A Case of Serotonin Syndrome in the Setting of Dextromethorphan-Based Cough Medicine, Tramadol, and Multiple Antidepressants

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Serotonin syndrome is a potentially life-threatening condition that is particularly relevant to both primary care and psychiatric clinical practice. Serotonin syndrome has been documented with increasing frequency in recent years, in part due to the increased use of selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and other serotonergic medications.[1–3] However, it is still relatively underdiagnosed and underreported.[1,4] We present a case of serotonin syndrome resulting from the use of dextromethorphan-based cough medicine in addition to multiple antidepressant and pain medications.

Case Report

Ms A, a 68-year-old woman with past psychiatric history of bipolar II disorder and past medical history of poorly controlled diabetes, hypertension, and hypothyroidism, presented to the emergency department of a large teaching hospital complaining of weakness and difficulty walking. She also reported recent nausea, vomiting, and diarrhea. She was found to have tachycardia, diaphoresis, dry mucous membranes, abdominal tenderness, and tremor but was afebrile, alert, and oriented. Initial laboratory studies were notable for elevated white blood cells (14×10^9/L), anion gap metabolic acidosis (gap 21, HCO_3 16 mmol/L), and elevated blood glucose (322 mg/dL). Computed tomography scans of the head and abdomen/pelvis revealed no acute abnormalities. Initially, emergency department staff were concerned for sepsis or diabetic ketoacidosis and treated her symptoms with intravenous ondansetron and normal saline before admitting her to the internal medicine service.

Table 1. Serotonergic Medications and Doses the Patient Was Taking at Admission

Medication	Dose
Duloxetine	60 mg by mouth 2 times/d (120 mg total)
Mirtazapine	45 mg by mouth at bedtime
Trazodone	350 mg by mouth at bedtime
Lamotrigine	200 mg by mouth daily
Gabapentin	1,200 mg by mouth 3 times/d (3,600 mg total)
Tramadol	50 mg by mouth 2 times/d (100 mg total)
Dextromethorphan/ guaifenesin	Dose unknown (over-the-counter preparation)

Further review of the patient's medical record revealed that she was being prescribed high doses of duloxetine, mirtazapine, trazodone, lamotrigine, gabapentin, and tramadol (Table 1). She had been stable on this regimen for several weeks. However, she had recently started taking over-the-counter dextromethorphan/guaifenesin for an upper respiratory infection. A thorough neurologic examination demonstrated bilateral fine tremors in hands, stiffness in elbows/wrists, inducible ankle clonus, lower extremity hypertonia, and diffuse hyperreflexia. A diagnosis of serotonin syndrome was made using the Hunter diagnostic criteria.[5] All serotonergic medications were held. She rapidly improved over the following 48 hours and was discharged home on a significantly simplified medication regimen.

Discussion

Serotonin syndrome can be challenging to recognize, given its often nuanced presentation and overlap with other clinical syndromes. The classic triad of autonomic instability (hypertension, tachycardia, diaphoresis), altered mental status (delirium, agitation), and neuromuscular findings (tremors, clonus, hyperreflexia) is often not present, particularly in mild or moderate cases.[1,6,7] Laboratory findings, such as metabolic acidosis and elevated white blood cell count, are nonspecific and may detract from the correct diagnosis.[2] Delays in diagnosis can result in inappropriate treatment that may prolong or even worsen serotonin syndrome. In the present case, the patient was initially administered another serotoninergic agent, ondansetron. Neuromuscular symptoms appear to be the most specific finding in serotonin syndrome.[7] Thus, the diagnosis is most accurately made through a thorough neurologic examination, as this case demonstrates. According to the

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Hunter diagnostic criteria, patients must have been exposed to 1 or more serotonergic agents and have at least 1 of the following findings: (1) spontaneous clonus, (2) inducible clonus plus agitation or diaphoresis, (3) ocular clonus plus agitation or diaphoresis, (4) tremor plus hyperreflexia, or (5) hypertonia plus temperature above 38°C plus ocular clonus or inducible clonus. These criteria are 84% sensitive and 97% specific to the diagnosis of serotonin syndrome.[5]

Psychiatrists and primary care physicians should be able to recognize and diagnose the syndrome early, given that the cause is often iatrogenic and the most commonly prescribed psychiatric medications are serotonergic.[3] In this patient's case, it was the additional use of a seemingly benign cough medicine containing dextromethorphan (which has been linked to serotonin syndrome[8]) that appears to have precipitated the syndrome. Thus, providers should also be closely aware of all medications, both psychiatric and nonpsychiatric and over-the-counter or prescribed, that their patients are taking.[3,4,9] They should especially seek to avoid situations of hazardous polypharmacy.

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