CASE REPORT

Serotonin syndrome: pills, thrills and shoulder aches

Malcolm Proudfoot, Joe Gormley

Department of Neurology,
Royal Devon & Exeter NHS
Foundation Trust, Exeter, UK

Correspondence to
Dr Malcolm Proudfoot,
m.proudfoot@gmail.com

SUMMARY

This case demonstrates an acute presentation of unwitnessed seizure causing typical injuries. Progress in hospital was complicated by worsening autonomic disturbance and agitation, typical for serotonin syndrome, suspected in light of recent selective serotonin reuptake inhibitor antidepressant initiation. Supportive care required treatment in the intensive care unit setting but full recovery ensued. This case not only reminds clinicians of the potential pitfalls in assessing postictal injured patients, but also that serotonin syndrome requires a high-index of diagnostic suspicion given the range of presenting features. Management ranges from simple withdrawal of the offending agent to specific therapies such as a cyproheptadine.

BACKGROUND

Serotonin syndrome is now a relatively common acute presentation given the widespread prescription of selective serotonin reuptake inhibitor medications.^{1 2} The potential pitfalls to the unwary physician include a failure to recognise the diverse clinical manifestations and variable tempo of the condition, lack of diagnostic suspicion owing to unsuspected pharmaceutical triggers and confusion with aetiological mimics. The present case demonstrates the evolution of the syndrome after an intriguing presentation following an un-witnessed seizure.

CASE PRESENTATION

A young adult presented to the emergency department by ambulance with shoulder pain in his dominant right arm. He had a medical background of asthma and mild depression but was not under specialist psychiatric review. He experienced the pain upon attempting to rise from his bed, where he had been watching television. He also experienced low thoracic back pain during the ambulance transfer. Clinically, the shoulder appeared to be dislocated without neurovascular compromise. Anterior dislocation was confirmed on plain x-ray (figure 1). While the treating team was preparing to reduce the joint, the patient had a 3 min generalised tonic-clonic seizure. Lateral tongue bite was noted. The shoulder was reduced by Rocker's method while the patient remained drowsy in the postictal period.

He was transferred to the medical admissions unit for further observation, whereby a second self-resolving seizure occurred. He recovered full consciousness promptly and denied any history of previous seizures or other neurological symptoms. Clinical examination was unremarkable with the exception of tachycardia at 110/min and blood pressure of 134/92 mm Hg. He had redislocated the

shoulder during the second seizure. CT head did not reveal any abnormality. Blood showed a creatine kinase (CK) of 9448 IU/l and a mild leucocytosis.

He was treated with a loading dose of sodium valproate, but subsequently upon attempting consent for orthopaedic theatre, was found to be mute and confused. Upon examination there was neither meningism nor focal neurology but an encephalopathy was suspected on account of his behaviour.

INVESTIGATIONS

Lumbar puncture was performed expeditiously. This returned clear cerebrospinal fluid at an opening pressure of 21 cm H₂O. One lymphocyte/ml was present and routine biochemistry was normal.

A more thorough collateral history was obtained. A selection of non-prescribed opiate and benzodiazepine medications were found in his room, receipts indicated that these had been purchased from an overseas internet-based retailer. He was also currently prescribed fluoxetine and codeine. Citalopram had recently been discontinued in favour of fluoxetine; his low mood was ascribed to a recent redundancy. A presumed diagnosis of polypharmacy overdose was made.

The following day he was noted to be febrile, tremulous and hyper-reflexic, hence serotonin syndrome was suspected. Blood test revealed a C reactive protein rise to 73, but his CK was normalising; paracetamol and salicylate levels were undetectable. Septic screen was negative and arterial blood gas revealed a normal acid-base balance. In the following days he became increasingly agitated and disordered in thought, diazepam provided transient relief. Electroencephalogram showed frontal theta runs only. Further negative investigations included porphyria, autoimmune, infectious and metabolic

Figure 1 Anterior dislocation of the shoulder.

To cite: Proudfoot M, Gormley J. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-008314

screens. An ECG revealed positive R waves in V1, consequently a CT pulmonary angiogram was organised to exclude pulmonary embolism. No significant lung pathology was noted, but compression fractures in two thoracic vertebrae were discovered, with preservation of the canal space. Spinal review recommended bed rest, pending further imaging via MRI.

TREATMENT

Ongoing myoclonus and opisthotonic episodes resulted in admission to the intensive care unit (ICU). Intravenous acyclovir was continued until viral PCR analysis was shown to be negative and sodium valproate was stopped in favour of phenytoin. An MRI under sedation (figure 2) confirmed the vertebral crush fractures to be recent, brain imaging was unremarkable. Closed reduction of the shoulder was performed under general anaesthesia the following day and the patient remained intubated and ventilated. Cyproheptadine was not started; this agent was not readily available and autonomic dysfunction was rapidly controlled once under sedation. Unfortunately his ICU stay was prolonged to 2 weeks by ventilator-acquired pneumonia with effusion, which required chest drain insertion. Although his fever was slow to resolve, his cognitive state had completely normalised at the time of his extubation in ICU.

