Altered Mental Status in an Octogenarian: How Frequently Should Serotonin Syndrome Be Kept in Mind?

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INTRODUCTION

Serotonin syndrome (SS) is a life-threatening complication of substances known to increase serotonin levels [1]. This can be caused by prescription drugs such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), etc. Venlafaxine is an SNRI, used in the treatment of depression and has been noted as one of the many drugs to precipitate serotonin syndrome [2]. Over the past few decades, the use of antidepressants in the United States has increased, causing SS to be more of a concern clinically. However, since SS is a diagnosis of exclusion and the presentation of symptoms ranges so widely, the condition may be overlooked, misattributed to other conditions, or misdiagnosed on presentation [2].

ABSTRACT

An 89-year-old female presented with altered mental status and hypertensive emergency. She was diagnosed with SS due to venlafaxine and oxycodone use. The presentation, diagnosis, and management are detailed. This case highlights the importance of keeping serotonin syndrome as a differential diagnosis in patients using serotonin and norepinephrine reuptake inhibitors, especially in vulnerable populations such as octogenarians. We present a case of SS caused by venlafaxine use, a serotonin-norepinephrine reuptake inhibitor indicated in the treatment of the major depressive disorder, generalized anxiety disorder, and panic disorder.

CASE PRESENTATION

An 89-year-old female with a past medical history of right lung lower lobe adenocarcinoma, pheochromocytoma, essential hypertension, hyperlipidemia, type 2 diabetes mellitus, COPD, and chronic diastolic heart failure presented to the ED with altered mental status. The patient's social history was negative for alcohol, tobacco, and illicit drug use. Relevant home medications include venlafaxine and oxycodone. On presentation, the patient was awake but not alert or oriented and not able to follow commands. The patient was in severe distress and appeared agitated. She was experiencing diffuse abdominal pain to palpation with no rebound or guarding. Musculoskeletal examination showed +1 bilateral lower extremity edema and generalized rigidity with muscle hypertonicity. Bilateral hands were closed in a fist. The bilateral upper extremities showed a tremor. Deep tendon reflexes could not be evaluated due to excessive muscle rigidity and shivering. The skin was warm, moist, flushed, and diaphoretic. The rest of the physical examination was within normal limits. Initial vitals are listed in table 1:

BP	HR	RR	O_2	T
242/106 mmHg	108 bpm	36 bpm	98% on 4L	102.2˚F

Table 1: Patient's vitals upon presentation.

CASE PRESENTATION CONTINUED

The blood pressure was treated with sublingual nitroglycerin and improved to the 140s mmHg and then later rebounded up to the 180s mmHg. EKG showed sinus rhythm with a heart rate of 98 bpm and a first-degree atrioventricular block. EKG also showed a normal axis with no significant ST segment or T -wave abnormalities. CT of the head shown in figure 1 revealed no acute intracranial process but showed progression of diffuse cerebral atrophy, chronic microangiopathic ischemic changes, and an old lacunar infarct in the right basal ganglia. CXR shown in figure 2 showed left perihilar hazy ill-defined opacity. The patient was started on ceftriaxone and doxycycline for possible pneumonia. Venlafaxine and oxycodone were stopped. Urinalysis was unremarkable.
Relevant findings from labs are shown in table 2.

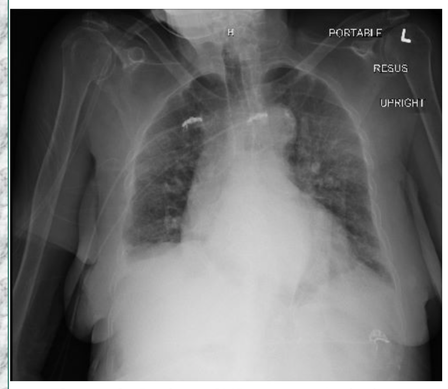

Figure 2: Patient CXR upon admission.

