CASE REPORT

Pendular nystagmus associated with venlafaxine overdose: a forme fruste of the serotonin syndrome?

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Dr Aravinthan Varatharaj,
a.varatharaj@gmail.com**SUMMARY**

We describe a case of pendular nystagmus as a previously unreported side effect of venlafaxine, and speculate to its importance in the recognition of the serotonin syndrome. In particular, we discuss the importance of identifying incomplete forms of the syndrome, such as those presenting with predominantly ocular manifestations, as is in our case.

BACKGROUND

Drugs which interfere with serotonin metabolism are commonly used for their psychoactive properties. Venlafaxine is a serotonin–norepinephrine reuptake inhibitor (SNRI) widely prescribed as an antidepressant. An important complication of these drugs is development of the serotonin syndrome, which in its complete form presents with a triad of neuromuscular, autonomic and mental hyperexcitability. In this case, we demonstrate pendular nystagmus as a new adverse effect of venlafaxine which has not previously been reported, and speculate that the aetiology may reflect an incomplete form of the serotonin syndrome.

CASE PRESENTATION

A 54-year-old woman ingested 3 g of venlafaxine in a modified-release preparation (40 tablets of 75 mg). She presented to the emergency department 4 h after ingestion, reporting blurred vision, dry mouth, nausea and vomiting. She denied co-ingestion of alcohol or any other substances, and was not on any regular medication.

On examination, temperature was 36.4°C, pulse 101 bpm, blood pressure 142/89 mm Hg and oxygen saturation 98% on room air. She was calm, alert and oriented. She was not sweaty, shivery or tremulous. Muscle tone was normal. All reflexes were markedly brisk but there was no limb clonus, and plantars were downgoing. Examination of eye movements demonstrated binocular horizontal pendular nystagmus with the eyes in the primary position (see [video 1](#)). Amplitude of nystagmus decreased with lateral gaze and was increased by central visual fixation. There was no ophthalmoplegia, and smooth pursuit and saccadic eye movements were preserved.

INVESTIGATIONS

An ECG showed sinus rhythm with right axis deviation and right bundle branch block, with a corrected QT interval of 415 ms. Routine blood tests were within normal limits, with a creatine kinase level of 132 units/L (range 0–145). Paracetamol

and salicylate levels were undetectable. Venous blood gas analysis showed normal acid–base balance.

TREATMENT

Initially, she reported severe nausea and vomiting, which was relieved by intravenous administration of 50 mg cyclizine. The patient was then observed overnight, with antiemetics and oral diazepam as required.

OUTCOME AND FOLLOW-UP

The patient managed to sleep and, by the next day, there was complete resolution of nystagmus and brisk reflexes. She was seen by the psychiatric team and discharged.

DISCUSSION

Serotonin, also known as 5-hydroxytryptamine, functions in the CNS as a neurotransmitter. The serotonin syndrome describes the clinical manifestations of an excess of serotonin at central nerve synapses. The typical cause is drugs which increase synaptic serotonin, commonly selective serotonin reuptake inhibitors (eg fluoxetine, paroxetine and citalopram) and SNRIs (eg venlafaxine and duloxetine). The clinical spectrum is broad, and a number of diagnostic criteria have been developed.^{1 2} In its complete form, the syndrome comprises a triad of neuromuscular excitability (tremor, rigidity, clonus and hyper-reflexia), autonomic disturbance (fever, shivering, sweating, tachycardia and mydriasis) and altered mental state (agitation and hypervigilance).

Pendular nystagmus is an involuntary oscillation of the eyes that occurs with a sinusoidal waveform, unlike jerk nystagmus which displays a fast and slow phase. Numerous causes have been described,³ and an association of binocular horizontal pendular nystagmus with serotonin toxicity is well recognised^{2 4}; although in much of the literature, the abnormality is described as ‘ocular clonus’, in parity with limb clonus. To our knowledge, isolated pendular nystagmus as a sign of serotonin toxicity has never been described, nor has pendular nystagmus as a consequence of venlafaxine overdose.

We suspect that our case represents an incomplete form (‘forme fruste’) of the serotonin syndrome. The absence of other clinical features of serotonin toxicity and the normal investigations precluded a diagnosis of the complete serotonin syndrome, and the case would not have met either the Sternbach or Hunter criteria.^{1 2} Recognition of such incomplete forms is important, as the

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Video 1 Binocular horizontal pendular nystagmus, reduced in amplitude by lateral gaze, and increased by central visual fixation.

serotonin syndrome is not a side effect per se; it is part of the clinical spectrum that results from agonism of central serotonin receptors, which is exploited for therapeutic effect by psychotropic medications. Adverse consequences of increased serotonin levels may occur at therapeutic doses, and if overlooked, one might inadvertently precipitate the full-blown serotonin syndrome with an increased dose of the causative agent or addition of another provocative drug. Also, with the use of modified-release preparations, the development of the complete syndrome may take longer than anticipated, and the presence of incomplete toxicity may herald clinical deterioration.

Learning points

- ▶ The serotonin syndrome occurs as a result of drugs which increase synaptic serotonin, commonly selective serotonin reuptake inhibitors and serotonin–norepinephrine reuptake inhibitor.
- ▶ In its complete form, the syndrome presents with a triad of neuromuscular, autonomic and mental hyperexcitability.
- ▶ Incomplete forms may occur and should be treated seriously, to avoid deterioration to the complete syndrome.
- ▶ Ocular manifestations may be the predominant sign of serotonin toxicity.

Competing interests None.

Patient consent Obtained.

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