## When No Treatment Is the Treatment: Mental Illness–Related Case Report

Colette Raphaël and Ofer Agid

Can J Hosp Pharm. 2022;75(1):58-61

#### DOI: 10.4212/cjhp.v75i1.3063

#### INTRODUCTION

Reaching a diagnosis is often difficult, involving multiple steps. According to Balogh and others,<sup>1</sup> mental health diagnoses in particular are challenging, especially in terms of distinguishing between physical and mental health problems. Sometimes, physical conditions manifest as psychiatric ones, and vice versa.<sup>2,3</sup> Furthermore, there are concerns about missing psychiatric diagnoses and potential problems with overtreatment, as seen in prescribing cascades.<sup>4</sup> Indeed, diagnosis is an inferential process, with conclusions that may change over time and that may include misdiagnoses. This case report highlights how a patient with a complex presentation was incorrectly given a diagnosis of severe mental illness and treated accordingly for more than a decade before the deprescribing of unnecessary medications provided new insights into the correct diagnosis.

#### CASE REPORT

A 56-year-old married man was referred to the electroconvulsive treatment (ECT) department.\* However, the referral was deferred because the patient's extensive list of pharmaceuticals included many mood stabilizers that were incompatible with ECT. Before proceeding further with the planned ECT, the patient was transferred to the Psychosis Coordinated Care Service (PCCS) of the Centre for Addiction and Mental Health (Toronto, Ontario) for clarification of the diagnosis, as well as review and optimization of his pharmaceutical treatment.

During the first meeting at the PCCS, the patient stated his current inability to function properly. The patient had worked for 28 years on the assembly line of a motor vehicle company and had taken medical leave after a myocardial infarction. He was last employed at the company 7 or 8 years before the current presentation. He reported it was hurtful "being told I wasn't good enough to go back to work." He also reported, "I've always been a bit of a worrier but never to this extent." Indeed, after the myocardial infarction, he was forcing himself to do daily activities.

On assessment, the patient had poor eye contact. He was sedated and fell asleep on several occasions. He described his mood as low. He stated that he felt tired and reported insomnia, despite taking 5 medications to help with sleep. He also felt that people were watching him: they "stare at me." He reported auditory hallucinations (not commanding), telling him what he should and should not do—mostly instructing him not to leave his house, to be more careful, and so on. Overall, the patient found his situation disturbing and upsetting.

When questioned about his understanding of his diagnosis, the patient reported misunderstanding. He indicated that he had searched for and found information about schizoaffective disorder, which apparently listed "all my symptoms". He therefore assumed that he "had that or something close to that". He reported his appreciation of the role of medications and the risks of stopping them. There were no adherence issues.

Apart from the excessive sedation, the patient's symptoms had not remitted over the years, despite the overabundance of prescribed medications.

The patient's illness was notable for symptoms of depression and anxiety that seemed to have commenced 6 to 9 months after his father died of heart disease. Apparently, his father's death was traumatic to the patient, and he turned to alcohol. In 2010, the patient himself had a myocardial infarction, followed a year later by a motor vehicle crash while he was intoxicated. This event was, as he described it, a wake-up call, and he stopped drinking. Upon admission to the PCCS, there were no reports of substance use apart from nicotine dependence and caffeinism.

The patient's medical and psychiatric problems requiring hospitalization and treatment had started about a decade before the current presentation, after the myocardial infarction. In terms of medical treatment, it appeared that the usual medications known to reduce cardiovascular risk

<sup>\*</sup>The patient provided verbal consent for publication of this report.

after myocardial infarction, such as angiotensin-converting enzyme inhibitors, statins,  $\beta$ -blockers, and acetylsalicylic acid,<sup>5</sup> were prescribed. In addition, the proton pump inhibitor (PPI) pantoprazole, for treatment of gastroesophageal reflux disease, had been part of the patient's regimen since 2009. The patient was also being treated for diabetes. In terms of psychiatric treatment, the patient was taking a large number of psychotropic agents, as discussed further below.

