A psychiatric whodunit: Serotonin syndrome in the emergency department

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ABSTRACT

Serotonin syndrome is a life-threatening reaction associated with serotonergic agents. Its mortality is estimated around 11%, hence prompt diagnosis is necessary [1]. Given the variability of its presentation, physicians often misdiagnose this devastating condition. We present a case of serotonin syndrome seen in the Emergency Department by an on-call psychiatric resident and review the Hunter Serotonin Toxicity Criteria, emphasizing the importance of physician familiarity with these criteria.

Keywords: Serotonin Syndrome; Paroxetine; Emergency Department

1. INTRODUCTION

Serotonin syndrome is a life-threatening reaction associated with serotonergic agents. Its mortality is estimated around 11%, hence prompt diagnosis is necessary [1]. Given the variability of its presentation, physicians often misdiagnose this devastating condition. We present a case of serotonin syndrome seen in the Emergency Department by an on-call psychiatric resident.

2. CASE

A 28-year old male was brought to the ED for altered mental status (AMS). He presented shirtless, shoeless, diaphoretic, pale with dilated pupils and chapped lips, and smelled of urine. He was oriented only to self, and screaming incoherently while thrashing about on the bed. Initial vitals showed his blood pressure was 139/74, his heart rate was 120, his respirations were 18 breaths per minute, and his temperature was 98.3 degrees Fahrenheit. The ED physician had ordered labs including a CBC, CMP, urinalysis, urine toxicity, BAL, and TSH. The results of these labs were all within normal limits. A psychiatric consult was requested by ED staff as the etiology for this presentation was unclear.

Upon consultation the psychiatry resident noted the patient to be repeating specific phrases including “Mississippi, Mississippi, I’m in the military” and “I need to know the date”. He denied any pertinent medical or substance abuse issues, and denied taking any daily medications. He could not provide collateral contact information, and was not carrying a wallet or phone for any further information to be obtained. Medical records contained one note from six years prior detailing outpatient treatment for depression, for which he was discharged due to non-compliance. Given his history of depression, unstable vital signs and combative behavior he was initially thought to have either purposefully or accidentally overdosed on drugs or medications. As his lab work did not identify any substances in his system, the resident became concerned about serotonin syndrome and neuroleptic malignant syndrome (NMS), prompting him to order a CPK. Serotonin syndrome and NMS were considered as the patient’s presentation, lab results, and physical exam did not direct the ED staff or psychiatry resident to a diagnosis, and the resident evaluating the patient wanted to rule out life-threatening psychiatric causes. His CPK level was found to be 264 U/L. In males total CPK limits are 32 - 267 U/L [2].

Given the patient’s elevated CPK level, he was re-examined by the psychiatric resident who was looking for signs consistent with serotonin syndrome or NMS. The patient displayed mild muscle rigidity but no myoclonus was present, and his rigidity was considered unimportant. Without myoclonus the resident incorrectly thought that serotonin syndrome was ruled out. Upon discussion of the case with the supervising staff, it was considered that the patient’s agitation could be due to intoxication with PCP that was not detected by his UDS. The staff recommended administering vitamin C, which can disperse PCP from fat cells allowing PCP to then be detected. 1 gram of vitamin C was administered, and repeat UDS did not detect PCP. At this point the patient’s agitation required medication. Over 40 minutes, he received 4 mg IV lorazepam and 20 mg olanzapine, neither of which was effective. He calmed mildly after placed in soft 4-point restraints. A CT scan was considered, but
risks outweighed the benefits. The decision was made to consult the ICU as although his diagnosis remained unclear, he required constant monitoring. Upon ICU evaluation, vital signs shifted to the following: BP 98/55, HR 140, RR 18. Despite the fluctuations in his vitals, the ICU was unconvinced of the severity and decompensating nature of his illness, instead attributing it to intoxication with some unknown substance. However, they did agree to admit the patient to provide supportive care and continuous monitoring.

In the ICU, AMS continued for which he was given olanzapine (40 mg) and lorazepam (6 mg). He remained disoriented with fluctuating vitals until day number four of admission, when his vital signs stabilized, his agitation resolved and he was fully oriented and able to effectively communicate. The patient was now able to report the name of his outpatient psychiatrist. Informed of patient status, his psychiatrist came to the ICU with two important documents. The first was a color-coded list of the patient’s previous doctors and their 20 different treatment courses over the past ten years. His past diagnoses included bipolar I disorder, bipolar II disorder, attention deficit hyperactivity disorder, post traumatic stress disorder, and major depressive disorder. The second item the physician provided was a hand-drawn timescale of visits until day number four of admission, when his vital signs stabilized, his agitation resolved and he was fully oriented and able to effectively communicate. The patient was now able to report the name of his outpatient psychiatrist. Informed of patient status, his psychiatrist came to the ICU with two important documents. The first was a color-coded list of the patient’s previous doctors and their 20 different treatment courses over the past ten years. His past diagnoses included bipolar I disorder, bipolar II disorder, attention deficit hyperactivity disorder, post traumatic stress disorder, and major depressive disorder. The second item the physician provided was a hand-drawn timescale of medications done by the patient. It involved unconventional medications and dosing schedules being taken by the patient prior to his admission. His morning medications included alprazolam (1 mg), aspirin (81 mg), dextroamphetamine/amphetamine (30 mg), fish oil (1000 mg), lamotrigine (100 mg), paroxetine (40 mg), and a vitamin B6 tablet.

