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Serotonin Syndrome in an Elderly Patient on Dual Antidepressant Therapy: A Case Report

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Background and importance

Serotonin syndrome (SS) is an uncommon potentially life-threatening adverse drug reaction caused by excessive serotonergic activity, **usually related to drug interactions or high-dose antidepressant therapy**. In **older adults**, **diagnosis** is particularly **challenging** due to **atypical presentations**, **multiple comorbidities**, and **polypharmacy**. Pharmacists play a key role in identifying drug-related risks and supporting early recognition.

Aim and objectives

To describe the case of an **81-year-old man admitted** after traumatic brain injury associated with hypotension, with a history of atrial fibrillation on rivaroxaban and bisoprolol, hypertension, prior ischaemic stroke without sequelae, and depression treated **with clomipramine 150 mg/day and venlafaxine 300 mg/day**. Relevant comorbidities included benign prostatic hyperplasia and orthostatic hypotension.

Material and methods

During hospitalisation, the patient developed **fever >39 °C**, **progressive somnolence**, **generalised tremor**, and **rigidity**. Laboratory tests showed CK 9100 U/L, AST 883 U/L, ALT 391 U/L, creatinine 1.87 mg/dL, and hypernatremia. EEG excluded seizures. Considering his medication history, **SS was suspected**. Neuroleptic malignant syndrome was considered less likely due to the absence of antipsychotics, though CK elevation and rigidity raised diagnostic uncertainty. **Empirical therapy with oral cyproheptadine** (12 mg initial dose followed by 2 mg every 2 h, maximum 32 mg/day) was started together with supportive measures. Bromocriptine was later added to cover potential diagnostic overlap.

Results

Over the following days, the patient showed **progressive clinical improvement**: fever resolved, myoclonus decreased, consciousness and orientation improved, and CK values declined. After psychiatric consultation, **antidepressant therapy was switched to desvenlafaxine** due to its lower risk of orthostatic hypotension and serotonergic toxicity. Beta-blocker therapy was also adjusted to minimise hypotensive episodes. The patient continued recovery in a rehabilitation unit.

Conclusions

This case highlights the **diagnostic complexity of SS in geriatric patients under polypharmacy**, particularly when dual antidepressant therapy is involved. Clinical overlap with other syndromes, such as neuroleptic malignant syndrome, can delay recognition. **Pharmacist involvement in medication review was crucial to identify the causative agents and propose safer alternatives**. Early detection and tailored pharmacological management are essential to reduce morbidity in this vulnerable population.