CLINICAL VIGNETTE

Serotonin Syndrome with Associated Hepatitis

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Case Presentation

A 20-year-old female with depression, anxiety, and PTSD presented to the emergency room with tremors. The patient reported worsening tremors, generalized weakness, lightheadedness, palpitations, night sweats, fevers, and anorexia for three weeks. About one month prior she was admitted to a psychiatric hospital and started on escitalopram. Prior to this hospitalization, the patient was taking sertraline 100mg daily and quetiapine 100mg at bedtime. The patient also acknowledged using alcohol, tobacco, mushrooms, and cannabis reportedly laced with fentanyl. However, her last use of any illicit substance was about 3 weeks prior to her current presentation, shortly after her psychiatric hospital discharge.

The patient's initial vitals were temperature of 36.5 degrees Celsius, heart rate of 96 beats per minute, blood pressure of 114/75 mmHg, respiratory rate of 19, and oxygen saturation of 99% on room air. Physical exam was notable for a resting tremor, anxiousness, bilateral hyperreflexia, bilateral clonus, but was otherwise normal. Laboratories included a normal complete blood count, basic metabolic panel, international normalized ratio, thyroid stimulating hormone level, and acetaminophen level. The aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were elevated at 79 U/L (normal range 13-62 U/L) and 176 U/L (normal range 8-70 U/L), respectively. Infectious hepatitis serologies were negative. Abdominal ultrasound demonstrated a minimally course and echogenic liver, suggestive of a nonspecific hepatitis.

The patient was diagnosed with serotonin syndrome with associated hepatitis. All serotonergic medications were stopped. She was treated with intravenous fluids and lorazepam as needed for symptom management. The patient was monitored in the hospital for four days until her symptoms improved enough that she was able to ambulate and reliably eat on her own. The patient's AST and ALT were checked daily and remained similarly elevated during the hospitalization. The patient was advised to abstain from serotonergic and illicit substances and was to follow up with her primary care physician and psychiatrist. Unfortunately, she was lost to follow up.

Discussion

Serotonin syndrome (SS) is an iatrogenic, drug-induced syndrome caused by increased serotonin activity in the central nervous system from serotonergic drugs. SS is typically caused by overdose of a serotonergic agent or the concomitant use of two or more serotonergic antidepressants. This patient was taking both sertraline and escitalopram, two selective serotonin reuptake inhibitors (SSRIs), which combine to overstimulate serotonin receptor subtype 1A (5-HT_{1A}). She was also taking quetiapine, an atypical antipsychotic, which is a serotonergic receptor 5-HT_{2A} antagonist. The use of atypical antipsychotics alone rarely increases the risk of SS, but when combined with serotonergic agents, increases the risk of SS by relatively enhancing the activity of 5-HT_{1A}.[1]

SS is a clinical diagnosis, which depends on identifying autonomic instability, neuromuscular signs, and cognitive-behavioral changes. The clinical presentation is variable and non-specific, which makes the diagnosis challenging. The Hunter Criteria is currently the best diagnostic criteria; it is fulfilled if the patient has been exposed to a serotonergic agent and meets any of the following conditions: (1) spontaneous clonus; (2) inducible clonus and agitation or diaphoresis; (3) ocular clonus and agitation or diaphoresis; (4) tremor and hyperreflexia; or (5) hypertonia and temperature greater than 38 degrees Celsius and ocular clonus or inducible clonus.[2] The incidence of SS is rising, as more serotonergic drugs are being prescribed and there is greater clinical recognition of the syndrome.

This patient was also found to have moderately elevated transaminases. Although rare, hepatotoxicity from SSRIs has been reported. Asymptomatic elevations of transaminases have been documented in 0.9% of patients receiving sertraline.[2] SSRI-induced hepatotoxicity presents with a predominantly hepatocellular injury pattern or a mixed obstructive and hepatocellular injury pattern. There have been several case reports demonstrating that elevated transaminases can also be seen in SS.[2-4] This case provides further evidence to suggest that SS may cause an associated hepatitis. Usually, the elevated transaminases associated with SS will downtrend as the patient's symptoms improve. The presented patient's AST and ALT remained stable during her inpatient stay, but she was lost to follow up. Notably, the presented patient's AST and ALT elevation may have alternatively been related to a drug-induced liver injury from her illicit drug use. However, this was less likely given her reported sobriety for 18 days.

Management of SS involves mainly supportive care, discontinuation of serotonergic drugs, and treatment with benzodiazepines. Benzodiazepines reduce muscle rigidity and shorten

the duration of SS, but have no effect on mortality.[5] SS often resolves within 24 hours of initiating care. In severe cases, SS can be sustained for longer periods of time and lead to death. In this patient, escitalopram, sertraline, and quetiapine were stopped, and her symptoms improved.

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