“When Therapy Turns Toxic: Lessons from a Dalfampridine Overdose Case“

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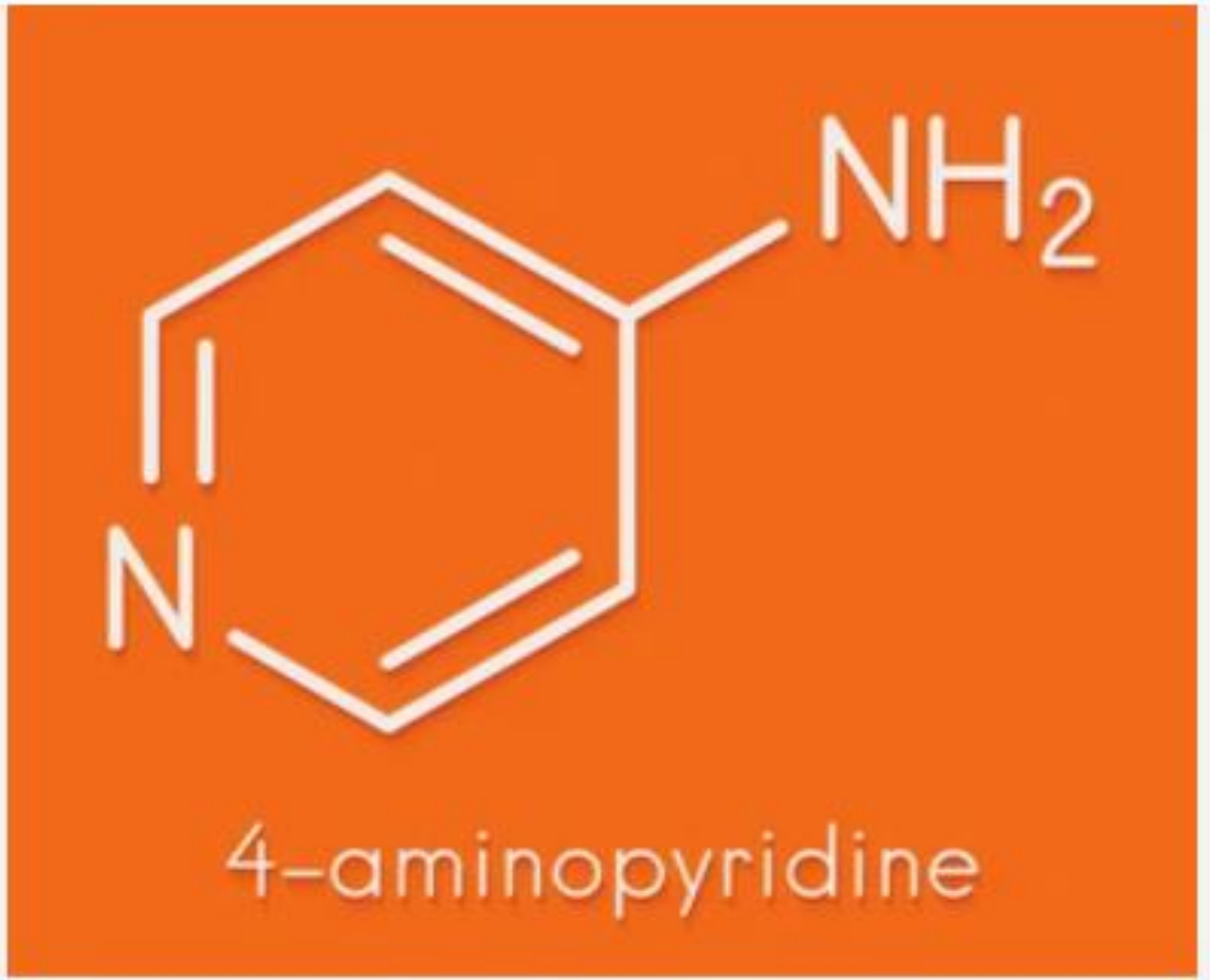
BACKGROUND AND AIM

- Dalfampridine, a selective potassium channel blocker, enhances conduction in demyelinated axons by stabilising membrane excitability, resulting in improved neurological function.
- It significantly restores ambulatory capacity in multiple sclerosis and spinal cord injury (SCI) without modifying disease progression.
- Aim: To provide an in-depth discussion of clinical manifestations and management strategies for a case of 4-aminopyridine intoxication



CASE DETAILS

A 23-year-old lady with history of spinal cord injury and psychiatric illness ingested a significant quantity of dalfampridine approximately tenfold recommended daily dose.

