

CASE REPORT

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Serotonin Syndrome with Escitalopram and Concomitant Use of Cocaine: A Case Report

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Introduction: Serotonin syndrome is a potentially life-threatening condition caused by excessive serotonergic activity in the central nervous system. It is characterized by mental status changes (eg, confusion, agitation, lethargy, coma), autonomic instability (eg, hyperthermia, tachycardia, diaphoresis, nausea, vomiting, diarrhea, dilated pupils), and neuromuscular hyperactivity (eg, myoclonus, hyperreflexia, rigidity, trismus). Serotonin syndrome classically occurs in patients receiving two or more serotonergic drugs, but it can occur with monotherapy. We report a case of a 20-year-old man who developed serotonin syndrome resulting from overdose of Escitalopram with concomitant use of cocaine. It is a very important area in medicine as serotonin syndrome should be suspected especially in drug abusers who are being treated with psychotropic agents for mental illnesses.

Keywords: serotonin syndrome, escitalopram, cocaine, overdose, poisoning

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Case Report

A 20-year-old male patient was admitted for altered mental status and agitation of unknown etiology. His past medical history was notable for depression and anxiety for which he had recently begun treatment with Escitalopram (selective serotonin re-uptake inhibitor), Qetiapine (atypical antipsychotic), and Clonazepam (benzodiazepine). Approximately four hours prior to admission, he had snorted multiple crushed tablets consisting of Percocet, Escitalopram 20 mg, Quetiapine 100 mg and Clonazepam because of abdominal pain and worsening feelings of sadness. He was found at home by his parents. He was noted to be very agitated and disoriented. He was brought immediately to the emergency department. His parents couldn't specify the exact amount of the ingested medications. It was also reported that he had been using cocaine for one year for recreational purposes. The exact time of his last recreational cocaine use couldn't be determined as patient was non-cooperative.

On admission, the patient was confused, lethargic, non-communicative, disoriented and agitated with Glasgow coma scale score of 10. His physical examination was significant for tachycardia (133 beats/minute), elevated body temperature (101.4 °F), slow and shallow breathing (11 breaths/minute), diaphoresis and generalized anxiousness. Neurologic exam was positive for hyperreflexia, clonus on dorsiflexion of the feet, and muscular rigidity. The patient's respiratory rate gradually decreased with accompanying desaturations to 80% necessitating intubation with mechanical ventilation. His laboratory results revealed no abnormalities including the urine drug screen. Computerized tomography of the head and lumbar puncture were also unremarkable.

Serotonin syndrome was considered after ruling out infection and cerebrovascular accidents as potential etiologies for the patient's condition. Escitalopram was withheld, and the patient was aggressively hydrated with intravenous fluids. He received one dose of Lorazepam (2 mg IV push) for agitation. Within 24 hours, the patient's mental status had improved and he was able to be extubated. By the second hospital day, the patient was declared medically stable and transferred to the psychiatric ward. Percocet (oxycodone/acetaminophen), Clonazepam and Qetiapine (serotonin, dopamine and adrenergic

antagonist with negligible anticholinergic properties) are known to depress CNS function and may have contributed to patient's mental status but the clinical history and physical exam with autonomic instability (hyperthermia, tachycardia, diaphoresis) and neuromuscular hyperactivity (hyperreflexia, rigidity, and myoclonus) pointed more towards serotonin syndrome with the main culprits being escitalopram and cocaine as they both increase serotonin activity in the brain. Cocaine blocks the serotonin uptake and therefore combination with escitalopram is potentially significant.

This case represents a rare incidence of serotonin syndrome occurring after an intentional overdose of escitalopram. As such, it highlights the importance for physicians to maintain a high suspicion for serotonin syndrome as a potential diagnosis when encountering an agitated and confused patient known to be on serotonin-modifying drugs.

Escitalopram is a selective serotonin reuptake inhibitor (SSRI), used to treat depression and generalized anxiety disorder. Therapeutic doses range from 10 mg/day to 20 mg/day. Our patient's dose was 20 mg/day. Common side effects seen with escitalopram use are nausea, constipation, diarrhea, dizziness and impotence. An adverse effect of escitalopram, as with other SSRIs, is the Serotonin syndrome.¹ The symptoms are variable and can easily be missed.¹ No single receptor appears to be responsible for the development of the Serotonin syndrome, although several studies suggest that agonism of serotonin-1A (5-HT_{1A}) and serotonin-5A (5-HT_{2A}) receptors contribute substantially to the condition.² Cocaine prevents serotonin uptake and its combination with escitalopram may lead to serotonin syndrome.⁹

