

Amitriptyline Intoxication - Unanticipated Complications

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Abstract:

Amitriptyline is a tricyclic antidepressants (TCAs) recommended for depression¹. However, these medications can also be abused. The prevalence of patients suffering from overdose intoxication is anticipated to rise as a result of easy availability to TCAs. A 41 year old male with alleged history of consumption of multiple TCA over doses. Despite initial treatment including intravascular lipid emulsion, sodium bicarbonate infusion, supra ventricular tachycardia occurred soon after arrival and went into cardiac arrest. A high concentration of amitriptyline was identified in his blood samples on arrival, for which plasmapheresis was done. EEG was done due to sudden development of myoclonic jerks which showed diffuse brain dysfunction not specific to any etiology. Emergency CT brain was done in view of dilated and non-reactive pupils, and absent brainstem reflexes which showed diffuse cerebral edema, started on anti edema measures and MRI brain did not show any specific etiology of sudden onset cerebral edema which confirmed amitriptyline overdose as the cause of cerebral edema. Amitriptyline has the potential to lead to serious side effects like cerebral edema, irreversible central nervous system damage, and deadly arrhythmia.

Keywords: Amitriptyline, supra ventricular tachycardia, lipid emulsion, plasmapheresis

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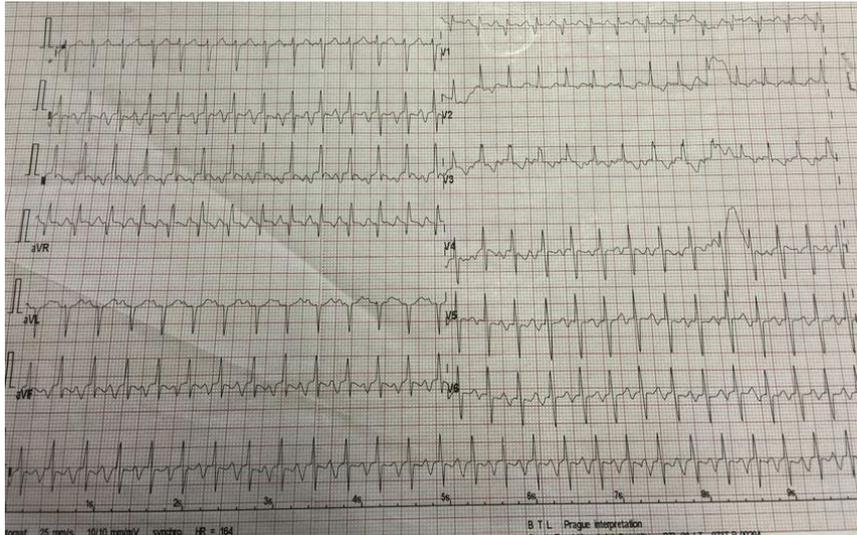
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I. INTRODUCTION

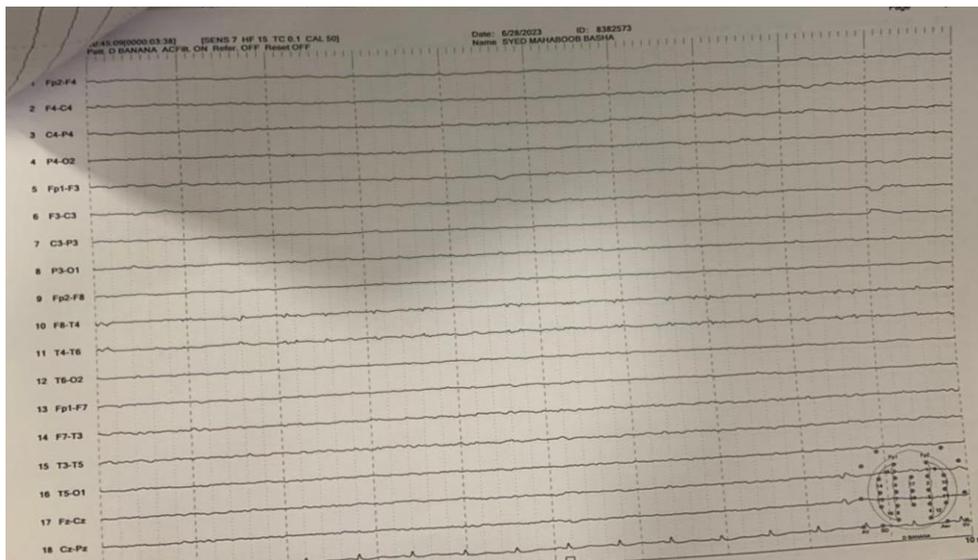
- Amitriptyline is one of the tricyclic antidepressants (TCAs), FDA approved medication to treat major depressive disorder (MDD) in adults¹. Other indications include anxiety, post-traumatic stress disorder, insomnia, chronic pain (diabetic neuropathy, fibromyalgia), irritable bowel syndrome, interstitial cystitis (bladder pain syndrome), migraine prophylaxis, post-herpetic neuralgia, and sialorrhea. Amitriptyline has been used for post-COVID headaches.
- However, these medications can also be abused, which can result in coma, deadly refractory ventricular arrhythmia, and various other conditions
- By inhibiting the norepinephrine or serotonin transporter (NET or SERT) in presynaptic terminals, amitriptyline promotes noradrenergic or serotonergic neurotransmission. Compared to other TCAs, amitriptyline is more sedative and has stronger anticholinergic effects.
- It is anticipated that the number of patients experiencing overdose intoxication will rise with ready availability to TCAs. We recently treated a patient who had uncommon but fatal side effects from amitriptyline overdose.

