

A Case of Serotonin Syndrome Following Cyproheptadine Withdrawal

To the Editor: Serotonin syndrome is a life-threatening complication related to the drug interactions involving altered serotonin levels. The majority of cases known so far are related to the overdose of proserotonergic drugs, especially antidepressants such as selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, and monoamine oxidase inhibitors. Other drugs such as triptans, opioid analgesics, and antiemetics such as metoclopramide are also documented to cause serotonin syndrome. Very few cases of serotonin syndrome have been reported to be associated with the withdrawal of the serotonergic antagonist with concomitant use of a serotonergic agent.¹⁻³ One such case has been reported due to clozapine withdrawal with concomitant use of citalopram hydrobromide.⁴ We report a rare case of a patient who developed serotonin syndrome during withdrawal of cyproheptadine with concomitant use of a therapeutic dose of sertraline.

Case report. Ms A, a 63-year-old woman, presented to the psychiatry outpatient department with a history of low mood, lethargy, lack of interest in routine activities, loss of appetite, occasional crying spells, and disturbed sleep. Ms A felt hopeless and worthless and often had death wishes. There was no history of any medical illness. She was treated with sertraline 50 mg daily and lorazepam 2 mg at night if needed. After a month, she reported partial improvement, as there were no crying spells or feelings of worthlessness or hopelessness. But, she still had occasional sadness and loss of appetite. Thus, the dose of sertraline was increased to 100 mg and cyproheptadine (syrup) 4 mg twice daily was added to improve her appetite. After 3 weeks, Ms A reported improved appetite, and her depressive symptoms remitted. Cyproheptadine was stopped after 6 weeks, and she continued to receive sertraline 100 mg. Within 24 hours of stopping cyproheptadine, Ms A was brought back to the hospital in a confused state; she was also agitated. Her temperature was 102°F, her pulse was 120 beats/minute, and her blood pressure was 160/100 mm Hg. She also had tremors in her hands. On neurologic examination, muscle twitching (myoclonus) was observed in all the limb muscles with exaggerated deep tendon reflexes. Detailed history revealed no other drug use

except sertraline. Laboratory parameters, ie, total blood count, renal and liver function tests, blood sugar, serum electrolytes, electrocardiogram, and chest X-ray, were within normal limits. The brain magnetic resonance image revealed no abnormality except age-related atrophic changes. On the basis of her history, sertraline was stopped and cyproheptadine was restarted at 4 mg every 6 hours, along with lorazepam 2 mg to control the agitation. Ms A improved within 24 to 48 hours. The fever subsided, her blood pressure returned to normal, and she regained her muscle power gradually.

There are no clear-cut criteria for the diagnosis of serotonin syndrome, but in the case of Ms A, the diagnosis was made on the basis of her symptom profile, the exclusion of possible medical causes, her history of cyproheptadine withdrawal, and her improvement with reinstitution of cyproheptadine. Ms A had serotonin syndrome, which developed after sudden withdrawal of cyproheptadine (5HT₂ antagonist) due to unopposed action of sertraline (serotonergic agent) even at a therapeutic dosage. Withdrawal of cyproheptadine led to a sudden increase in the levels of serotonin, leading to serotonin syndrome.

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