Serotonin Syndrome Masquerading as Status Epilepticus following Ingestion of Tranylcypromine and Clomipramine and L-Tryptophan: A Case Report

Serotonin syndrome (SS) is a rare but possibly catastrophic side effect of medications that affect serotonin levels in the central nervous system, which is marked by a change in the mental status, intensifying neuromuscular activity and autonomic instability. The case report presented here illustrates a real-life scenario where self-treatment with an off-label monoamine oxidase inhibitor (MAOI) and clomipramine resulted in a fatal drug reaction, leading to SS. A patient presented with symptoms of abnormal jerky movements with altered sensorium masquerading as status epilepticus. However, the medical refractoriness, transient autonomic dysfunction, electroencephalogram (EEG) pattern at the bedside, and augmented early laboratory values of creatinine kinase led to the diagnosis of SS.

A 23 year-old male was referred to the Fortis Emergency Department (ER) with a history of acute altered sensorium in the last 4 hours and abnormal jerky movements of the extremities. He was treated with midazolam and shifted to the ER. On arrival to ER, the patient was obtunded with frequent jerks of all limbs, diagnosed as status epilepticus, and treated with parenteral administration of lorazepam, midazolam, levetiracetam, and fosphenytoin, but the jerking of extremities still persisted. He was intubated, ventilated, and a midazolam infusion was started. There was a transient fever spike of 102ºF. Due to persistence of continuous jerks, an EEG was ordered, which revealed alpha coma. This led to the probability of the diagnosis of acute toxic encephalopathy. His blood pressure was elevated to 220/110 mm of Hg, which was corrected with labetalol. His parents confirmed the history of bipolar disorder and the patient being treated with clomipramine and sodium valproate. With the constellation of acute altered sensorium, jitteriness, and autonomic dysfunction, a possibility of SS was likely. The symptoms and elevated serum Creatine phosphokinase (CPK) triggered the need for a blood toxicity screening with a stomach lavage.

His CPK level was extremely high, at 12,000 IU/ml [Figure 1]. As per the medication history, use of off-label tranylcypromine with L tryptophan was ascertained, which clinched the diagnoses. Interaction between tranylcypromine and clomipramine leading to complex and deadly SS was identified. After the clear understanding of the actual diagnosis, the midazolam and propofol infusions were suspended and the patient was started on cyproheptadine. On the third day, the patient was weaned off the ventilator. He remained agitated and disoriented for the next 72 hours, most likely as a result of the serotonergic effects wearing off, which abated on treatment with oral diazepam and quetiapine during this period. There was a gradual improvement on day 7 and he was fully oriented to time and place.

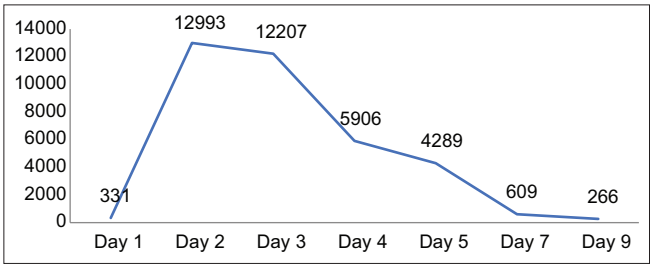

Figure 1: Creatinine kinase levels

SS is a life-threatening emergency and prompt diagnosis can help prevent unnecessary delay and incorrect treatment.[1,2] The current case highlights the outliers in the treatment response which prompted a good review of the patient's current medications. Otte *et al*. described approximately 40 case reports, all published before 1973, describing adverse reactions encountered by patients who received TCAs and MAOIs. Drug–drug interactions, lethal doses, and concurrent use of other psychoactive drugs or ingestion of tyramine-containing food were common complicating factors in many of these cases. The current scenario illustrates that the patient was abusing off-label prescription usage of MAOI and L – tryptophan for the excitatory effects. He was also taking prescribed clomipramine [tricyclic antidepressant (TCA) class] which on interaction with MAOI and L-tryptophan caused serious adverse effects. He had high-grade fever with elevated blood pressure, highlighting the importance of being wary of the very transient and episodic symptoms which may be misleading. Clinical presentation with repetitive jerks was a good learning point in the case as these jerks were non-epileptic, confirmed with a simultaneous bedside EEG, which revealed an alpha coma, resulting in tapering of anti-seizure medications and starting treatment with cyproheptadine 12 mg daily[3] and gradually increasing to 32 mg/day. In individuals with profound coma, alpha coma is an EEG pattern characterized by diffuse or broad rhythmic activity in the alpha frequency band. Hypoxic–ischemic encephalopathy, encephalitis, head trauma, metabolic problems, and drug overdose are some of the most prevalent etiologic reasons for this pattern.[2] The patient had non-reactive EEG alpha activity [Figures 2 and 3], which fulfills the criteria of alpha coma.[2] The EEG diagnosis helped clinch the suspicion of a toxic encephalopathy, which was invaluable in the early treatment of this patient. The absence of burst suppression or any spike wave activity on the EEG and the presence of an alpha coma, helped the de-escalation of anti-seizure medications and initiate the toxic screen work-up.

