

Serotonin Syndrome in the Intensive Care Unit Following Orthotopic Heart Transplantation: A Case Report

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Case Report

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Abstract

The diagnosis of serotonin syndrome in the ICU population is challenging due to its relative complexity and clinical unfamiliarity. Our report is based on a clinical presentation of a 64 year-old female on chronic SSRI therapy who underwent orthotopic heart transplantation (OHT), followed by hyperthermia and autonomic instability. The symptoms were related to the subsequent vasoplegic syndrome requiring methylene blue. The purported offending agents were discontinued and her symptoms improved over the next several hours. Although serotonin syndrome is uncommon and becomes a difficult diagnosis to make, clinicians need to recognize it early.

Keywords: Serotonin Syndrome; Methylene Blue; Intensive Care Unit.

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Introduction

Serotonin syndrome is a potentially life threatening adverse drug reaction caused by excessive activation of postsynaptic serotonin receptors in the central nervous system [1]. Clinically, the syndrome is manifested as autonomic instability, mental status abnormalities, neuromuscular changes and hyperpyrexia [2]. Due to the potentially wide spectrum of presentation and overall physicians' lack of familiarity with the disease, serotonin syndrome becomes a difficult diagnosis to make, particularly in the intensive care unit (ICU) setting. Generally this syndrome is caused by an overdose with a single agent either intentionally or by accident, nevertheless the majority of severe cases result as an interaction between two or more agents that enhance serotonin transmission [1].

Case Presentation

We describe the case of a 64 year-old female who underwent

orthotopic heart transplantation (OHT). The patient has a history of non-ischemic cardiomyopathy with a left-ventricular assist device (LVAD), hypertension, gastro-esophageal reflux disease, asthma, monoclonal gammopathy, and depression. She was found to have a malfunctioning LVAD which placed her in to category IA for transplantation. After an appropriate donor became available, OHT was performed with no major intraoperative complications noted. Following her transplant surgery, she was brought to the intensive care unit intubated on several vasopressors and inotropes for refractory shock. She remained hypotensive despite large doses of vasopressors; therefore methylene blue was used for refractory vasoplegic syndrome. As the effects of general anesthesia subsided, there were no focal abnormalities noted in her neurologic evaluation. As a result of ondansetron administration for nausea, she progressively developed dilated pupils, ocular clonus, and diffuse muscle rigidity. She subsequently became febrile to 105.7 degrees Fahrenheit, with a bilateral ankle clonus on physical exam. Delayed malignant hyperthermia and neuroleptic malignant syndrome were clinically ruled out, and serotonin syndrome was suspected. The patient's clinical history as well as pharmacologic treatment including sertraline, methylene blue and ondansetron all implicated serotonin syndrome as a cause for her abnormal neurologic findings. The purported offending agents were discontinued, and she was treated symptomatically with cyproheptadine, acetaminophen, lorazepam and active cooling. Over the next several hours, her neurologic symptoms improved and her fever subsided. She experienced a full neurologic recovery, and was subsequently discharged home in stable condition.

Discussion

Serotonin syndrome is an uncommon but fatal diagnosis, infrequently encountered in the critical care setting. The serotonin syndrome is often described as a clinical triad of mental-status changes, autonomic hyperactivity, and neuromuscular abnormalities, but not all of these findings are consistently present in all patients with the disorder [2]. Serotonin syndrome has been observed in all age groups, including newborns and the elderly.

The increasing use of serotonergic agents in medical practice increased the frequency of this diagnosis [3].

Generally, non-specific symptoms are identified first during the mild phase, and rapidly progress to a life threatening toxicity [2]. There is an extensive list of drugs and drug interactions responsible for the development of this syndrome.

A landmark paper published by Dunkley et al. in 2003 introduced a set of rules known as Hunter's Criteria in order to diagnose this syndrome [4]. The diagnosis is founded on the presence of recent use of a serotonergic agent within the past five weeks. There is no single lab test to confirm the diagnosis of this syndrome. The clinical picture commonly includes hypertension and tachycardia. Our scenario was clouded due to the fact that all the initial symptoms were noticed in a critical care transplant recipient with augmented hemodynamic parameters.

Methylene blue is commonly used as an antidote in cyanide toxicity. It has been used in an off-label fashion for vasoplegic syndrome following cardiopulmonary bypass. What is sometimes not known is that this drug is a potent monoamine oxidase inhibitor (MAOI), which increases free levels of serotonin in the CNS [5].

Discontinuation of precipitating agents as well as adequate management of agitation, hyperthermia, and autonomic instability is essential. Agitation should be promptly treated with benzodiazepines, and active cooling should be employed. Anti-pyretics should not be intended to treat hyperthermia resulting from muscle contraction, without hypothalamic involvement. Autonomic instability from MAOI should be treated with direct-acting vas-

oactive amines in order to avoid an exaggerated response from indirect agents. Cyproheptadine, a 5-HT_{1A} & 2A antagonist is commonly used to block serotonergic effects, although its efficacy has not been clinically studied.

Conclusion

The diagnosis of serotonin syndrome in the ICU population is challenging due to its relative complexity and clinical unfamiliarity. Diagnosis is mostly dependent on history, physical examination and clinical suspicion. The utilization of complex pharmacologic agents in the ICU could act as confounding factor for diagnosis of serotonin syndrome. Our case represents a case of serotonin syndrome involving a post-cardiac transplant patient on chronic SSRI therapy who underwent (Cardiopulmonary Bypass) CPB, with subsequent vasoplegic syndrome requiring methylene blue in the critical care setting.

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