Introduction

- Naltrexone, an opioid antagonist at the Mu receptor used in the treatment of opioid use disorder and alcohol use disorder, also acts as an antagonist at the μ-1 (HT3) serotonin receptor, increasing levels of serotonin in the brain (1).
- Naltrexone’s synergistic effect with multiple serotonergic agents leads to serotonin syndrome, a syndrome of excess serotonergic activation leading to symptoms such as clonus, autonomic instability, and delirium (2).
- Naltrexone can also increase the propensity for delirium by rapidly unbinding opioids from receptors if opioids have been used recently, precipitating severe withdrawal (6).
- This case is a presentation of concurrent severe opioid withdrawal and serotonin syndrome after first-time use of naltrexone in the setting of recent opioid use.

Patient History

- Patient is a 49-year-old female with a past psychiatric history of bipolar disorder, PTSD, schizophrenia, and opiate use disorder, who presented to the emergency department via EMS with a chief complaint of full body spasms for approximately 4 hours after taking naltrexone for the first time for opioid use disorder.
- Other symptoms included diaphoresis, muscle spasms, autonomic instability, and restlessness.
- She reported that she had recently stopped buprenorphine after 1 month, with last use approximately 8 days prior to arrival. She voluntarily discontinued this due to perceived lack of benefit.

Physical Exam

- In the ED, patient’s vital signs were temperature 97.6F, heart rate 108, respiratory rate 17, blood pressure 138/65 and SpO2 97% on room air. Records indicate the patient was alert and oriented.
- Physical exam was notable for diaphoresis and tachycardia as well as occasional 2-3 second periods of stiffening of upper and lower extremities with no loss of consciousness and self-resolution.
- HENT, eyes, pulmonary, abdominal, musculoskeletal and psychiatric portions of the exam were unremarkable.

Laboratory/Imaging Results

- Labs were significant for: CPK elevation.
- CMP, CBC, TSH, TP were within normal limits.
- β-HCG, salicylate, acetaminophen, COVID-19 testing were negative.
- QTC was prolonged at 627.

Pathophysiology

- Serotonin syndrome is a potentially life-threatening syndrome that is often caused by the use of multiple serotonergic agents from numerous drug classes, resulting in increased levels of serotonin in the body, leading to overactivation of 5-HT receptors, particularly 1A and 2A (3).
- As a result of this increase in serotonin leading to overactivation, patients often present with mental status changes and neuromuscular and autonomic hyperactivity leading to spontaneous or inducible clonus, ocular clonus, agitation, diaphoresis, hyperreflexia, hypertension, tremors or fever (4).

Differential Diagnoses

Differential diagnoses of conditions include Naltrexone-induced opioid withdrawal and Serotonin syndrome.

Hospital Course

- In the ED, she was treated with a total of 4mg Lorazepam which was ineffective.
- Given continued uncontrolled spasms and autonomic instability with prolonged QTC interval, she was admitted to the hospital for further evaluation and treatment.
- Overnight, she became confused, disoriented, and agitated with visual hallucinations and attending to internal stimuli.
- Patient was initially treated with phenobarbital with concern for alcohol withdrawal resulting in delirium. This was quickly discontinued due to sedation.
- Further symptoms of inducible clonus with agitation, hyperreflexia, and hypertension were found, and serotonin syndrome was diagnosed based on Hunter Criteria (2).

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Table 2: Signs and symptoms of serotonin syndrome and opioid withdrawal

Conclusion

This case demonstrates the continued need for diligent and cautious medication monitoring and prescribing given the broad breadth of serotonergic action in medications and substances. This case also highlights the recognition of overlapping pathology. Serotonin syndrome and opioid withdrawal are two syndromes with overlapping symptomology and agent etiology but with separate prognosis, severity, and treatment. Effective treatment of this patient relied on identification of the two different pathologies and concurrent treatments.

References