The PCCS treatment team suspected the occurrence of prescribing cascades,<sup>4</sup> a type of polypharmacy that occurs when an adverse drug event is misinterpreted as a new medical condition, and a second medication is prescribed. With the involvement of the patient, his wife, and an interdisciplinary team (psychiatry, pharmacy, and nursing), a clinical process map was applied and a deprescribing treatment plan was created. The patient and his wife were in full agreement with the plan. Both were motivated and wanted the removal of unnecessary medications. With the patient's consent, the PCCS team contacted his primary care provider, who had been prescribing all the medications, and his community pharmacy and informed them that the PCCS team would take over prescribing to ensure coordination of care and appropriate monitoring. All of the parties agreed. Weekly meetings were scheduled for psychiatric evaluation and close monitoring during the planned 6-month deprescribing period. A safety plan was also put in place to allow for inpatient admission in case of deterioration in the patient's mental state.

The goal was to eliminate unnecessary medications, improve safety, and permit a clearer diagnosis, thus improving the patient's quality of life.

#### DISCUSSION

Whereas polypharmacy is generally defined as the routine use of 5 or more medications,<sup>6</sup> psychiatric polypharmacy involves the concurrent use of 2 or more psychiatric medications.<sup>7,8</sup> The occurrence of polypharmacy does not necessarily denote the inappropriate or incorrect use of medications; however, in this patient's case, the medication regimen appeared to confer more risks than benefits. This situation led to the reconsideration of treatment through a deprescribing approach.

This patient's psychiatric regimen involved a plethora of drugs for which indications, times of initiation, and intended duration were unclear. Indeed, over the years he had been given various diagnoses related to psychotic and mood symptoms, such as depression, bipolar disorder – depressive type, bipolar I disorder with psychotic features, schizophrenia, and most recently schizoaffective disorder – bipolar type. In fact, the ECT referral had been intended to improve the patient's mental state, given his continuing symptoms and lack of response to the numerous pharmaceuticals in his regimen (listed in Table 1).

The patient had 2 psychiatric hospitalizations (in 2012

and 2013) for apparent depression with suicidal ideation. As previously noted, there may be an evolution of diagnoses over time, especially in mental health. In this case, the patient's depression might have been related to his myocardial infarction, ongoing grief after his father's death, or nonpsychiatric drugs that induce negative psychological adverse effects. Additionally, the suicidal ideation could have been an adverse effect related to his prescribed medications. In any event, there had been several trials of antidepressants and anxiolytics over the previous decade without persistent improvement in symptoms. This situation prompted the referral for ECT and recommendations for future changes in therapy, such as augmentation with the antipsychotic lurasidone or initiation of clozapine for treatment-resistant schizophrenia.

Evidently, the patient's polypharmacy was an obstacle to clear diagnosis, given the presence of too many confounding factors. Deprescribing was needed because the risk of interactions with other medications or conditions and the risk of cumulative harms outweighed any potential benefits.

The medications were tapered and discontinued in an orderly fashion, starting with 2 medical agents, pantoprazole and propranolol, that were deemed unlikely to be necessary at the time of consultation. Indeed, given their known psychiatric side effects, they were most likely confounding other therapies. For instance, the long-term use of PPIs (i.e., longer than 1 year) may result in serious medical adverse events<sup>9</sup> and psychiatric symptoms such as depression, agitation, confusion, and disorientation. Other psychotic problems associated with PPIs include auditory and visual hallucinations.<sup>10,11</sup> The pantoprazole had been initiated in 2009 (a decade before), around the same time the myocardial infarction was diagnosed. The PCCS team questioned whether this agent had been prescribed because of confusion about the patient's symptoms. The product monograph for pantoprazole<sup>12</sup> further reports potential adverse effects of nervousness, tremor, sleep disorders, hyperlipidemias and lipid increases (triglycerides, cholesterol), depression (and associated aggravations), and disorientation (and associated aggravations). The agent was deemed inappropriate, and was therefore tapered and discontinued.