II. Case Presentation

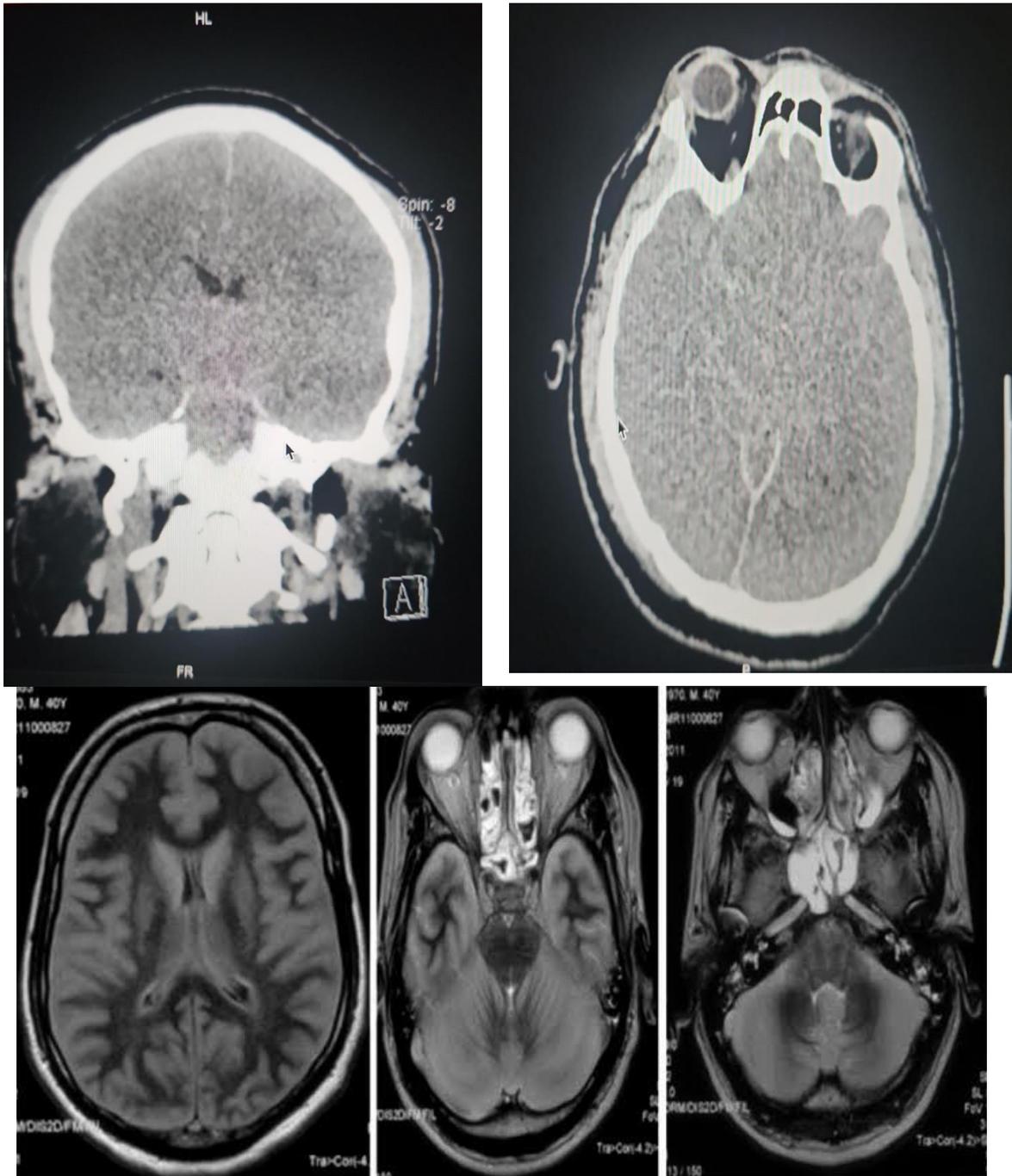
- A 41 year old male with no significant past medical history brought in an ambulance, presented with complaints of alleged history of consumption of multiple Tri-cyclic Anti-depressant over dose approximately 60 tablets -1500 Mg .
- His vital signs were as follows: Glasgow Coma Scale (GCS) score: E1 V1 M1 (Eye opening (E), best verbal response (V), best motor response (M)); heart rate: 150 beats per minutes; blood pressure: 100/70 mm Hg; respiratory rate: 14 breaths per minutes; SpO₂: 90% on room air. Both pupils were 4 mm, equal and sluggish reactive to light. Blood test results on arrival were as follows: pH 7.317, P_{CO2}: 45.1 mm Hg, P_{O2}: 61.7 mm Hg, HCO₃: 22.4 mmol/L, lactate: 2 mmol/L. His blood reports showed hyponatremia and hypokalemia and other blood parameters were within normal limits. Urine for drug abuse panel showed positive for Tri-cyclic Anti-depressant (TCA)
- ECG showed sinus tachycardia. 2D echo showed no cardiac abnormality. Patient was intubated in view of low GCS and anticipated risk of aspiration.