Approximately 2 hours later, relatives found her having profuse diaphoresis and vomiting, followed by multiple episodes of generalised tonic-clonic seizures without regaining consciousness.

She was brought to the emergency where she was intubated and mechanically ventilated due to a profoundly low Glasgow coma scale score and impending respiratory failure. Initial treatment included aggressive fluid resuscitation, but persistent hemodynamic instability required inotropic support.

MRI brain was done (Figure 1), and EEG revealed epileptiform activity (Figure 2). Gastric lavage was done and a laxative was administered to enhance drug elimination

Despite management as refractory status epilepticus with metabolic correction, she remained unresponsive to treatment initially. Anti-seizure medications were titrated.

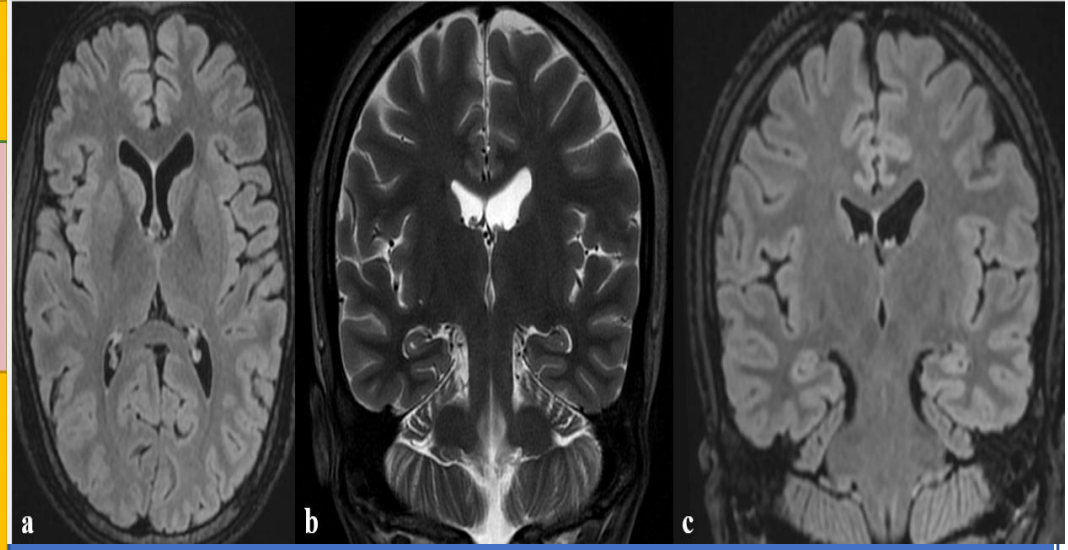


Figure 1:The axial FLAIR MRI (a), oblique coronal T2 (b), and FLAIR (c) did not show any obvious abnormality to explain seizures. No acute seizure-related changes were demonstrated

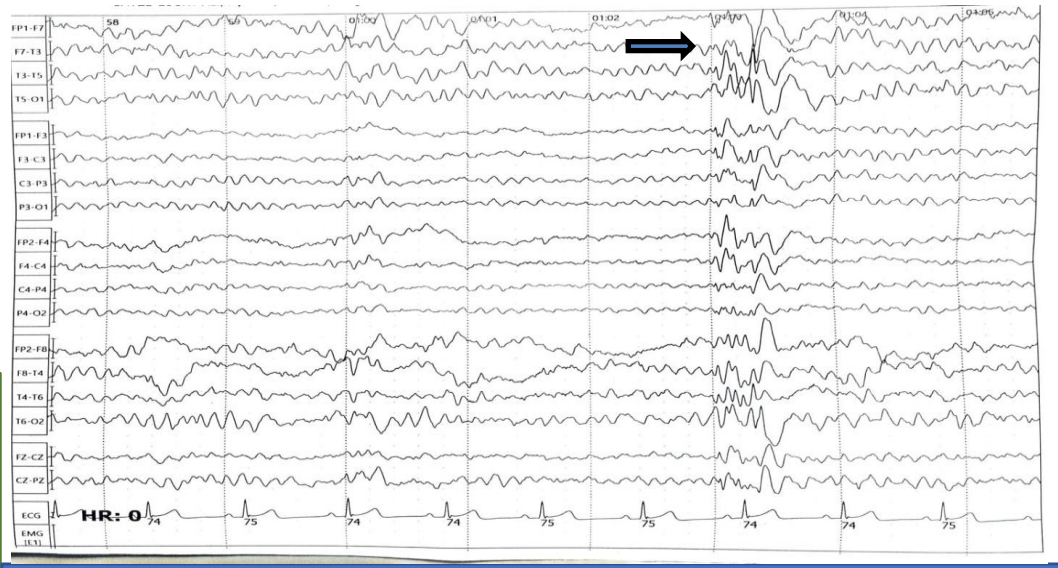


Figure 2 : EEG done in drowsy state showed diffuse mild cerebral dysfunction with generalized epileptiform discharges (black arrow)

OUTCOME

After 36-hours stay in the ICU, she achieved seizure control and was successfully extubated following hemodynamic stability

Follow-up EEG demonstrated complete resolution of epileptiform discharges with diffuse mild cerebral dysfunction (Figure 3).

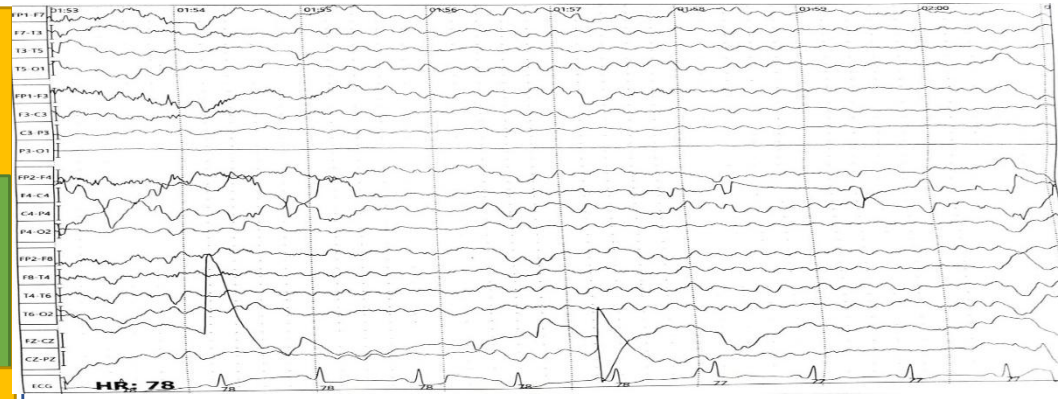


Figure 3: EEG done in awake state showed diffuse mild cerebral dysfunction with resolution of discharges

Although dalfampridine serum levels were unavailable, the medication history and constellation of autonomic instability, cholinergic signs, pulmonary edema, and refractory seizures precisely mirrored the established toxidrome of dalfampridine overdose.

- **DISCUSSION**
- This case emphasises the necessity for a detailed understanding of clinical manifestations and management strategies in dalfampridine intoxication. Due to its narrow therapeutic window, overdose can cause severe neuroexcitability, manifesting as delirium, seizures, and autonomic dysfunction.
- While clinical trials **report < 1% seizure incidence**, real-world data reveal a heightened risk among vulnerable individuals, often leading to under-recognition of toxicity.
- **Management is primarily supportive, emphasising airway protection, hemodynamic stabilisation and controlling CNS hyperexcitability with sedatives. Collaboration with toxicology experts is essential for optimal outcomes.**

CONCLUSION

- **Dalfampridine is a potent neurofunctional agent. However, overdose can lead to life-threatening complications, most notably status epilepticus. Vigilant awareness and timely identification are paramount, with psychiatric assessment and intervention strongly advised in all cases of intentional overdose to mitigate recurrence risk**.

References: 1) Goodman AD, Brown TR, Krupp LB, et al. Sustained-release oral fampridine in multiple sclerosis: a randomized, double-blind, controlled trial. Lancet. 2009;373(9665):732–738

2)Xiong R, et al. Post-marketing safety surveillance of dalfampridine. Front Pharmacol. 2023;14:1226086