The diagnosis of Serotonin syndrome is made clinically. It is characterized by mental status changes (eg, confusion, agitation, lethargy, coma), autonomic instability (eg, hyperthermia, tachycardia, diaphoresis, nausea, vomiting, diarrhea, dilated pupils), and neuromuscular hyperactivity (eg, myoclonus, hyperreflexia, rigidity, trismus).¹ The combination of SSRIs with other serotonergic drugs (eg, tryptophan, illicit drugs like cocaine and MDMA, "ecstasy") or drugs with serotonin properties (eg, lithium, meperidine, triptans) can lead to serotonin syndrome.³ Serotonin syndrome classically occurs in patients receiving two or more serotonergic drugs,

**Table 1.** Timeline of the events for the patient.

Time	Pulse	RR	Temp	BP	Pulse ox
0100 AM	133	10	101.4	140/69	Blood, urine cultures, chest x-ray and head CT done
0130	131 (ativan 2 mg given)	10	100.3	135/66	Ceftriaxone and Vancomycin given
0235	122	8	99.9	135/65	93%
0240	112	8	99.9	109/52	99%
		Intubated (CMV-TV 500, PEEP 5, FiO ₂ 40%, R 20)	Rapid sequence intubation		ABG: pH 7.19, pCO ₂ 70.9, pO ₂ 177, HCO ₃ 26.5
0330	91	20	99.7	103/51	99%
					ABG: pH 7.47, pCO ₂ 28.2, pO ₂ 213, HCO ₃ 20.3
0350	75	20	99.5	115/66	99%
0430	75	20	99.8	126/84	100%

but it can occur with monotherapy. Selective serotonin reuptake inhibitor (SSRI) monotherapy has an incidence of 0.5 to 0.9 cases of SS per 1000 patient-months.³ Concomitant use of an SSRI with a monoamine oxidase inhibitor (MAOI) poses the greatest risk of developing Serotonin syndrome. The Hunter Serotonin Toxicity Criteria are used to diagnose serotonin syndrome and require the presence of one of the following classical features or groups of features: spontaneous clonus, inducible clonus with agitation or diaphoresis, ocular clonus with agitation or diaphoresis, tremor and hyperreflexia, hypertonia, temperature above 100.4 °F (38 °C), and ocular or inducible clonus.³ There are no specific laboratory tests to diagnose Serotonin syndrome. Laboratory and other diagnostic tests are used to rule out alternative explanations of symptoms. Blood 5-HT levels are not useful because it is the local concentration at nerve terminals that is responsible for the physiologic effects.^{4,5} A strong clinical suspicion, known exposure to serotonergic agents, demonstration of specific signs and symptoms, and exclusion of other medical and psychiatric conditions are required for the diagnosis.

Key differential diagnoses to the serotonin syndrome are the other potentially life-threatening hyperthermic syndromes: neuroleptic malignant syndrome (NMS), malignant hyperthermia and anticholinergic poisoning.³ However, important points in history and physical examination facilitate the distinction between the three. NMS is a reaction to several antipsychotic drugs, eg, such as chlorpromazine and haloperidol.⁵ NMS is due to dopamine receptor blockade and it

usually starts with muscular rigidity followed by hyperthermia and altered consciousness. Unlike the serotonin syndrome, NMS is exclusively caused by dopaminergic drugs. Symptoms develop over days and resolve over days to weeks.⁵ In the serotonin syndrome, the onset and resolution of symptoms occur within hours. Most patients present within 6 hours of increasing dosage, starting a new drug, or taking an overdose. A history of neuroleptic usage combined with the presence of bradykinesia or “lead pipe” rigidity on examination distinguishes the NMS from that caused by serotonin excess.⁵ It is important to note that serotonergic agents include nonprescription drugs, illicit drugs, and diet supplements. The time line of events for the patient is listed in Table 1.

Malignant hyperthermia (MH) is a rare life-threatening condition that is usually triggered by exposure to certain drugs used for general anesthesia; specifically, the volatile anesthetic agents and the neuromuscular blocking agent, succinylcholine. It is due to an abnormally increased release of calcium from the sarcoplasmic reticulum.^{6,7} Susceptibility to MH is often inherited as an autosomal dominant disorder, for which there are at least 6 genetic loci of interest, most prominently the ryanodine receptor gene (RYR1).⁶ The syndrome occurs within minutes of exposure to the anesthetic agents, unlike Serotonin syndrome, and presents with muscular rigidity, a hypermetabolic state reflecting increased oxygen consumption and increased carbon dioxide production, metabolic acidosis, and hyperthermia.⁷ The onset of symptoms, history of exposure to anesthetic agents,



family history, and physical examination positive for skin mottling and hyporeflexia may distinguish malignant hyperthermia from serotonin syndrome.⁸ On the other hand, anticholinergic syndrome (ACS) is produced by the inhibition of cholinergic neurotransmission at muscarinic receptor sites. The distinguishing feature of anticholinergic syndrome is dryness of the skin compared with diaphoresis in serotonin syndrome.

