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PATIENT SAFETY NETWORK

Acute Care Admission of the Behavioral Health Patient

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The Case

A 25-year-old man presented to the emergency department (ED) with a 3-week history of abdominal pain, nausea and vomiting, and weakness. His medical history included Crohn disease with ileocolectomy and ileostomy; chronic pain; schizophrenia and major depression with prior suicide attempts; and narcotic abuse with hydrocodone. Medications included mesalamine, clonidine, tramadol, haloperidol, olanzapine, venlafaxine, potassium chloride, and magnesium oxide. The patient was disabled, participated in an intensive case management program (ICM), and lived in supportive housing.

The ED work-up was consistent with acute pancreatitis and the patient was admitted to the hospital. A gastroenterology (GI) consult noted that olanzapine can cause pancreatitis. In addition, the GI consult described how the patient requested a reduction in the haloperidol dose because he felt overmedicated. The GI consult declined the patient's request and suggested that changes in the haloperidol dose, as well as the decision to discontinue olanzapine, should be made by the patient's psychiatrist.

Despite this advice, the medical team discontinued the olanzapine without consulting the patient's psychiatrist. The patient's condition improved and he was discharged to home. The discharge summary documented that the patient was instructed to follow up with his primary care provider, his gastroenterologist, and his psychiatrist in 1 week, and to inform his psychiatrist that olanzapine had been discontinued. Tragically, 2 weeks after discharge the patient committed suicide.

The Commentary

The case highlights the life-threatening potential of major mental illness, the complexities of caring for patients with both mental and physical illness, and the risks associated with inadequate care coordination for this population. At the heart of the case is the decision to discontinue olanzapine, an atypical antipsychotic medication, in a young man with severe mental illness who presented with acute pancreatitis.

The development of the medication class known as antipsychotics, beginning with the introduction of chlorpromazine in 1951, heralded a new era in the management of severe mental illness. Prior to that date,

there was no effective pharmacotherapy to quell the symptoms associated with these illnesses, and patients were often institutionalized and managed with restraints. With chlorpromazine, not only was there an 80% reduction in the use of restraints, but for the first time some patients were safely discharged from hospital.(1) The developers of chlorpromazine were awarded the 1957 Lasker Clinical Medical Research Award.

Over the subsequent decade, other antipsychotics were developed, most with greater potency (including haloperidol), each with the presumed mechanism of action of dopaminergic antagonism. Adverse motor effects associated with this antagonism (e.g., Parkinsonism and dystonia) were described and were considered to be essential for treatment effectiveness. However, the emergence of delayed-onset choreiform movements (tardive dyskinesia) raised alarm, as these symptoms were functionally impairing and in many cases irreversible.

In the closing decades of the 20th century, an antipsychotic named clozapine was noted to have fewer adverse motor effects and perhaps greater efficacy when compared with the earlier medications in this class. However, clozapine had significant potential for hematologic toxicity, which led to a search for agents that might preserve its advantages without this problem. Ultimately, a series of "second generation" antipsychotics were developed targeting both serotonergic and dopaminergic mechanisms. These agents showed equivalent efficacy to the older agents in treating the psychotic symptoms of schizophrenia (i.e., hallucinations and delusions) but with apparently lower rates of tardive dyskinesia. These medications, which included clozapine, but also olanzapine, risperidone, and quetiapine, were termed "atypical."

In part related to this perceived neurological safety profile, and in part related to studies showing efficacy in other conditions beyond schizophrenia, the use of atypical antipsychotics grew tremendously.(2) As with the first generation antipsychotics, the risks of the second generation antipsychotic medications became clearer with expanded use over time. These medications, but especially clozapine and olanzapine, have been associated with impairments in the metabolism of both lipids and sugars, leading to hypertriglyceridemia, diabetes mellitus, and significant weight gain.(3,4) Use of these medications therefore requires careful metabolic monitoring, as patients with severe mental illness have elevated risks of cardiovascular death.(5)

In this case, the patient presented with acute pancreatitis. As suggested by the GI consultant, there have been published case series showing a relationship between the use of atypical antipsychotics (especially clozapine and olanzapine) and the development of pancreatitis.(6,7) However, a larger scale study has recently suggested that this linkage is explained by confounding variables, particularly alcohol use.(8) Although the pancreatitis did resolve after discontinuation of olanzapine in the present case, excessive alcohol use (and sobriety while hospitalized) may have played a role in the onset and resolution of the GI distress.

