
Case report

Serotonin syndrome in the differential diagnosis of spinal cord compression

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Key words: antidepressants; serotonin syndrome; serotonin uptake inhibitors; sertraline; spinal cord compression

Introduction

Serotonin syndrome (SS) is an iatrogenic complication of antidepressants and other drugs which potentiate serotonergic activity. It is typically provoked by drug interactions, though cases attributable to single drug therapy are increasingly recognised. SS has been reported more frequently in recent years due to increased use of SSRIs and other implicated drugs, together with better recognition of the condition.

SS may be difficult to recognise because it presents a wide variety of symptomatology and severity.¹ Clinical features classically include disturbances of cognition and behaviour, autonomic nervous system function, and neuromuscular activity.

This case report describes sertraline-induced SS in a patient with metastatic carcinoma of the prostate whose clinical features mimicked spinal cord compression.

Case history

BB, an 85 year old with prostate cancer and vertebral metastases was commenced on sertraline 50 mg od for depression.

Admission was requested three weeks later because he had “gone off his legs”. He had been bedbound for three days, following several weeks of deteriorating mobility. He complained of lumbar back pain and urinary retention. He was acutely unwell and his family reported

confusion and visual hallucinations. There was no change in bowel habit or sphincter control.

On admission he was taking sertraline, lansoprazole, metoclopramide, celecoxib, codanthrusate, metoprolol, morphine m/r and i/r, lisinopril, frusemide, amiloride, megestrol, isosorbide mononitrate, fluconazole with regular goserelin implants. He had not taken over-the-counter remedies.

He was drowsy with intermittent agitation and disorientation. There was a pronounced coarse tremor affecting all limbs. He had full power in the upper limbs. The lower limbs were weak and he was unable to stand. There was marked hypertonicity and hyperreflexia affecting the lower limbs more than the upper limbs with bilateral ankle clonus and upgoing plantars. He complained of numbness of his lower limbs but there was no objective sensory deficit. His pulse rate was 72/min (paced) and he was apyrexial.

His spastic paraplegia was strongly suspicious of spinal cord compression though the hyperreflexia in the upper limbs and other non-specific neurological features including confusion were untypical. MRI was contraindicated as he had a pacemaker and his general condition was too poor to consider invasive neuroimaging.

The alternative diagnosis of drug toxicity was considered. Despite the fact that he had only been exposed to one serotonergic agent in standard dosage we made a provisional diagnosis of SS and discontinued sertraline and metoclopramide. Supportive therapy including intravenous rehydration was commenced and his condition gradually improved with no further specific intervention. The confusion improved within days and he regained full power, normal reflexes and urinary function within two weeks. A clinical diagnosis of sertraline induced SS was substantiated by this favourable course.

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Discussion

SS is an iatrogenic disorder which occurs when serotonergic activity is increased as a result of single drug therapy or, more commonly, drug interaction. Implicated drugs include MAOIs, SSRIs, tricyclics, dextromethorphan, pethidine, tramadol, buspirone, lithium, carbamazepine and fentanyl.

Our case is unusual in that single drug therapy with an SSRI in standard dose was implicated. Such idiosyncratic reactions are increasingly recognised,² and with greater understanding of the cytochrome P450 group of enzymes it is likely that an underlying pharmacogenetic predisposition will be identified.³ Age-related changes in the pharmacokinetics of antidepressants are also relevant,⁴ indicating that the overall safety of SSRIs may have been significantly overestimated.

SS is easily missed because of its protean manifestations and the lack of any definitive diagnostic test. Sternbach characterised a classical cluster of symptoms including agitation, confusion, hypomania, myoclonus, hyperreflexia, diaphoresis, shivering, tremor, diarrhoea, incoordination and fever.⁵ Mild cases present with limited symptoms. More severe cases demonstrate disordered cognition and muscular hyperactivity with myoclonus, shivering, rigidity and hyperthermia. Untreated patients are at risk of multiple organ failure as rhabdomyolysis precipitates renal failure, hepatic dysfunction, disseminated intravascular coagulation and cardiovascular collapse. A non-specific rise in creatine kinase is the only regularly observed biochemical marker.

Neuromuscular features are most commonly reported and in a large series of cases lower limb abnormalities were more commonly demonstrated with hyperreflexia, rigidity and bilateral positive Babinski sign.⁶ There is no previous report of a case mimicking spinal cord compression.

The differential diagnosis of SS includes neuroleptic malignant syndrome and drug-induced parkinsonism. In our case, the predominance of pyramidal weakness and rigidity in the context of known vertebral metastases suggested the previously unreported differential diagnosis of spinal cord compression.

Management of SS is largely supportive and the prognosis is favourable in all but the most serious cases. Serotonergic medication should be discontinued. Symptomatic

measures should be introduced as necessary: paracetamol and external cooling for hyperthermia, propranolol and/or cyproheptadine for their antiserotonergic effect and midazolam for myoclonus or convulsions.⁷ A minority of severe cases require admission to an intensive care unit for prevention and treatment of multiple organ failure. Caution is required in prescribing additional drugs for symptom control. Morphine and paracetamol are safe analgesics, though fentanyl may be contraindicated. Mirtazapine is the drug of choice if continuing antidepressant therapy is required.⁷

This case report demonstrates the need for vigilance in the detection of an increasingly common iatrogenic condition. Palliative care patients who are often exposed to antidepressants in the context of polypharmacy are at particular risk of SS. Our case draws attention to the high index of suspicion appropriate in this group of patients and the importance of considering SS in the differential diagnosis of spinal cord compression.

Acknowledgements

Acknowledgements to Inga Andrew for help and advice.

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