

INTRODUCTION

Managing patients with polypharmacy overdose poses significant diagnostic and therapeutic challenges, particularly when overlapping toxicities contribute to a complex or atypical clinical presentation. We present a case of a patient who developed features consistent with both serotonin syndrome and cholinergic crisis following an overdose involving both agents.

CASE DESCRIPTION

A 29-year-old Chinese gentleman with a history of depression on sertraline and donepezil intentionally overdosed on both medications following a domestic conflict. He experienced multiple episodes of vomiting post ingestion. On arrival at the emergency department, he was confused with a GCS of E4V1M4. Vital signs were: temperature 37.0°C, BP 166/108 mmHg, HR 66 bpm, RR 30 bpm, SpO₂ 97% on room air, and glucose 8.5 mmol/L. Examination revealed quadriparesis with rigidity and hypersalivation, without clonus or other clear features of cholinergic crisis.

Blood investigations were within normal limits. ECG showed sinus tachycardia, and urine toxicology was negative. He later developed worsening respiratory distress with SpO₂ dropping to 88% on high-flow oxygen, requiring intubation. He was treated with intravenous atropine and benzodiazepines, admitted to ICU, extubated on day three, and discharged in stable condition following psychiatric assessment.

DISCUSSION

Early recognition of overlapping toxidromes is crucial in cases of polypharmacy overdose, which may exert opposing pharmacologic effects. Sertraline toxicity may lead to serotonin syndrome while donepezil overdose may cause cholinergic toxicity. The simultaneous ingestion of these two agents can result in atypical or attenuated presentations, as certain features of one toxidrome may mask or counterbalance those of the other—potentially delaying diagnosis and appropriate treatment. For instance, donepezil-induced bradycardia may be masked by sertraline-associated tachycardia, or serotonergic hyperactivity may obscure signs of cholinergic neuromuscular weakness. Therefore, maintaining a high index of suspicion and recognizing the subtle interplay of symptoms is essential. Notably, oximes are not indicated in donepezil overdose, as it is a reversible cholinesterase inhibitor.

CONCLUSION

This case underscores the need for early recognition of mixed toxidromes, where opposing effects may obscure clinical features. Timely diagnosis and targeted supportive care are essential to optimize outcomes.

REFERENCES

- (1) Liu Y, Yang H, He F, Xu P, Tong H, Liu Y, Ni J, Zhang Q, Wang J. An atypical case of serotonin syndrome with normal dose of selective serotonin inhibitors: A case report. *Medicine (Baltimore)*. 2019 May;98(19)
- (2) Delirrad, M., Ahmadi, H., & Aghakhani, N. (2024). Donepezil overdose and its atypical clinical presentations: A case report. *Journal of Research in Clinical Medicine*, 12(2)
- (3) Little, K., Lin, C. M., & Reynolds, P. M. (2018). Delayed serotonin syndrome in the setting of a mixed fluoxetine and serotonin antagonist overdose. *American Journal of Case Reports*, 19, 604–607.

Keywords: Toxidromes , Serotonergic-Cholinergic Interaction, Polypharmacy

