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SEROTONIN SYNDROME CAUSED BY VENLAFAXINE (LATE ONSET)

# ABSTRACT

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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 in- duced 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. Se- verity ranges from mild , self limiting symptoms to severe cases with rhabdomyolysis and renal failure.

The syndrome was first described in animal mod- els in the 1950s. Reports of serotonin syndrome have become increasingly frequent since the 1960s in hu- mans. Serotonin sundrome has previously been thought to occur when a patient concomitantntly receives 2 an- tidepressants, especially the combination of a monoam- ine oxidase inhibitor and a monoamine reuptake inhibi- tor. 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 concomi- tant use of venlafaxine with other antidepressant medi- cation1-3. However, there are case reports with monotherapy when the patient was overdosed or re- ceived a therapeutic dosage4.

Out of some146 published cases of serotonin syn- drome with SSRIs and related drugs, venlafaxine is im- plicated in 16 of these.

Our case report illustrates serotonin syndrome in- duced 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 in- crease in the dose of venlafaxine.

# CASE HISTORY

B is a 54 year old man of Indian Gujrati 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

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increasingly withdrawn and non-communicative with gradual decline in interest in day-to-day activities and family issues with delusions of impoverishment and ni- hilism. 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 re- ported myoclonic jerks which became worse after addi- tion of amisulpride and lithium. He also became con- fused and unsteady. Laboratory investigations showed CK 183 ( normal range less than 130) The rest of the biochemical and haematological tests were within nor- mal 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 achy 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 emer- gency for jerky movements of head and limbs, gross ataxia and fluctuating consciousness. He appeared to be gasping for breath and was not maintaining his air- way on his back. He had profound involuntary move- ment of his head and limbs. He had decreased con- sciousness. 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 un recordable. , 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.

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 bezodiazepines (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 fol- lowed up for 12 months(upto the writing of this report) with no recurrence of involuntary movements, confu- sion or ataxia.

# DISCUSSION

We believe that this was a case of Serotonin Syn- drome 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 me- dulla and, perhaps of overstimulation of 5HT2 recep- tors5.

A large number of drugs and drug and drug com- binations have been associated with the serotonin syn- drome. These include MAOIs, TCAs, SSRIs, opiate an- algesics, 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 fol- lows; 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 fea- ture.

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 incoher- ently and has prominent myoclonus, whereas a patient with NMS is immobile, mute and staring 7.

The presentation of our patients in his first hospi- tal 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 antipsy- chotic. 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 mani- festation may present with subacute or chronic symp- toms. 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 pa- tients may dismiss symptoms as inconsequential or symp- toms 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 ad- mission 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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