC056- EF. Rockville, MD: Agency for Healthcare Research and Quality. September 2011. www.effectivehealthcare.ahrq.gov/reports/final.cfm.
- Bond DJ, Hadjipavlou G, Lam RW, McIntyre RS, Beaulieu S, Schaffer A, Weiss M; Canadian Network for Mood and Anxiety Treatments (CANMAT) Task Force: The Canadian Network for Mood and Anxiety Treatments (CANMAT) task force recommendations for the management of patients with mood disorders and comorbid attention-deficit/hyperactivity disorder. *Ann Clin Psychiatry* 2012; 24:23–37
- Lam RW, Kennedy SH, Grigoriadis S, McIntyre RS, Milev R, Ramasubbu R, Parikh SV, Patten SB, Ravindran AV; Canadian Network for Mood and Anxiety Treatments (CANMAT): Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. III. Pharmacotherapy. *J Affect Disord* 2009; 117(Suppl 1):S26–S43
- Rush AJ, Warden D, Wisniewski SR, Fava M, Trivedi MH, Gaynes BN, Nierenberg AA: STAR*D: revising conventional wisdom. *CNS Drugs* 2009; 23:627–647
- Fava M: The combination of buspirone and bupropion in the treatment of depression. *Psychother Psychosom* 2007; 76:311–312



NOTES