A similar rationale was applied for the  $\beta$ -blocker propranolol. Although it is common for a  $\beta$ -blocker to be prescribed after myocardial infarction,<sup>5</sup> the dose appeared incongruent (too low) for this purpose. Additionally, propranolol had been introduced in 2016, approximately 5 years after the infarction. The reason for its use remained nebulous (although arrhythmia or akathisia was surmised). Notably, propranolol has psychiatric adverse effects that include visual hallucinations, auditory hallucinations, depression, and paranoid psychosis.<sup>13-15</sup> These adverse reactions have all diminished in this patient after withdrawal of the drug.

Furthermore, because propranolol has  $\beta$ -adrenergic blocking activity, it may block premonitory signs and

#### **TABLE 1. Patient's List of Medications**

Medications before Deprescribing	Suspected Diagnoses and Date of Initiation	Medications after Deprescribing
Acetylsalicylic acid 81 mg qAM	Post-myocardial infarction; about 2010	Acetylsalicylic acid 81 mg qAM
Asenapine 5 mg S/L qHS	Trial of new antipsychotic medication; about 2019	—
Atorvastatin 80 mg once daily	Post-myocardial infarction; about 2010	Atorvastatin 80 mg once daily
Canagliflozin 100 mg qAM	Diabetes inferred; date of initiation unknown	Canagliflozin 100 mg qAM
Clonazepam 0.25 mg BID + clonazepam 0.5 mg qHS + clonazepam 0.25 mg every other day PRN (per community pharmacy, taken regularly by patient)	Anxiety; date of initiation unknown	_
Lamotrigine 300 mg once daily	Mood stabilizer; date of initiation unknown	—
Lithium 450 mg BID	Mood stabilizer; date of initiation unknown	—
Metformin 500 mg BID	Diabetes inferred; date of initiation unknown	Metformin 500 mg BID
Multivitamin with minerals once daily	Supplement; date of initiation unknown	Multivitamin with minerals once daily
Nitroglycerin 0.4 mg PRN for chest pain	Post-myocardial infarction; about 2010	Nitroglycerin 0.4 mg PRN for chest pain
Pantoprazole sodium 40 mg once daily	Possible GERD; about 2009	—
Pregabalin 150 mg once daily	Anxiety; date of initiation unknown	—
Propranolol 10 mg TID	Diagnosis unknown; date of initiation unknown	—
Ramipril 10 mg once daily	Post-myocardial infarction; about 2010	Ramipril 10 mg once daily
Risperidone 4 mg once daily	Trial of new antipsychotic medication; about 2020	—
Venlafaxine 112.5 mg once daily	Anxiety and depression; date of initiation unknown	—
Zopiclone 7.5 mg qHS and during the day if required (per community pharmacy, taken regularly by patient)	Insomnia; date of initiation unknown	-
Agents added temporarily during PCCS admission to supp Quetiapine, up to 75 mg qHS Olanzapine, up to 15 mg qHS	oort sleep Sleep optimization; about 2020 Trial of new antipsychotic medication: about 2020	_

BID = twice daily, GERD = gastroesophageal reflux disease, PCCS = Psychosis Coordinated Care Service, PRN = as needed, qAM = in the morning, qHS = at bedtime, S/L = sublingual, TID = 3 times daily.

symptoms (such as changes in pulse rate and blood pressure) of acute hypoglycemia, a condition that may contribute to mood fluctuations. In this patient, unrecognized hypoglycemia might have been caused or exacerbated by the hypoglycemic agents he was taking. The propranolol was also discontinued.

The same systematic approach, based on clinical experience, judgment, and evidence, guided the deprescribing process for each medication as listed in Table 1. We are of the opinion that the deprescribing process was successful. At the time of writing, the patient was doing well. The ECT was deemed unnecessary, and the referral was therefore cancelled.

#### CONCLUSION

Although polypharmacy can be appropriate if thoughtfully applied, it is often harmful. In fact, it is possible that this patient's diabetes was a metabolic side effect related to past use of antipsychotics. Moreover, there is little evidence that polypharmacy enhances clinical outcomes.<sup>8</sup> In this case, all psychotropics were ceased with no adverse consequences for the patient. This case report illustrates the adage that sometimes "less is more". Minimizing prescribing cascades<sup>4</sup> and deprescribing when appropriate can be powerful tools to clarify diagnoses and improve safety and patient outcomes. The 6-month period of deprescribing for this patient highlighted the necessity for ongoing medication review and management by both prescribers and dispensers and led us to the conclusion that the patient did not have a severe mental illness.

