

CITALOPRAM-INDUCED SEROTONIN SYNDROME: A CASE REPORT

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Serotonin syndrome is a disorder resulting from excess stimulation of serotonin and is associated with drug interaction, single-drug therapy, and overdose. We report a case involving a 32-year-old man who developed sudden agitation, diaphoresis, subjective fever, tremor, and insomnia. These symptoms were related to doubling the dose of citalopram in combination antidepressant therapy. Discontinuation of the agent resulted in early notable clinical resolution after 1 week. This is a rare report of serotonin syndrome induced by citalopram polytherapy. Although serotonin syndrome is rare, clinicians need to recognize it early.

Key Words: serotonin syndrome, citalopram
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Serotonin syndrome is a disorder resulting from excess stimulation of serotonin (5-hydroxytryptamine, 5-HT), especially 5-HT_{1A} and 5-HT₂ receptors, in the brainstem and spinal cord [1,2]. The onset of serotonin syndrome is observed within 24 hours following administration or overdose of the serotonergic agent [2]. It is characterized clinically by the sudden onset of a triad of symptoms consisting of cognitive or behavioral changes (agitation, hypomania, confusion), autonomic instability (hyperthermia, diaphoresis, diarrhea, mydriasis, tachycardia), and neurologic changes (hyperreflexia, myoclonus, tremor, incoordination, rigidity). Other causes such as infection, substance abuse, or withdrawal must be excluded before making a diagnosis of serotonin syndrome [2,3]. Because serotonin syndrome is rare [4,5], most general practitioners are unaware of the condition [6]. We report a case of serotonin syndrome that was related to doubling of the dose of citalopram in combination drug therapy, and that

subsided after discontinuation of the offending drug. The syndrome has rarely been reported in association with citalopram, an antidepressant [2]. We emphasize the need for increased awareness of this syndrome when using this agent.

CASE PRESENTATION

A 32-year-old man had been diagnosed with major depressive disorder associated with a stressful internship 5 months before he presented to our clinic. He had been taking citalopram (20 mg/day), flupentixol (0.5 mg/day), and melitracen (10 mg/day) for more than 3 months. He had recently self-initiated an increase in his dose of citalopram to 40 mg/day due to worsening depressive mood. Two days later, he suffered from agitation and insomnia. In our clinic, he was alert and complained of insomnia, diaphoresis, subjective fever, tremor, agitation, constipation, and dry mouth. He denied any other substance abuse.

On physical examination, his blood pressure was 112/80 mmHg, heart rate was 108 beats/min, and temperature was 36.5°C. The neurologic examination was unremarkable. Laboratory tests revealed a white blood cell count of 4.38 ×

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10⁹/L, hemoglobin of 9.49 mmol/L, serum creatinine of 87.5 µmol/L, glutamic-pyruvic transaminase (GPT) of 19 U/L, and thyroid-stimulating hormone of 1.1 mU/L.

Initial therapy consisted of citalopram discontinuation, sedation, and stool-softening agents. Two days later, the patient showed gradual improvement. Another week later, he was considered adequately recovered for psychiatric evaluation in our clinic.

DISCUSSION

Our patient met the diagnostic criteria for serotonin syndrome according to Sternbach's description [3], which has been widely used [4]. He exhibited three of the symptoms commonly associated with serotonin syndrome: agitation, diaphoresis, and tremor after increased ingestion of a serotonergic agent. Alternative diagnoses were ruled out either by history or by laboratory examination.

Differential diagnosis of serotonin syndrome includes neuroleptic malignant syndrome (NMS), dystonic reaction, hyperthyroidism, tetanus, malignant hyperthermia, and other disorders that produce muscle rigidity, and includes toxicities of certain drugs such as cocaine, monoamine oxidase inhibitors, amphetamines, lithium, and other drugs [7]. Patients with serotonin syndrome are frequently misdiagnosed with NMS [8]. This is especially true in patients taking both neuroleptic and serotonergic agents. NMS is often confused with serotonin syndrome because mental status changes, autonomic dysfunction, and neuromuscular abnormalities characterize both disorders. One feature distinguishing NMS from serotonin syndrome is the lead-pipe rigidity associated with the former disorder compared with the clonus and hyperreflexia seen with serotonin syndrome. In addition, both the onset and resolution of symptoms are faster in serotonin syndrome [7]. In our patient, the lack of altered consciousness, severe autonomic changes, muscle rigidity, and elevated GPT levels made the diagnosis of NMS less likely [8]. In addition, there was no evidence of the other differential diagnoses described above.

Citalopram is a selective serotonin reuptake inhibitor

(SSRI) antidepressant that produces a net increase in 5-HT₁-mediated transmission. Flupentixol is a phenothiazine antipsychotic agent, and melitracen is a tricyclic antidepressant. Coadministration of citalopram, flupentixol, and melitracen has not been reported to result in serotonin syndrome. In our patient, no evidence of serotonin syndrome was noted during drug combination therapy for more than 3 months. However, doubling the dose of citalopram resulted in the onset of agitation, diaphoresis, and tremor after 2 days. Management of serotonin syndrome includes discontinuation of the offending serotonergic agent, supportive therapy and, possibly, the use of serotonin antagonists [9]. Our patient improved gradually within 2 days after citalopram was discontinued. His condition improved completely after another week.

Although citalopram is a relatively safe antidepressant, serotonin syndrome needs to be considered when prescribing this agent alone or in combination with other drugs. With the increased use of SSRIs in the management of psychiatric disorders, the importance of recognizing this syndrome cannot be overemphasized.

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Citalopram 引起之血清素症候群 — 病例報告

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血清素症候群是一種由於使用單一種血清素抑制劑，或合併使用其他藥物所造成血清素接受器過度刺激的副作用。我們發現一位三十二歲接受抗憂鬱藥物治療的男性，由於服用加倍劑量的 **citalopram** 之後；突然出現情緒不安、冒冷汗、自覺發熱感、肢體顫抖及失眠的症狀。經門診治療停用 **citalopram** 一週之後，上述臨床症候群逐漸緩解。這是一則少見的合併藥物治療中，**citalopram** 導致的血清素症候群案例。縱使臨床上，發生血清素症候群的機率不高，但隨著憂鬱症被人重視且抗憂鬱藥物的使用日漸頻繁。臨床醫師應該對血清素症候群有進一步的認識與瞭解。

關鍵詞：血清素症候群， **citalopram**

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