At noon he took alprazolam (1 mg) and dextroamphetamine/amphetamine (15 mg). This was followed by another dose of both alprazolam (1 mg) and dextroamphetamine/amphetamine (30 mg) at 3 p.m. His bedtime regimen consisted of clonazepam (2 mg), fish oil (1000 mg), lamotrigine (100 mg), prazosin (3 mg) and zolpidem (10 mg). This large, inconsistent amount of medication was due to his doctor-shopping behavior, as he was seeing at least four providers at once. When confronted with this information, he readily confessed both his inappropriate behavior and his suicide attempt. Prior to admission, he had become suicidal and had taken a 90-day supply of paroxetine followed by ondansetron to prevent vomiting. The attempt was lethal in intent, and had it not been for aggressive hydration, monitoring of vitals, and treatment with benzodiazepines, could have ended in completed suicide.

3. DISCUSSION

3.1. Overview

Serotonin syndrome, a life-threatening reaction to serotonergic medications, can be produced by any serotonergic drug. A search of PubMed with keywords “serotonin syndrome” revealed a variety of sources too innumerable to discuss in this brief case report review, but did clarify the illness. Its proposed etiology is stimulation of 5-HT2A receptors, causing excess intrasynaptic 5-hydroxytryptamine [2]. This syndrome more frequently occurs after administration of a second serotonergic agent, and is also referred to as serotonin toxicity. Medications from many different classes have serotonergic properties, such as the antibiotic linezolid, the pain medication tramadol, and the antitussive dextromethorphan. Although any serotonergic agent can be the cause, some medications are more likely to precipitate serotonin syndrome than others. It should be noted that the most common symptom of serotonin syndrome is myoclonus, present in 57% of cases, but it is not necessary for diagnosis [1,2].

3.2. Diagnosis

The true incidence of serotonin syndrome is unknown. Diagnosis involves known exposure to a serotonergic agent with alterations in cognition and behavior, autonomic nervous system, and neuromuscular activity. No diagnostic blood test exists, but with extreme muscle rigidity CPK may be elevated [1]. Compiled from an SSRI-alone overdose database, The Hunter Serotonin Toxicity Criteria is used in diagnosis. The Hunter Serotonin Toxicity Criteria is as follows: Diagnosis is made in the presence of a serotonergic agent with spontaneous clonus, inducible clonus with agitation or diaphoresis, ocular clonus with agitation or diaphoresis, hyperreflexia with tremor, or if hypertonic with a temperature over 38°C with ocular or inducible clonus. If the patient fails to meet the above criteria, the diagnosis is not serotonin toxicity [3].

In terms of a differential diagnosis, NMS must be ruled out. Most researchers view the core symptoms of NMS as fever with muscle rigidity, however as with serotonin syndrome, its presentation is quite variable [4]. Adityanjee et al. proposed a complex research criteria for NMS in 1999 which can help with diagnosis of NMS. Their work suggests that severe (Type I) NMS can be diagnosed if all of the following are present: altered sensorium, extrapyramidal symptoms, hyperpyrexia, autonomic dysfunction, recent ingestion of dopamine deplete or cessation of antiparkinsonian or anticholinergic medication, not due to other condition, and one of another supporting conditions is present (elevated CPK, leukocytosis, low serum iron, elevated LFT’s, myoglobinuria). Less severe types II-IV involve meeting less of the above criteria. Our patient’s presentation was similar and would meet several of these criteria as well. Unfortunately, the presence of a dopaminergic or a serotonergic agent was not known, nor was the physician examining the patient.
using Hunter Criteria or Adityanjee Rules to rule out serotonin syndrome or NMS [5-7].

3.3. Treatment

Treatment is necessary for every case of serotonin toxicity, with mortality estimated at 11%. Supportive care is essential, but no guidelines exist for the use of serotonin antagonists. Providers should first cease all serotonergic agents and admit to hospital, with severe cases requiring ICU transfer. The most common cause of death is hyperthermia. [1] Most patients improve within 24 hours; 25% of patients require endotracheal intubation and neuromuscular Benzodiazepines are nonspecific serotonin antagonists and likely also work by relaxing the patient, but cyproheptadine appears most effective. The reasoning behind this is unclear, but likely involves histamine receptors. Doses from 4 to 12 mg orally can be repeated in 2 hours if no response to the initial dose is noted. It is, however, only available orally. Cyproheptadine should be discontinued if no response is noted after 32 mg. Responders are given 4 mg every 6 hours for 48 hours. Chlorpromazine antagonizes 5-HT2A receptors, and can be given intramuscularly but blocks dopamine receptors and can exacerbate NMS, increase rigidity and hypotension, and lower the seizure threshold. Bromocriptine and other dopamine agonists should not be used, and dantrolene, a muscle relaxant, should only be considered in cases of malignant hyperthermia. Once recovered, serotonergic agents should be avoided, and if necessary risks vs. benefits should be discussed with the patient and close monitoring should be initiated, as the incidence of recurrence is unknown [1]. Our patient received multiple lorazepam doses, and despite ICU reluctance was given proper hydration and vital sign monitoring. Had he needed intubation or muscle paralysis, he would have received it rapidly.

4. CONCLUSION

With the frequent misdiagnosis and high mortality of serotonin syndrome, all physicians, not just psychiatrists, should familiarize themselves with the Hunter Serotonin Toxicity Criteria.

REFERENCES


