

SEROTONIN SYNDROME CAUSED BY VENLAFAXINE (LATE ONSET)

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ABSTRACT

Serotonin Syndrome is a disorder induced by pharmacological treatment with serotonergic agents. A case of a 54 year old man with Serotonin Syndrome after 15 weeks of 375 mg Venlafaxine use is presented.

Key words: Serotonin Syndrome, Venlafaxine.

INTRODUCTION

Serotonin Syndrome is an iatrogenic disorder induced by pharmacological treatment with serotonergic agents that increase serotonin activity in both central and peripheral serotonergic systems. It is characterized by a clinical triad of mental-status changes, autonomic hyperactivity and the neuromuscular abnormalities. Severity ranges from mild, self limiting symptoms to severe cases with rhabdomyolysis and renal failure.

The syndrome was first described in animal models in the 1950s. Reports of serotonin syndrome have become increasingly frequent since the 1960s in humans. Serotonin syndrome has previously been thought to occur when a patient concomitantly receives 2 antidepressants, especially the combination of a monoamine oxidase inhibitor and a monoamine reuptake inhibitor. But reports suggest that this syndrome can happen even when the patients receives only 1 antidepressant.

Venlafaxine induced serotonin syndrome has been reported, most case reports describe concomitant use of venlafaxine with other antidepressant medication¹⁻³. However, there are case reports with monotherapy when the patient was overdosed or received a therapeutic dosage⁴.

Out of some 146 published cases of serotonin syndrome with SSRIs and related drugs, venlafaxine is implicated in 16 of these.

Our case report illustrates serotonin syndrome induced by venlafaxine monotherapy. To our knowledge this is the first case report in which the onset of full blown serotonin syndrome was several weeks after the increase in the dose of venlafaxine.

CASE HISTORY

B is a 54 year old man of Indian Gujarati origin. He is married with two grown up children. His illness started 9 years ago, after he was made redundant from his job as a crane operator of 22 year duration. He became

increasingly withdrawn and non-communicative with gradual decline in interest in day-to-day activities and family issues with delusions of impoverishment and nihilism. He was given a diagnosis of depression with mood congruent psychotic symptoms and treated over time with various antidepressants, antipsychotics and lithium.

On 225 mg of venlafaxine, he showed only partial improvement. After admission to psychiatric unit, the dose was increased to 300mg. After this increase B reported myoclonic jerks which became worse after addition of amisulpride and lithium. He also became confused and unsteady. Laboratory investigations showed CK 183 (normal range less than 130). The rest of the biochemical and haematological tests were within normal limits. An EEG and brain scan were also normal. Myoclonic jerks improved after stopping amisulpride and lithium.

His venlafaxine was increased to 375 mg once daily after which he was discharged back to community.

Case notes have recorded, history of aching legs, myoclonic jerks and unsteady gait some weeks after the increase in the dose of venlafaxine.

15 weeks after the increase in the dose of venlafaxine, B was admitted to the medical ward in emergency for jerky movements of head and limbs, gross ataxia and fluctuating consciousness. He appeared to be gasping for breath and was not maintaining his airway on his back. He had profound involuntary movement of his head and limbs. He had decreased consciousness. His pupils were equal and reactive. Power and reflexes could not be tested formally. The tone in muscles was decreased. He also developed marked psychomotor agitation.

On examination, his pulse was 87, RR24 and BP unrecordable. Temperature was 37.2. On investigation U&Es and TFTs were within normal limits. AST was 93, blood glucose 15.4 and CK was 1652. ESR was not done and CRP was 8.

Urine dip test showed proteinuria and haematuria. No growth was found on culture.

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ECG was of poor quality but no abnormality was found.

No infective or metabolic cause was found.

His venlafaxine was stopped immediately. He was given supportive treatment including benzodiazepines (lorazepam and midazolam) and Benztropine . B made complete recovery within 72 hours.

He was subsequently treated with lofepramine and aripiprazole for his psychiatric symptoms and was followed up for 12 months(upto the writing of this report) with no recurrence of involuntary movements, confusion or ataxia.

DISCUSSION

We believe that this was a case of Serotonin Syndrome that was precipitated by monotherapy with venlafaxine. The clinical features of this episode and their rapid resolution on discontinuation of venlafaxine support this.

Serotonin syndrome is the result of overstimulation of 5 HT-1a receptors in central grey nuclei and the medulla and, perhaps of overstimulation of 5HT2 receptors⁵.

A large number of drugs and drug and drug combinations have been associated with the serotonin syndrome. These include MAOIs, TCAs, SSRIs, opiate analgesics, over the counter cough medicine, antibiotics, weight educing agents, antiemetics, antimigraine agents, drugs of abuse and herbal products.

The serotonin syndrome encompasses a range of clinical findings. The diagnosis serotonin syndrome is guided by the Sternbach's criteris:⁵ which are as follows; recent change of a potent serotonin agent; no history of substance abuse or infectious or metabolic disease; absence of any antipsychotic drug; and 3 of the following symptoms:-

1. change in the finding of the mental status
2. agitation
3. myoclonus
4. hyperreflexia
5. diaphoresis
6. shivering
7. tremor
8. diarrhea
9. Incoordination
10. fever

Our patient had 4 of these criteria (change in the mental status, agitation, myoclonus, incoordination).

Clonus (inducible, ocular and spontaneous) by some clinicians is considered to be the most important finding in establishing the diagnosis of the serotonin syndrome⁶. Clonus was our patient's main clinical feature.

The principal dd is NMS.Both NMS and SS can be fulminant, and patients may present with delirium, hy-

perthermia, rhabdomyolysis, dilated pupils, tachycardia, diaphoresis and rigidity and blood pressure changes and a rise in CK.

The main difference lies in the clinical gestalt : typically a patient with SS is agitated, speaks incoherently and has prominent myoclonus, whereas a patient with NMS is immobile, mute and staring ⁷.

The presentation of our patients in his first hospital stay (in psychiatric unit) could have been due to NMS, but re-emergence of symptoms after stopping amisulpride makes it unlikely. During second episode of serotonin syndrome, our patient was not on any antipsychotic. Only one case report of NMS has been connected to venlafaxine , this was associated with a single dose of venlafaxine in a patient previously on trifluoperazine ⁷.

In our case report the onset of serotonin syndrome is delayed for several weeks after the increase in the dose of venlafaxine. Typically the onset is considered to be rapid, 60% of patients with the serotonin syndrome present within 6 hours after initial use of medication, an overdose or a change in dosing⁶, patients with mild manifestation may present with subacute or chronic symptoms. Some case reports have shown a delay of upto 2 weeks. One reason for delay in our case report could be that mild symptoms of serotonin syndrome could have been present throughout. Symptoms could be missed because of its protean manifestation. Clinician and patients may dismiss symptoms as inconsequential or symptoms such as anxiety or akathisia may be misattributed to the patient's mental state⁷. Our patient complained of akathisia on discharge from hospital after his first admission and was prescribed procyclidine for that. The reason for sudden deterioration in his condition remains unclear. There is no indication that he took any over the counter drugs with serotonergic properties which might act as a contributory factor.

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