

sudden death.⁷ Accidental ingestion of foreign bodies, while rare, may now be added to the list of serious complications.

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Serotonin syndrome due to venlafaxine overdose

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Abstract

A case is presented of serotonin syndrome after deliberate overdose of the antidepressant venlafaxine. The mechanism, diagnosis, and management of this disorder is discussed.

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Keywords: serotonin syndrome; overdose; venlafaxine

Case report

A 28 year old male with a previous history of chronic fatigue syndrome and depression presented one hour after taking an overdose of 40, 75 mg venlafaxine tablets. On arrival he was conscious, but unable to speak, with a coarse tremor of his upper limbs and rigid lower limbs, with marked clonus present in his ankles. He was not taking any other prescribed or illicit drugs, did not smoke, and seldom used alcohol. He was tachycardic with a rate of 160 beats/min, hypertensive with blood pressure 174/83 mm Hg, flushed, and diaphoretic. His temperature was 36.6°C. An electrocardiogram showed sinus tachycardia with normal morphology. Arterial blood gases were normal.

On the basis of the history and clinical findings a diagnosis of serotonin syndrome was made. He was resuscitated with 2 litres of 0.9% saline over two hours and charcoal given via a nasogastric tube. Chlorpromazine 12.5 mg was given intravenously to control the tremor. Fifteen minutes later his condition had improved such that he could answer questions by nodding or shaking his head. At this stage he was pyrexial with an axillary temperature of 38.5°C.

Thirty minutes after administration of the chlorpromazine the patient suffered a seizure, treated with an intravenous bolus of 2 mg midazolam. A second dose of chlorpromazine was given three hours after the overdose when rigidity returned. His pyrexia responded to cooling and the chlorpromazine. Creatine kinase peaked at 1307 U/l (normal range 20-260) at 16 hours after the overdose. Renal function was normal throughout and urinalysis unremarkable. He recovered completely and was discharged after 48 hours.

Discussion

This is the second reported case of serotonin syndrome after venlafaxine overdose,¹ although in the previous case the patient had taken paroxetine two weeks previously.

Venlafaxine (Efexor, Wyeth Pharmaceuticals) is a chemically distinct antidepressant with unique action and efficacy. It has a faster onset of action than both selective serotonin reuptake inhibitors and tricyclic antidepressants and appears to inhibit reuptake of serotonin, noradrenaline, and dopamine. The main indication for venlafaxine is major depressive disorder, particularly seriously depressed melancholic patients. Overdosage with venlafaxine has been reported to cause profound central nervous system depression requiring intubation,² generalised seizure,³ and serotonin syndrome as mentioned above, although most patients are asymptomatic. Of patients who report symptoms, somnolence is the commonest.

Serotonin syndrome is a symptom complex resulting from increased biological activity of serotonin. Symptoms include altered mental status, neuromuscular irritability, and autonomic instability. Previously it has been seen almost exclusively in the context of polypharmacy in patients on serotonergic medication, most frequently monoamine oxidase inhibitors, tricyclic antidepressants, or selective serotonin reuptake inhibitors, all of which increase the half life of serotonin in the synaptic cleft. Most reported cases have occurred shortly after an increase in the dose of a serotonergic drug or the addition of another. Diagnosis is clinical, since laboratory abnormalities are non-specific. Symptoms are due to synaptic serotonin concentration alone, hence blood serotonin values are unhelpful.

Diagnostic criteria⁴ are:

(A) The recent addition of increase in the dosage of a drug which enhances serotonin activity or availability;

(B) The absence of abused substances as well as metabolic or infectious causes;

(C) No recent addition or increased dose of neuroleptic;

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Table 1 Drugs used in serotonin syndrome

Chlorpromazine	25 mg intramuscular ⁷
Cyproheptadine	4 mg every 2–4 hours (0.5 mg/kg/day) ^{8,9}
Propranolol	20 mg three times a day by mouth ¹⁰
Methysergide	2–6 mg/24 hours ¹¹
Benadryl	50 mg intramuscular ¹²
Clonazepam	0.5 mg intravenous ¹³

(D) The presence of at least three of altered mental status, agitation, tremor, shivering, diarrhoea, hyperreflexia, myoclonus, ataxia, or fever.

Differential diagnoses include sepsis, neuroleptic malignant syndrome, sympathomimetic overdose, heat stroke, anticholinergic toxicity, delirium tremens, baseline psychiatric symptoms, and lethal catatonia. There is considerable overlap with neuroleptic malignant syndrome, and many patients may be taking both antidepressants and neuroleptic drugs. Patients with neuroleptic malignant syndrome tend to be more toxic, with a higher fever and myoclonus is uncommon, the muscle rigidity tending to be leadpipe.

Severity ranges from mild, self limiting symptoms that spontaneously resolve to severe cases with rhabdomyolysis and renal failure. In one study, 70% of cases resolved within 24 hours, although 40% required intensive care unit admission.⁷ Mortality is estimated at 11%.

The basic principles of management are the prompt discontinuation of serotonergic medications and provision of adequate supportive care. With this management most cases resolve within 24 hours. Supportive care includes fluid resuscitation for dehydration, rhabdomyolysis and hypotension, and active cooling in high fever.

If symptoms are severe or persistent a number of drugs may be used, most of which block postsynaptic serotonin receptors (table 1⁶). Hyperthermia (temperature >40.5° C) indicates severe disease with significant complications and mortality. Drugs may be used to limit excessive muscle contraction, which contributes to fever, rhabdomyolysis, and musculoskeletal respiratory failure. The most widely used are benzodiazepines, particularly clonazepam, which will control myoclonus and prevent seizures. Theo-

retical arguments exist for the use of β blockers, which act at 5-HT_{1A} receptors, in addition to their negative chronotropic effect.

Several authors report successful treatment with chlorpromazine,⁷ a relatively potent 5HT₂ antagonist, although it may lower the seizure threshold, as occurred in this case. Cyproheptadine is also reported to be effective.^{8,9} Management of complications such as seizures, ventricular tachycardia, or respiratory compromise involve standard techniques.

Summary

Serotonin syndrome is a potentially life threatening condition which may be seen in the emergency department in patients taking antidepressants, the early recognition and treatment of which is vital if morbidity and mortality are to be avoided. The diagnosis should be considered in patients presenting with altered mental state, fever, or neuromuscular changes. The increasing use of venlafaxine and other potent serotonergic drugs in potentially suicidal patients may result in increasing numbers of such patients presenting to emergency departments with symptoms of serotonin syndrome following deliberate overdose.

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Puffer fish poisoning

Jonathan Field

Abstract

Regarded by many as a delicacy, puffer fish (*Lagocephalus scleratus*) is a lethal source of food poisoning with a high mortality. It contains tetrodotoxin which can cause death by muscular paralysis, respiratory depression, and circulatory failure. A case of mild intoxication is reported and the literature reviewed.

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Keywords: puffer fish; tetrodotoxin; food poisoning

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Case report

A 36 year old Korean seaman presented to the accident and emergency (A&E) department at 0300 hours. He was accompanied by a shipmate who indicated, in broken English, that he had been poisoned by an unusual type of seafood that he'd caught and prepared himself about 4–5 hours previously. He identified the puffer (toad) fish photographed in Straun Sutherland's book of *Australian Animal Toxins*.¹

On examination he was having some difficulty breathing and articulating. His pulse rate