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Serotonin Syndrome after a Single Dose of Sertraline: A Case Report

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ABSTRACT

Backgrounds: Serotonin Syndrome is a rare and life-threatening drug reaction that occurs with increased serotonin activity in the brain as a result of taking therapeutic doses or excessive amounts of serotonergic-acting drugs or using multiple serotonergic-acting drugs together. It is characterized by neuromuscular abnormalities, autonomic hyperactivity, and cognitive/behavioral changes. **Case:** In our case, we describe a serotonergic syndrome, which developed as a result of the use of a therapeutic single dose serotonergic drug in a 15-year-old girl and its treatment. **Conclusions:** The determination of the history of serotonergic drug use, early recognition of the mental, autonomic, and neurological finding triad, and the early application of supportive medical treatments ensure the effective and successful management of the case.

Keywords: Serotonin Syndrome, sertraline, supportive therapy

INTRODUCTION

Serotonin Syndrome (SS) is a life-threatening toxic condition that occurs when serotonergic drugs are used at therapeutic levels, taken in toxic doses, or consumed together with more than one agent with serotonergic effects. SS is a syndrome with a wide range of symptoms that can easily be overlooked when presented with mild symptoms. These symptoms occur as a result of excessive activation of 5-HT (hydroxytryptamine) receptors in the central nervous system, vascular endothelial cells, and platelets. Some antidepressants, antibiotics, migraine medications, cough medications, narcotic agents, dietary supplements, and analgesics are accused in the etiology of SS [1,2]. Sudden discontinuation of some drugs also causes SS [3-5]. Although clinically a triad of neuromuscular abnormalities, autonomic hyperactivity, and changes in consciousness is expected, all symptoms may not be present in each patient [3]. While tremor and diarrhea are observed in mild cases, severe symptoms, such as high fever, metabolic acidosis, rhabdomyolysis, renal failure, epileptic seizures, and delirium may occur in more severe cases [5]. When the patient has a history of serotonergic drug use, SS should be suspected and caution should be exercised in case of side effects, such as rigidity, tremor, sweating, mydriasis, and hypertension [4]. The first approach in its treatment is to discontinue the serotonergic agent used, to provide

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intravenous hydration, to give supportive treatments, and to control agitation [2].

We present a case of serotonin syndrome, who received the medication after the diagnosis of major depressive disorder, a condition observed less frequently after the first dose of sertraline 25 mg, and describe the approach to its treatment.

THE CASE PRESENTATION

A 15-year-old girl was brought to our pediatric emergency department by her mother with complaints of abdominal pain, nausea, weakness in the legs, chills, and shortness of breath. Her medical history revealed the use of Sertraline 25 mg tablets due to a diagnosis of depressive disorder and her complaints started approximately 6 hours after ingesting the first dose. The patient did not have any other drug or substance use history, and she did not have any additional diseases.

The general condition of the patient was moderate to good, conscious, oriented and agitated. The Glasgow Coma Score was rated as 14. In the vital follow-ups, fever was 37.2 °C, arterial blood pressure was 137/90 mmHg, and heart rate was 97/min. On physical examination, her pupils were isochoric and light reflex was bilaterally reactive. The patient complained of nausea, vomiting, abdominal pain, diarrhea, sweating, tremor, weakness, dizziness, shortness of breath, weakness in the bilateral legs, and inability to walk. In the physical examination, except for tachypnea and loss of muscle strength in the legs, other system examinations were evaluated as normal. The patient's self-care was inadequate, she appeared anxious in the mental state evaluation, but did not demonstrate any psychotic symptoms.

In the initial examinations, the creatine kinase (CK) value was >2150 mg/dl (reference range: 0-145 mg/dl), CK-MB: 56 mg/dl (ref. range: 0-24mg/dl), phosphorus: 5.01 mg/dl (ref. range: 2.5-4.5), AST: 64.5IU/L (0-35IU/L), and the blood gas analysis revealed mild metabolic acidosis (pH: 7.34, pCO2: 41.9 mmHg, HCO3: 20.4 mEq/l). Other blood test results were among the reference values. No pathology was detected in the imaging studies. The medication was discontinued, IV hydration therapy was started, and the Department of Child and Adolescent Psychiatry was consulted with the preliminary diagnosis of 'Serotonin Syndrome'.

In the control blood tests taken at the 24th hour of the patient's follow-up, the measurements were: CK 1288 mg/dl, CK-MB 36.5 mg/dl, and blood pH 7.39. The patient's general condition was good; she was conscious, her vitals were stable, and her physical complaints regressed. The patient was discharged with an outpatient check-up appointment.

At the 48th and 72nd hours of the outpatient clinic controls, it was observed that the general condition of the patient was better, her vitals were stable, and her symptoms regressed further. In addition, CK, CK-MB values were decreased in the control blood tests taken.

Discontinuation of the serotonergic drug, regression of symptoms after IV hydration therapy, complete resolution of all symptoms within one week of follow-up, and regression of values to the normal reference ranges in blood tests supported our diagnosis of "Serotonin Syndrome".