#### References

 Balogh EP, Miller BT, Ball JR; Committee on Diagnostic Error in Health Care; Board on Health Care Services; Institute of Medicine. *Improving diagnosis in health care*. National Academies Press (US); 2015 Dec 29 [cited 2019 Dec 29]. Available from: https://doi. org/10.17226/21794

- McKee J, Brahm N. Medical mimics: differential diagnostic considerations for psychiatric symptoms. *Ment Health Clin*. 2016;6(6):289-96.
- Keshavan MS, Kaneko Y. Secondary psychoses: an update. World Psychiatry. 2013;12(1):4-15.
- McCarthy LM, Visentin JD, Rochon PA. Assessing the scope and appropriateness of prescribing cascades. J Am Geriatr Soc. 2019;67(5):1023-6.
- Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction—executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction) [published correction appears in *J Am Coll Cardiol.* 2005;45(8):1376]. *J Am Coll Cardiol.* 2004;44(3):671-719.
- Medication safety in polypharmacy: technical report. World Health Organization; 2019 [cited 2019 Dec 29]. Available from https://apps. who.int/iris/handle/10665/325454
- Kukreja S, Kalra G, Shah N, Shrivastava A. Polypharmacy in psychiatry: a review. *Mens Sana Monogr.* 2013;11(1):82-99.
- Sarkar S. Psychiatric polypharmacy, etiology and potential consequences. *Curr Psychopharmacol.* 2016; 6:12.
- Proton pump inhibitors: hypomagnesemia accompanied by hypocalcemia and hypokalemia. *Can Adverse React Newslett*. 2011 [cited 2019 Dec 29];21(3):1-2. Available from https://www.canada.ca/content/ dam/hc-sc/migration/hc-sc/dhp-mps/alt\_formats/pdf/medeff/ bulletin/carn-bcei\_v21n3-eng.pdf
- 10. Florentin M, Elisaf MS. Proton pump inhibitor-induced hypomagnesemia: a new challenge. *World J Nephrol*. 2012;1(6):151-4.

Canada's

- 11. Novotny M, Klimova B, Valis M. PPI long term use: risk of neurological adverse events? *Front Neurol.* 2019;9:1142.
- Ava-pantoprazole [product monograph]. Avanstra; 2011 [cited 2019 Dec 29]. Available from https://pdf.hres.ca/dpd\_pm/00012502.PDF
- Teva-propranolol [product monograph]. Teva Canada Ltd; 2011 [cited 2019 Dec 29]. Available from https://pdf.hres.ca/dpd\_pm/00014382. PDF
- 14. Cunnane JG, Blackwood GW. Psychosis with propranolol: still not recognized? *Postgrad Med J.* 1987;63(735):57-8.
- 15. Gershon ES, Goldstein RE, Moss AJ, van Kammen DP. Psychosis with ordinary doses of propranolol. *Ann Intern Med.* 1979;90(6):938-9.

**Colette Raphaël**, RPh, BPharm, BCPP, MHA, CHE, is with the Centre for Addiction and Mental Health, Toronto, Ontario.

Ofer Agid, MD, is with the Centre for Addiction and Mental Health, Toronto, Ontario.

Competing interests: None declared.

Address correspondence to: Colette Raphaël Centre for Addiction and Mental Health 1001 Queen Street W Toronto ON M6J 1H4

email: colette.raphael@camh.ca

Funding: None received.

Acknowledgments: The authors would like to thank Maria Reyes, manager of the Psychosis Coordinated Care Service, and her dedicated interprofessional team, who embrace recovery and work together to help people with severe mental illness live well and better.

Online: Jan 29 - Feb 6



# **Hospital Pharmacy Conference**

## What's new at #CSHPTogether2022

7 timely keynotes Live Q&A for all sessions Preliminary results of the Hospital Pharmacy in Canada Survey Social events: Trivia night and the Dueling Piano Kings Returning: Posters, awards, games, & exhibits

### **Register at CSHP.ca**