- After admission to intensive care, bicarbonate boluses was given and 4th hourly ABG monitoring was done to maintain an alkaline p^H and serum sodium monitoring 6th hourly to maintain serum sodium between 145-150meq/dl. Patient developed ,1 episode of supra ventricular tachycardia and was treated with Sodium bicarbonate injection infusion, followed by an episode of cardiac arrest , for which cardio-pulmonary resuscitation (CPR) was given as per advanced cardiac life support (ACLS) protocol and return of spontaneous circulation (ROSC) was achieved. Two cycles of plasmapheresis was done in view of severe toxicity and was started on intravenous intra-lipid emulsion infusion. Patient developed involuntary jerky movements of the body – suggestive of myoclonus, Electroencephalogram (EEG) was done which showed diffuse brain dysfunction and not specific to any etiology.



Emergency CT brain was done in view of dilated and non-reactive pupils, and absent brainstem reflexes which showed diffuse cerebral oedema, started on anti-oedema measures and MRI brain was done which did not show any specific etiology of sudden onset cerebral oedema which confirmed amitriptyline overdose as the cause of cerebral oedema. After extubation, patient was not alert with GCS E3V2M3 was transferred to a rehabilitation centre



III. Discussion:

- Amitriptyline, which is classified as a TCA, is commonly used to treat depression. Amitriptyline is one of the TCAs that has a lengthy elimination half-life that often lasts longer than 24 hours. It is extremely lipophilic and has a wide distribution volume in the vasculature. Amitriptyline's elimination half-life varies from 31 to 46 hours. TCAs enter the digestive system quickly and undergo first-pass effect metabolism. The therapeutic index of TCAs is narrow, and therefore, the ingestion of 10 to 20 mg/kg is potentially life-threatening¹.
- Usually, amitriptyline toxicity sets in 2-4 hours after consumption. Hypotension, seizures, CNS depression, and arrhythmias including QT prolongation are common symptoms of overdosing².
- Amitriptyline overdose was found to be the most common pathological clinical signs such as tachycardia, altered consciousness, and coma, and the most common pathologic laboratory findings were leukocytosis, hyperglycemia, and hyponatremia and other potentially life-threatening complications.

- Absence of early clinical and laboratory findings in identifying the patients at risk of life-threatening complications such as arrhythmia, seizure, and respiratory depression during the amitriptyline poisoning is a serious problem³.
- Our case presented two unique symptoms during the clinical course: (1) cerebral edema (2) myoclonic jerks derived from irreversible brain damage.
- Bicarbonate administration was recommended as treatment of TCAs overdose by the guidelines, and Intravenous Lipid Emulsion infusion is predicted as other treatment⁴.
- Levine *et al* reported a successful case of a patient with cardiac arrest after amitriptyline overdose treated with Intravenous Lipid Emulsion infusion⁵.
- As far as we know, few previous studies of irreversible brain damage caused by amitriptyline intoxication have been published. Although the majority of severe cases of amitriptyline intoxication present comatose within 24 hours, Roberge and Krenzelo reported a unique case with a prolonged coma lasting more than 5 days and loss of brain stem reflexes⁶. We cannot determine why our patient developed irreversible brain damage. Although VT occurred, the MRI findings were not typical of hypoxaemia. Overdose of amitriptyline might be associated with irreversible brain damage. Further studies on amitriptyline intoxication are needed.

IV. Conclusion:

- Despite intravenous lipid emulsion and plasmapheresis, the common tricyclic antidepressant amitriptyline has the potential to lead to serious side effects like cerebral edema, irreversible central nervous system damage, and deadly arrhythmia.
- Physicians need to be aware of these potentially fatal side effects of amitriptyline overdose.

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