The potential benefits of discontinuing the olanzapine would need to be considered in the context of potential disruption in a psychiatrically fragile patient. Indeed, even from the brief history provided, we note that he was at elevated risk for suicide. Patients with schizophrenia have a lifetime suicide rate of nearly 5%.(9) When combined with the additional risk factors of prior suicide attempts, depressive symptoms, chronic pain, medical illness, substance abuse, and disability with unemployment, the risk of self-harm

would be even greater. Any shift in his medication regimen or social situation would therefore need careful consideration.

Antipsychotic discontinuation has been associated with a number of neuropsychiatric sequelae, which may have contributed to the outcome in this case. Based on several meta-analyses, discontinuation of antipsychotics, especially when done abruptly, is associated with higher rates of relapse to psychosis.(10) Rather than simply a recurrence of illness, this iatrogenic effect has been thought to be a "supersensitivity psychosis," presumably related to dopamine receptor up-regulation after chronic medication–related receptor blockade. At least one case report has described this pattern with olanzapine.(11) Withdrawal dyskinesias, presumably related to dopaminergic sensitivity, are also described.(12) Additional discontinuation symptoms, related to the complex pharmacology of atypical antipsychotics, include myoclonus (likely due to serotonergic hyperactivity) and cholinergic rebound, with nausea, vomiting, headaches, and insomnia.(13)

Although unaware of any specific studies linking olanzapine withdrawal to suicide, we note two indirect lines of evidence that may be of relevance. Antidepressant discontinuation has been associated with higher rates of suicide, presumably via a serotonergic mechanism that may be shared by some atypical antipsychotics.(14) In addition, antipsychotic medications have been found to be protective against suicide in large epidemiologic studies. Although initially thought to be limited to clozapine, a recent study of patients with schizophrenia who had prior suicide attempts found that those on all antipsychotics (especially olanzapine) were less likely to die by suicide over the time window they studied.(15)

Unfortunately, in this case, the olanzapine was stopped without psychiatric oversight and evaluation of these risks. The failure to recognize the importance of changing the psychiatric medication by the non-psychiatric physician may reflect training inadequacy, barriers to addressing psychiatric medicine due to stigma, privacy concerns, and/or a lack of appreciation among physicians of the severity, disability, pain, and impact of relapse of major psychiatric disorders. Maybe psychiatric consultation was difficult to obtain, as it is in some acute care hospitals. An additional factor was the assumption, likely unrealistic in this case, that this patient with severe mental illness would be capable of coordinating several outpatient appointments and transferring critical medical information from the inpatient stay. Perhaps most striking was the fact that this patient was already enrolled in an intensive case management program, and the case presentation does not describe direct communication between the inpatient team and the case managers. Had the program been notified and included in the discharge process, it could have helped to coordinate the aftercare plan, including home visits to assist with monitoring.

This tragic case reflects both positives and negatives about our health care system. We can save patients with potentially fatal conditions like pancreatitis, but with respect to communication and coordination, we often fall well short of the mark. In the absence of other technology to monitor the brain and mind, communication and coordination are the keys to caring for patients with mental illness—and when they break down, the consequences can prove devastating.

Take-Home Points

- Mental illness can be life threatening. Risk of suicide should be considered in all hospitalized patients with mental illness.
- Although abrupt discontinuation of psychiatric medication may sometimes be indicated, the neuropsychiatric consequences must be considered. Expert consultation is generally warranted.
- Mental illness and medical illness are highly comorbid and require close care coordination—particularly between inpatient and outpatient caregivers—to obtain successful outcomes on both fronts.

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