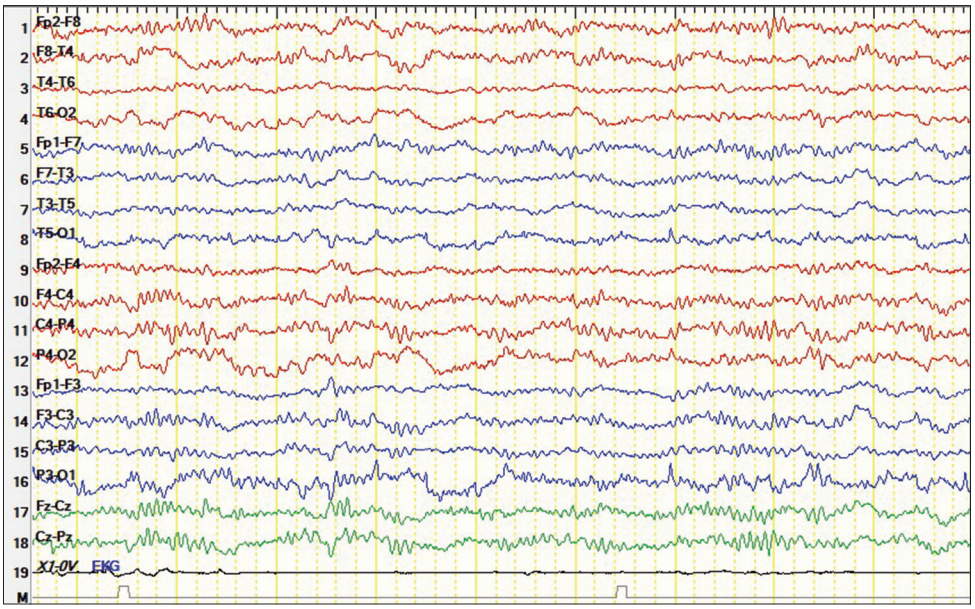

Figure 2: Abnormal EEG showing alpha coma

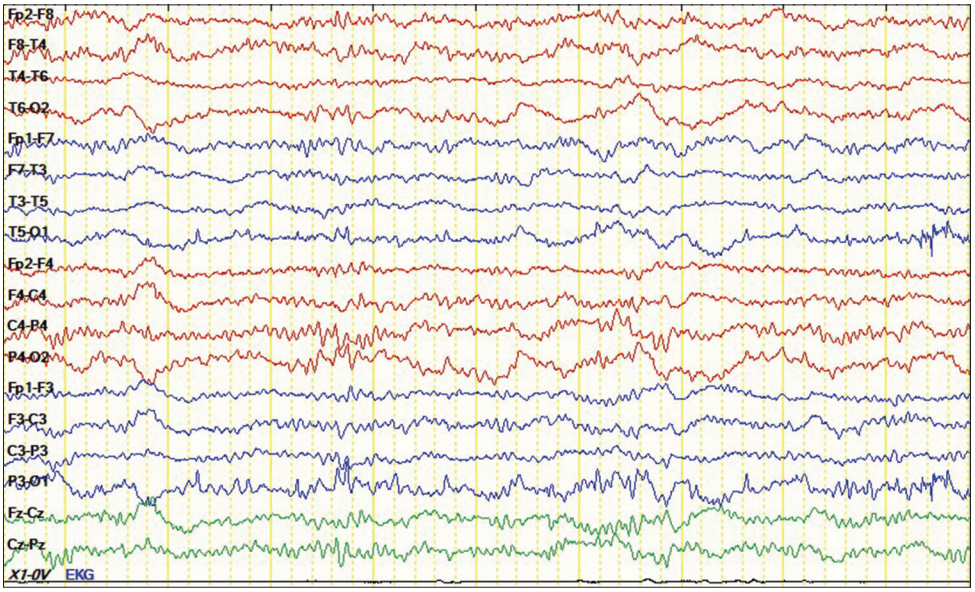

Figure 3: Abnormal EEG showing alpha coma

Because of the risk of SS, combination of TCAs and MAOIs are not recommended. Washout period of 14 days between antidepressant MAOI and starting TCA therapy or vice versa is required to avoid dangerous consequences such as SS. Patients who were stable on a single serotonergic drug but developed SS after taking MAOIs or TCAs or tryptophan have been described in multiple case reports. The majority of these medicines can increase central serotonergic activity by inhibiting serotonin reuptake, lowering serotonin metabolism, or stimulating serotonin receptors directly.[4]

Combination of tryptophan and MOAIs causes behavioral and neurological problems, according to tryptophan labeling (e.g., disorientation, confusion, agitation, myoclonus, and hyper-reflexia).[5]

Emerging use of serotonergic medications for various psychiatric illnesses increases the prevalence of SS. Concurrent use of two or more of these drugs may lead to the risk of serotonin poisoning, resulting in autonomic, neuromuscular, and neurological symptoms including serotonergic overstimulation.[6] Death is certain due to SS, and a minority of cases are benign. As a result, psychiatrists and general practitioners must be aware of this syndrome and be able to detect it early.[7] EEG can help diagnose SS from other mental illnesses. The current case scenario highlights the importance of reconciling patient's self-medication

for the appropriate diagnosis and treatment of SS and also serve the community at large by prevention of the deadly syndrome.

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Conflicts of interest

There are no conflicts of interest.

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