Successful management of serotonin syndrome relies upon prevention, early recognition, and supportive care. Combinations of serotonergic medications should be avoided and at least 2 to 4 weeks should pass between discontinuation of an MAOI and initiation of another serotonergic agent.⁶ Acute management is based on 2 simple principles: discontinuation of all serotonergic medications and provision of necessary supportive care. Severe forms of the syndrome may require aggressive measures, including neuromuscular-blocking agents, mechanical ventilation, benzodiazepines (for sedation), and external cooling.⁶ Mild cases generally resolve within 24 to 72 hours with conservative therapy and removal of the causative drugs. Patients who are severely hyperthermic with temperatures $> 41^{\circ}\text{C}$ (106°F) should be given IV sedation, paralyzed, and intubated. Cooling blankets can be used for patients with mild to moderate hyperthermia.

In addition, pharmacologic therapy in the acute management of serotonin syndrome includes benzodiazepines (Lorazepam or Diazepam) and nonspecific serotonin receptor blockers such as cyproheptadine, chlorpromazine, methysergide, and propranolol.⁶ Benzodiazepines are used for control of agitation and preferred over physical restraints. The efficacy of cyproheptadine in the treatment of serotonin syndrome has been documented.⁴ Atypical antipsychotic agents with serotonin antagonist properties (eg, olanzapine 10 mg SL) have been tried with some success. There is no role of acetaminophen in the management of serotonin syndrome.

Conclusion

This case shows a rare incidence of serotonin syndrome with Escitalopram use and concomitant abuse of cocaine.⁹ It is very important that physicians are familiar with the signs and symptoms of Serotonin syndrome and should suspect it in anyone with altered

mental status who is taking serotonin-modifying drugs. Because of its protean manifestations, the illness can easily be missed while the patient is subjected to a variety of unnecessary tests. In addition, the offending agent may be continued, causing an exacerbation of the syndrome with devastating consequences. This case emphasizes the fact that drug abusers with mental illness on psychotropic pharmacological agents have a very high incidence of developing serotonin syndrome.

Author Contributions

Conceived and designed the experiments: HM, KK. Analysed the data: HM. Wrote the first draft of the manuscript: HM. Contributed to the writing of the manuscript: HM, KK. Agree with manuscript results and conclusions: HM, KK. Jointly developed the structure and arguments for the paper: HM, KK. Made critical revisions and approved final version: HM, KK. All authors reviewed and approved of the final manuscript.

Disclosures and Ethics

As a requirement of publication author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. Any disclosures are made in this section. The external blind peer reviewers report no conflicts of interest.

References

1. Sclar DA, Robison LM, Castillo LV, et al. Concomitant use of triptan, and SSRI or SNRI after the US food and drug administration alert on serotonin syndrome. *Headache*. Feb 2012;52(2):198–203.
2. Baptista G, Eiden C, Monguillot P, Philibert C, Jeandel C. Serotonin syndrome during treatment with low dose of escitalopram associated with miconazole mucoadhesive tablet: a suspected drug interaction. *Int Psychogeriatr*. Jan 17, 2012:1–3.
3. Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med*. 2005;352:1112–20.
4. Kumar BN, Shah R, Grover S. Serotonin syndrome while switching antidepressants. *Indian J Psychiatry*. Oct 2011;53(4):372.



5. McDermott M, Noordsy DL, Traum M. Neuroleptic malignant syndrome during multiple antipsychotic therapy. *Community Ment Health J.* Oct 30, 2011.
6. Nierenberg DW, Semperebon M. The central nervous system serotonin syndrome. *Clin Pharmacol Ther.* 1993;53:84–8.
7. Bhalla T, Maxey D, Sawardekar A, Tobias JD. Anesthetic management of a pediatric patient with neuroleptic malignant syndrome. *J Anesth.* Nov 19, 2011.
8. Migita T, Mukaida K, Kobayashi M, Hamada H, Kawamoto M. The severity of sevoflurane-induced malignant hyperthermia. *Acta Anaesthesiol Scand.* Mar 2012;56(3):351–6.
9. Klys M, Kowalski P, Rojek S, Gross A. Death of a female cocaine user due to the serotonin syndrome following moclobemide-venlafaxine overdose. *Forensic Sci Int.* Jan 30, 2009;184(1–3):e16–20. Epub Jan 7, 2009.