

Medicinal mishap

Serotonin syndrome precipitated by an over-the-counter cold remedy

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Case

A 46-year-old man presented to the emergency department with a three-day history of headache and vomiting, and one day of confusion and fevers. His medical history included an old spinal injury and his usual medications were methadone 70 mg daily, gabapentin 3.6 g daily and citalopram 40 mg daily. One week before admission he had a tooth extracted and two days later developed a 'head cold', from which he recovered.

At presentation the patient was febrile (39.1°C) and sweating. His pulse fluctuated between 80 and 140 beats/minute, and his blood pressure between 170/86 and 214/100 mmHg. He had a score of 12 on the Glasgow Coma Scale and was unable to sustain conversation. His dental socket looked clean and there was no clinical evidence of infective endocarditis, but he had generalised abdominal tenderness. Neurological examination revealed dilated reactive pupils and no meningism, but he had increased tone in both legs, with brisk reflexes and clonus at both ankles. Investigations revealed a white cell count of 21.1×10^9 , predominantly neutrophils, and a C-reactive protein of 15. Chest and abdominal X-rays and urine were normal.

The diagnosis was sepsis, probably from an intracerebral or abdominal source, so broad-spectrum antibiotics were started. However, the patient had a normal brain scan and the lumbar puncture found no evidence of infection. The patient's condition remained unchanged over the next 24 hours. An abdominal CT scan and an echocardiogram were ordered, but were normal.

On reviewing the history, the patient recounted taking 'Night and Day' capsules containing dextromethorphan as a cough suppressant for his head cold for two or three days before becoming unwell. A presumptive diagnosis of serotonin syndrome was made and the creatine kinase was found to be elevated (354 IU). After 48 hours without citalopram, the patient recovered fully.

Comment

Serotonin syndrome is a triad of mental-status changes, autonomic hyperactivity, and neuromuscular abnormalities¹, with a mortality of about 11%. It is caused by excessive stimulation of serotonin receptors, often as a result of interactions between serotonergic drugs.² Severe cases of serotonin syndrome can cause rhabdomyolysis, with raised creatine kinase and metabolic acidosis.¹

Many drugs have been implicated, including monoamine

oxidase inhibitors, selective serotonin reuptake inhibitors (SSRIs), opioid analgesics including tramadol, antimigraine treatments and antibiotics, for example linezolid. Over-the-counter cough and cold remedies have occasionally been implicated³, but no case reports involving dextromethorphan and citalopram were found in a literature search.

Several mechanisms may have contributed to the development of serotonin syndrome in this patient. Firstly, dextromethorphan is a potent inhibitor of serotonin reuptake, similar to SSRIs.⁴ The combination with citalopram would therefore be expected to markedly increase the concentration of serotonin at the synapse. Secondly, SSRIs act as cytochrome P450 2D6 inhibitors⁵, and although citalopram is a weak inhibitor, this may have contributed to elevated concentrations of dextromethorphan, which is a substrate of CYP 2D6.⁶ Finally, methadone increases brain serotonin in laboratory animals⁷, but the patient had been taking methadone and citalopram for two years, without ill-effect.

Estimates from previous studies are that 85% of doctors may be unaware of serotonin syndrome as a clinical entity.⁸ Some community pharmacists may also be unaware that serotonin syndrome can be precipitated by over-the-counter cold remedies. As it can cause significant morbidity and mortality, health professionals need to consider the possibility of serotonin syndrome. This case also shows the value of taking a thorough drug history, including over-the-counter preparations.

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References

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