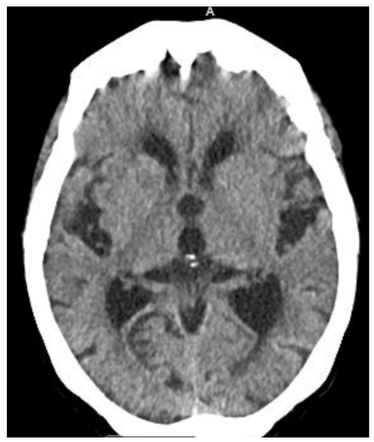

Figure 1: Head CT upon admission.

Lab Test	Value	Normal Value
WBC (mm^3)	24.2	4,500-11,000
Potassium (mMol/L)	3.2	3.5-5.1
AST (units/L)	178	13-39
ALT (units/L)	97	7-52
Urea Nitrogen (mg/dL)	28	7-25
Creatinine (mg/dL)	1.18	0.60-1.20
ABG pH	7.47	7.35-7.45

Table 2: Relevant labs upon admission.

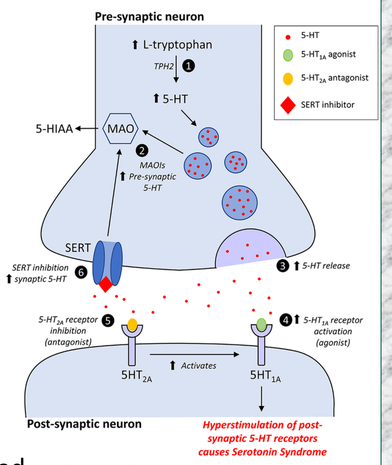

Figure 3: Mechanism of SS. (Scotton et al., 2019)

Troponin and BNP levels were elevated, however an EKG and echocardiography showed normal heart function.
The patient was symptomatically treated with Tylenol for fever, nitroglycerin for hypertension, and diazepam for agitation. The patient's mental status failed to improve despite 48-72 hours of antibiotics and she remained hypertensive despite medical therapy, therefore the patient was admitted to the ICU and cyproheptadine was administered, improving her blood pressure and mental status.

DISCUSSION

- SS is a rare and life-threatening condition caused by an excessive amount of serotonin that over activate the central and peripheral postsynaptic 5HT (5-hydroxytryptamine)-1A and 5HT-2A receptors [1]
- Leads to a triad of symptoms including altered mental status, neuromuscular abnormalities, and autonomic hyperactivity. SS presents with symptoms including hyperreflexia, myoclonus, rigidity, restlessness, delirium, confusion, diaphoresis, hypertension hyperthermia, mydriasis, and tachycardia [3]
- Opioids are known to precipitate SS [1]
- This patient was using an opioid and an SNRI, oxycodone, and venlafaxine, respectively
- Both medications have serotonin reuptake inhibitor characteristics, shown in figure 3, and the combination is thought to have caused SS in this patient
- The elderly population is more vulnerable to medication accumulation due to slower metabolic rates
- Venlafaxine is primarily metabolized in the liver by CYP2D6/3A3/4 isoenzymes, which makes patients with genetic polymorphisms more susceptible to serotonin syndrome [3]
- The diagnosis of serotonin syndrome should be done quickly for early supportive treatment to prevent morbidity and mortality
- History and physical exam findings are highly important in aiding diagnosis [1]
- Treatment involves removing offending substances, sedation, supportive care, oxygen, fluids, cardiac monitoring, and cyproheptadine [1]
- Educating the clinicians and patients may assist in minimizing the prevalence of SS [7]

CONCLUSION

- SS is a predictable and life-threatening condition caused by the overactivation of serotonin receptors
- Symptoms of altered mental status, muscular abnormalities, and autonomic dysregulation are present
- SS is precipitated by medications that elevate serotonin levels such as SSRIs, SNRIs, MAOIs, opioids, and TCAs
- Early recognition is critical to ensure appropriate resuscitative measures and to limit further use of drugs that can exacerbate symptoms
- Treatment involves the removal of the offending medication, sedation, paralytics, and serotonin antagonists depending on the severity of the condition

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