CONCLUSION

Serotonin Syndrome (SS) is a life-threatening drug reaction resulting from excessive serotonergic activation in the central and peripheral nervous system and is characterized by mental, autonomic, and neuromuscular dysfunctions. More than one serotonergic receptor responsible for this picture has been described in the literature. Of these, 5-HT1A is responsible for sleep regulation, thermoregulation, eating, neural inhibition, depression-related hypoactivation, and anxiety-related hyperactivation; 5-HT1B is responsible for muscle tone and movement; 5-HT2A is responsible for neural excitation, peripheral vasoconstriction, and platelet aggregation; 5-HT2B is responsible for smooth muscle contraction; 5-HT3 is responsible for nausea, vomiting, and anxiety; and 5-HT4 is responsible for gastrointestinal motility [6].

SS is a drug reaction that develops due to taking a serotonergic agent at high doses or using it together with another drug containing serotonin, but rare cases have also been reported in the literature when used at therapeutic doses. Symptoms appear within the first 24 hours after taking the drug, and cases are divided into three as mild, moderate, and severe SS according to the clinical situation [1,6]. Diarrhea and tremor may be seen in mild symptoms, while a course leading to coma and death may be observed in severe cases. Hyperreflexia and clonus being more prominent in the lower extremities are also important in the physical examination. Our case's complaints developed after the first dose of serotonergic drug use in the therapeutic range. The diagnosis of SS was clarified by consulting the child psychiatrist with the preliminary diagnosis of SS as a result of the current anamnesis and physical examination findings.

Neuroleptic malignant syndrome, dystonic reactions, encephalitis, and carcinoid syndrome are considered in the first line in the differential diagnosis of SS, especially in terms of neurological symptoms. The coexistence of hyperreflexia, flushing, and clonus are the most specific findings for SS [7].

Although there is no definitive guideline in the treatment of SS, improvement typically occurs within 24 hours in most cases with early diagnosis, discontinuation of triggering drugs, and early initiation of supportive treatment. However,

the findings may take longer depending on the half-life of the agent used or the state of its active metabolites. Considering the patient's clinical condition in terms of supportive treatments, intravenous hydration, external cooling, use of antihypertensive drugs, and the use of anxiolytic/sedative agents are recommended in agitated patients. In severe cases, mechanical ventilation support should be provided [2,7]. It is reported that benzodiazepine-derived drugs have an important place in the treatment because of their non-specific inhibition in the serotonergic system [6]. Lorazepam and diazepam can be used as the only treatment option in mild cases due to their effects in treating SS-related myoclonus [8]. Dantrolene can also be preferred in cases unresponsive to benzodiazepines, with severe muscle rigidity and hyperthermia [9]. In severe cases, antiserotonergic agents, such as cyproheptadine and methysergide are used [8,10,11].

The intensity of treatment is proportional to the severity of the symptoms. While discontinuation of the triggering drug and intravenous hydration is sufficient in mild cases, more aggressive treatment may be required in severe cases. In patients with life-threatening hyperthermia and muscle spasms, mechanical ventilation support and sedation may be needed [4,12].

Although many cases report that cyproheptadine, a 5-HT2A antagonist, is successful in antiserotonergic therapy, its use in treatment guidelines has not been finalized yet [13-16]. Atypical antipsychotic drugs with a 5-HT2A antagonist effect can be administered to patients. Olanzapine, which has forms that dissolve in the mouth, is used successfully in treatment, although its mechanism of action is unknown [17]. In severe cases, chlorpromazine, which provides ease of parenteral administration, can also be used [4,18,19].

To control hyperthermia, excessive muscle activity must be eliminated. In severe cases, muscle paralysis should be provided with non-depolarizing drugs, such as vecuronium, and respiratory support should be given to the patient by intubation. Antipyretic agents have no place in the treatment because hyperthermia in SS occurs due to excessive muscle activity independent of the thermoregulatory center [4].

Confusion and changes in consciousness may last for several days, and there is always a risk of death despite treatment [5,18].

Serotonin Syndrome may come to mind more frequently when more than one serotonergic agent is used, and patients with low-dose or single drug use or with milder clinical symptoms may be overlooked. Case reports of single-dose drug use are very rare in the literature. In a case report, a case of SS induced by 30 mg/day of duloxetine was reported [20]. It has been reported that the occurrence of serotonin syndrome with the first use and low dose SSRI may be due to the absence/lowness of congenital liver enzyme activity or hypersensitivity in the receptors [21].

Recognition of the clinic of serotonin syndrome is significant due to the increase in the frequency of depression in adolescence and the widespread use of antidepressant drugs. Therefore, detailed questioning of the drugs used is necessary for early diagnosis and intervention. As a result, the determination of the history of serotonergic drug use, early recognition of the mental, autonomic, and neurological finding triad, and the early application of supportive medical treatments ensured the effective and successful management of the case.

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