OUTCOME AND FOLLOW-UP

Psychiatric review back on the medical ward did not find any evidence of pervasive low mood or psychosis, he had made a complete physical and cognitive recovery. He was advised to restrict himself to prescribed medications only. He declined follow-up in the neurology clinic.

Figure 2 Thoracic vertebrae wedge fractures.

DISCUSSION

This case demonstrates several learning points. Seizures are well recognised to cause shoulder dislocations, typically posterior but anterior dislocations are also common and may have a higher rate of recurrence.³ The occurrence of fractures as a consequence of seizure is not common at around 1.1% of seizures requiring admission to hospital,⁴ but it is worth noting the masking of vertebral fractures by more obvious injuries elsewhere and the difficulty in conducting secondary survey for confused postictal patients.

The recognition of serotonin syndrome must be made on clinical grounds, although urinary serotonin levels may prove to be relevant.⁵ The diagnostic difficulty lies in the broad spectrum of severity from minor autonomic hyperactivity and mental state changes through to neuromuscular abnormalities with life-threatening consequences.⁶ Large population-based studies⁷ have provided more sensitive recognition tools than the original strict diagnostic criteria.⁸ The early features of tremor, anxiety and diarrhoea can progress through to clonus (inducible at first then spontaneous, lower limb predominant then ocular involvement), tachycardia, hypertension and hyperthermia.⁹ Serotonin syndrome should be considered an inevitable consequence of excess pro-serotonergic agents, but can also occur with therapeutic doses. Our case highlights the danger posed by the long half-life (7–15 days) of norfluoxetine, the active metabolite of fluoxetine¹⁰ and the risks of polypharmacy if coprescribed with other serotonergic drugs. The main differential diagnoses include the neuroleptic malignant syndrome (NMS), hopefully easily distinguishable by a drug history of recently commenced antipsychotics and also by the prominence of extrapyramidal features. Malignant hyperthermia is worth consideration in the context of recent general anaesthetic. Increasing availability of prescription medications from alternative sources merits considerable vigilance with drug histories. Serotonin syndrome can be caused by a diverse range of recreational drugs, medications (or even their withdrawal) and can also be precipitated by inhibition of cytochrome p450 metabolism.

Treatment is largely supportive, ensuring removal of the causative agent. Antipyretics are unhelpful since the hyperthermia is produced by prolonged intense muscular contraction which is best treated by benzodiazepines,¹¹ or if necessary, paralysis via non-depolarising agents. Cyproheptadine, a sedative histamine-1 antagonist with additional antiserotonin properties, has been used successfully and safely in cases of moderate severity,¹² however it is only available in tablet form. Chlorpromazine may be administered parentally but is associated with sedation plus hypotension and the potential to worsen misdiagnosed NMS.

Learning points

- ▶ Seizures cause injury but patients are frequently amnesic.
- ▶ An accurate drug history may be needed to consider unconventional sources.
- ▶ Serotonin syndrome requires high-diagnostic suspicion and careful management.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Isbister GK, Bowe SJ, Dawson A, *et al.* Relative toxicity of selective serotonin reuptake inhibitors (SSRIs) in overdose. *J Toxicol Clin Toxicol* 2004;42:277–85.
- 2 Kelly CA, Dhaun N, Laing WJ, *et al.* Comparative toxicity of citalopram and the newer antidepressants after overdose. *J Toxicol Clin Toxicol* 2004;42:67–71.
- 3 Bühler M, Gerber C. Shoulder instability related to epileptic seizures. *J Shoulder Elbow Surg* 2002;11:339–44.
- 4 Finelli PF, Card J. Seizure as a cause of fracture. *Neurology* 1989;39:858–60.
- 5 Brvar M, Stajer D, Kozelj G, *et al.* Urinary serotonin level is associated with serotonin syndrome after moclobemide, sertraline, and citalopram overdose. *Clin Toxicol Philadelphia PA* 2007;45:458–60.
- 6 Boyer EW, Shannon M. The serotonin syndrome. *New Engl J Med* 2005;352:1112–20.
- 7 Dunkley EJCJC, Isbister GKK, Sibbritt D, *et al.* The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. *QJM* 2003;96:635–42.
- 8 Sternbach H. The serotonin syndrome. *Am J Psychiatry* 1991;148:705–13.
- 9 Birmes P, Coppin D, Schmitt L, *et al.* Serotonin syndrome: a brief review. *CMAJ* 2003;168:1439–42.
- 10 Hiemke C, Härtter S. Pharmacokinetics of selective serotonin reuptake inhibitors. *Pharmacol Therapeut* 2000;85:11–28.
- 11 Nisijima K, Shioda K, Yoshino T, *et al.* Diazepam and chlormethiazole attenuate the development of hyperthermia in an animal model of the serotonin syndrome. *Neurochem Int* 2003;43:155–64.
- 12 Graudins A, Stearman A, Chan B. Treatment of the serotonin syndrome with cyproheptadine. *J Emerg Med* 1998;16:615–19.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow