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74. Successful Use of High-Dose Buprenorphine to Manage Precipitated Opioid Withdrawal Caused by Naltrexone LAI Administration

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Background: Patients frequently experience venous thromboembolic events (VTEs) while on clozapine (Paciullo 2008) and will need treatment for VTE. Riociguat is a treatment for pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension (CTEPH). This is an early (if not the first) case that highlights potential interactions between riociguat and clozapine in a patient that was diagnosed with CTEPH after dual antipsychotic usage, who also experienced clozapine toxicity in the setting of medical comorbidities.

Case: A 58-year-old male with schizoaffective disorder and CTEPH presented with several days of altered mental status, fatigue, gait changes, spastic movements, and dysarthria. His psychiatric medications included clozapine 300 mg daily, risperidone long-acting injectable 100 mg monthly, and valproic acid 1500 mg daily, which had been titrated over years for paranoia and aggression. After poor response to PDE-5 inhibitors, riociguat had been initiated for pulmonary hypertension (PH) six months prior and increased to 2.5 mg TID one month before presentation.

On examination, the patient exhibited delirium, spasmodic muscle movements, abdominal distention, and a shuffling gait. Objective findings were significant for a creatinine of 2.2 and a clozapine level of 1030. Clozapine was discontinued. The patient was transitioned to olanzapine for psychosis and agitation control. He required ICU care for his delirium and then resurging psychosis while his acute medical conditions resolved.

Discussion: Venous thromboembolic events may occur while on clozapine because of decreased nitric oxide release causing vasodilator dysfunction (Nair et al., 2019). This may have contributed to the diagnosis of CTEPH. Next, the etiology of clozapine toxicity in this patient is multifactorial. While riociguat and its metabolite M1 are not directly involved in the P450 metabolism of clozapine (Frey et al., 2018), riociguat is a substrate of the UDP-glucuronosyl-transferase system, which is also involved in clozapine metabolism. Additionally, riociguat is a weak to moderate inhibitor of P-glycoprotein, of which risperidone is a substrate, leading to increased risperidone levels and exacerbating the patient's Parkinsonism (Rickert et al., 2014). The patient's AKI and generalized inflammation impaired clozapine metabolism, further contributing to toxicity.

Conclusions: Clinicians should be aware of the possibility of indirect drug interactions, even when primary metabolic pathways do not overlap. Patients prescribed clozapine typically have a history of treatment failure with other antipsychotics, which may result in the use of dual antipsychotic therapy and an increased risk of developing severe PH, including the variant CTEPH. For patients with PH on dual antipsychotic therapy and riociguat, psychiatrists and cardiologists should monitor renal function, vital signs, and clozapine levels for potential toxicity.

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74. Successful Use of High-Dose Buprenorphine to Manage Precipitated Opioid Withdrawal Caused by Naltrexone LAI Administration

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Background/Significance: Naltrexone is a mu opioid receptor antagonist used in alcohol use disorder (AUD) to reduce craving and block the reward pathway. If administered in the presence of opioid agonist, however, it can precipitate opioid withdrawal. We present a case of a patient taking prescribed buprenorphine, who erroneously received long-acting naltrexone, causing opioid withdrawal, and successful management of the adverse effects with high-dose buprenorphine.

Case: A 59yo man with opioid use disorder (OUD) and chronic pain on buprenorphine-naloxone 8mg-2mg sublingual twice-daily, alcohol use disorder, and type 2 diabetes mellitus was admitted to the hospital for acute pancreatitis and diabetic ketoacidosis (DKA). During admission, alcohol was recognized as a contributing factor to pancreatitis and DKA, and his inpatient physician recommended naltrexone for reducing alcohol use. The patient accepted naltrexone 380mg intramuscular injection on the day of discharge. He did not receive oral naltrexone before receiving the injection. One day after discharge, he developed diarrhea, abdominal cramping, restlessness, anxiety, insomnia, and increased back pain. Three days post-discharge, the patient returned to the ED because symptoms were not improving, and was re-admitted. The following day, psychiatry was consulted for anxiety, insomnia, and agitation. A careful history elucidated that symptoms began one day after receiving naltrexone injection, though he continued taking buprenorphine-naloxone at his usual dose. He was diagnosed with opioid withdrawal caused by administration of injectable naltrexone. Hypothesizing that a higher dose of buprenorphine might overcome opioid receptor blockade by naltrexone, buprenorphine-naloxone was titrated to the clinical endpoints of alleviating opioid withdrawal and achieving analgesia, ultimately requiring 36mg of buprenorphine per day, which was well-tolerated. The patient was discharged with close outpatient follow-up, and successfully tapered down to his original maintenance buprenorphine dose by week 6 post-naltrexone injection.

Discussion: Opioid use—including prescribed opioid agonist therapy with buprenorphine—is one of the few absolute contraindications to naltrexone for AUD. Although existing literature describes strategies for acute pain management in the presence of an opioid receptor antagonist, there was limited evidence to guide management of chronic pain for this patient on long-term buprenorphine therapy who erroneously received long-acting naltrexone, which remains active for several weeks. Naltrexone's affinity for the mu opioid receptor (Ki 0.4-0.6nM) overlaps that of buprenorphine (Ki 0.21-1.5nM), but we hypothesized that administering significantly more buprenorphine could overcome naltrexone blockade—a strategy that was ultimately successful. The patient's clinical course and buprenorphine requirements correspond to the known pharmacokinetics of a single dose of LAI naltrexone: serum concentration peaks 2 hours post-administration and again 2-3 days post-administration; the concentration remains > 1ng/ml for approximately 35 days. This case illustrates the safety and feasibility of using high-dose buprenorphine to overcome naltrexone. With increasing promulgation of naltrexone for AUD and other indications (eg, for weight loss in combination with bupropion), along with potential fragmentation of care, providers must be prepared for similar scenarios.

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75. Identifying Early Presentation of Serotonin Syndrome in a 20-Year-Old Male Prescribed Clomipramine and Quetiapine: A Case Report

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Background: Serotonin syndrome can be challenging to diagnose due to its diverse etiology and varied symptomatology. Despite its severity, serotonin syndrome may present from mild to fatal, with symptoms such as autonomic instability, altered mental status, and neuromuscular excitation manifesting as muscle rigidity masking hyperreflexia and clonus. Due to masking of symptoms, early detection of serotonin syndrome can be challenging.

Case: A 20-year-old male with a past medical history of obsessive compulsive disorder (OCD) being treated with clomipramine 25 mg orally (PO) daily and quetiapine 100 mg PO daily arrived at the emergency department for agitation. He was found to be in sinus tachycardia with a heart rate (HR) around 140 beats per minute (BPM) with no medical or substance cause identified. He was medically stabilized, continued on his home medications, and transferred to the inpatient psychiatry unit, where he again became tachycardic at 175 BPM, with muscle rigidity, tremor, agitation, and diaphoresis. The patient's HR stabilized following administration of lorazepam 2 mg intramuscular (IM) and metoprolol 5 mg intravenous (IV), but he remained rigid and diaphoretic for several more hours. The patient reported that he took clomipramine in excess prior to admission, so clomipramine discontinued prior to discharge.

Discussion: In this case, muscle rigidity masked the hyperreflexia and myoclonus often used to diagnose serotonin syndrome, making it even more difficult to recognize. Additionally, collateral about the patient's excessive use of clomipramine, a potent serotonergic tricyclic antidepressant was not obtained early on.

Conclusion: Few cases of mild and masked serotonin syndrome have been reported, due to the difficulty in recognizing and quickly treating such cases. Cases of serotonin syndrome should continue to be reported in order to familiarize clinicians with the varied presentation.

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76. Abuse of a GLP-1 Agonist and Lithium Toxicity in Anorexia Nervosa: A Case Report

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Background: Anorexia nervosa is an eating disorder which poses unique treatment challenges and a high mortality rate (Attia 2025). Disordered eating itself has been significantly linked to self-esteem, body image, and use of social media (Aparicio-Martinez, 2019). With mass marketing of GLP1 agents and the presence of various direct-

to-consumer prescription platforms, the abuse potential of these agents in eating disorders is of significant concern. In addition, the rise of GLP1 use among individuals on psychotropic medications may have dosing implications. We describe a unique case of a patient with anorexia, inappropriate GLP1 use, and lithium toxicity.

Case: We present a woman in her 30s with a history of PTSD and anorexia nervosa who presented to the ER with altered mental status. Her psychotropic regimen included lithium. She was tachycardic, laboratory studies revealed electrolyte abnormalities and a lithium level of > 3. She required 2 sessions of emergent hemodialysis. After she gradually regained awareness, she reported a relapse of anorexia nervosa symptoms, leading to significant food restriction in the last few weeks. Furthermore, she reported using prescription tirzepatide injections for the past 6 weeks, which she obtained online after entering a false weight to qualify. During hospitalization, she progressively increased her meal consumption to 30-40%. At discharge, she expressed insight into the dangers of using tirzepatide and expressed anger for obtaining it so easily.

Discussion: GLP1 agents function via acting as agonists to glucagon-like peptide-1 (GLP1) and glucose-dependent insulinotropic polypeptide (GIP), which results in delaying gastric emptying and glucagon production inhibition (Collins, 2024). GLP1 agents carry significant side effects including diarrhea, nausea, vomiting, and dyspepsia, and are FDA-approved to treat type 2 diabetes mellitus and obesity (Collins, 2024). With targeting via social media algorithms, concern arises that these medications could cause morbidity and mortality in those with eating disorders. This case was complicated by the patient's lithium use and sheds light on the risk of lithium toxicity in patients taking GLP1 agonists. Mechanistically, GLP1 agents could cause diarrhea, leading to subsequent hypovolemia (Collins, 2024). This could result in impaired renal clearance, leading to lithium toxicity.

Conclusion/Implications: We present this case to spread awareness of potential abuse of GLP1 agents in patients with eating disorders and to warn about potential implications for such use with medications such as lithium. We must remain vigilant about screening patients for eating disorders and monitoring lithium levels closely when they are concurrently on GLP1 agents.

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77. Can Psychedelics Revolutionise OCD Treatment? Systematic Review and Meta-Analysis of Efficacy, Safety, and Patient Experiences

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