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THE STROKE THAT WASN'T- A CASE OF CLINICAL MIMICRY FROM WOLFSBANE TOXICITY

Dr. Suvasish Chakraberty[1], Dr. Feraz Nawaz[2], Dr. Judith Mattakkal Jose[3*], Dr. Mayank Butola[4], Dr. Mannat Narang[5]

[1]Dr. Suvasish Chakraberty, Chief & Head of Department, Department of Emergency Medicine & Urgent Care, Artemis Hospital, Gurugram, Delhi NCR, India.

[2]Dr. Feraz Nawaz, Attending Consultant, Department of Emergency Medicine & Urgent Care, Artemis Hospital, Gurugram, Delhi NCR, India.

[3*]Dr. Judith Mattakkal Jose, Attending Consultant, Department of Emergency Medicine & Urgent Care, Artemis Hospital, Gurugram, Delhi NCR, India.

[4]Dr. Mayank Butola, 2nd Yr Dr.N.B. Resident, Department of Interventional Cardiology & Cardiac Sciences, Artemis Hospital, Gurugram, Delhi NCR, India

[5]Dr. Mannat Narang, 2nd Yr Dr.N.B. Resident, Department of Critical Care Medicine, Artemis Hospital, Gurugram, Delhi NCR, India

***Corresponding Author:** Dr. Judith Mattakkal Jose
*Attending Consultant Department of Emergency Medicine & Urgent Care, Artemis Hospital, Gurugram, Delhi NCR, India.

ABSTRACT

Historically infamous for its pernicious toxins - Aconitum also known as Wolfsbane, Devil's Helmet and Monkshood is a common ingredient in Ayurveda where it is known as महाविषा mahavisha ("great poison") or वत्सनाभ vatsanabha ("root resembling the navel of a child") and is used in small quantities after undergoing a lengthy process of detoxification.

We present to you a case of Aconitum toxicity initially diagnosed at a primary care facility as a cerebrovascular accident and referred for tertiary centre care to our emergency department where the patient was promptly diagnosed, stabilized, treated and eventually discharged owing to a multidisciplinary collective effort by physicians belonging to the departments of Emergency Medicine, Critical Care Medicine & Cardiac Sciences.

INTRODUCTION

Fig 1. Botanical Illustration of Aconitum variegatum

Aconitum (Aconitum variegatum) is a genus of over 200 species of herbaceous perennial plants found in the mountainous parts of Europe, North America and Asia. Aconitum ferox being the subspecies endemic to the Asian subcontinent with its range extending in the eastern Himalayas from central Nepal eastward through to the north of West Bengal, Sikkim, Bhutan, Arunachal Pradesh and Assam[1]. Its biologically active metabolite - Aconitine is an alkaloid toxin notorious for its pestilential effects since times immemorial as early as Claudius, the fourth Roman emperor who was said to be killed by his wife Agripinna using Aconitum. Deaths of other historical figures along the lines of Socrates and Alexander the Great have also been hypothesised to the same bane. Such ingestions - both intentional and unintentional have resulted in fatalities across the globe in recent times[2].Beyond malicious and accidental, its use has been prevalent in ancient Chinese[3], Slovenian[4] and Ayurveda schools of alternate medicine[5].

CASE REPORT

A 36 year old female, 6 weeks post partum with no diagnosed comorbidities and nil known allergies was referred to our hospital from a primary care facility for tertiary neurointerventional care with a provisional diagnosis of ischaemic stroke. She was initially taken to the primary facility 6 hours ago after developing sudden onset right sided limb weakness, perioral parasthesias, dysarthria, generalised asthenia and abdominal discomfort which was diffuse over all quadrants and not associated with any other symptoms or aggravating factors. There was no history of seizure, fever, and trauma, loss of consciousness, chest pain, gastrointestinal or genitourinary complaints.
Upon arrival, her vital parameters were indicative of hemodynamic instability with a blood pressure of 80/40 mm Hg and bradycardia of 41 beats per minute. Blood glucose and point-of-care electrolyte testing findings were unremarkable.Blood gas analysis was indicative of metabolic acidosis arising out of lactatemia thereby ruling out hint of ventilation-perfusion mismatch per se.

A physical examination followed which revealed an atraumatic head; there was no pallor or icterus. No carotid bruit, engorged neck veins or peripheral oedema were observed. Her respiratory system

findings was normal with clear breath sounds. Heart sounds were heard without any rub or murmurs. The abdomen was soft, non-tender, without any distension seen or organomegaly felt on palpation.
A nervous system examination revealed a dull sensorium with a Glasgow Coma Scale (GCS) scoring of 9 (E2V2M5) owing to which an evaluation of power deficits was not done. Examination of muscle tone via Passive Range of Motion (PROM) testing revealed hypotonia in all four limbs. With multiple domains of the National Institutes of Health Stroke Scale (NIHSS) not being evaluated due to the poor sensorium, maximum possible scores were assigned to those items with the result being a high total of 32.
After drawing samples for baseline investigations, an atropine test of 0.5 milligrams intravenous (IV) push was done to which the patient responded well revealing no intrinsic conduction system disease. A fluid challenge followed to which she failed to respond and was started on vasopressor support of Noradrenaline titrated to response to attain and maintain a mean arterial pressure (MAP) of 65 mm Hg. The patient responded well to the support and an immediate improvement in her sensorium was observed. A 12 lead Electrocardiogram (ECG) obtained post inotropic and chronotropic stabilisation revealed premature ventricular contractions with ventricular bigeminy for which a Cardiac Sciences consultation was sought and meanwhile, the patient was shifted to Radiology for an emergent Magnetic Resonance (MR) study of the brain which was Selectively Stroke Sequenced (SSS) with the NeuroIntervention team held on standby.

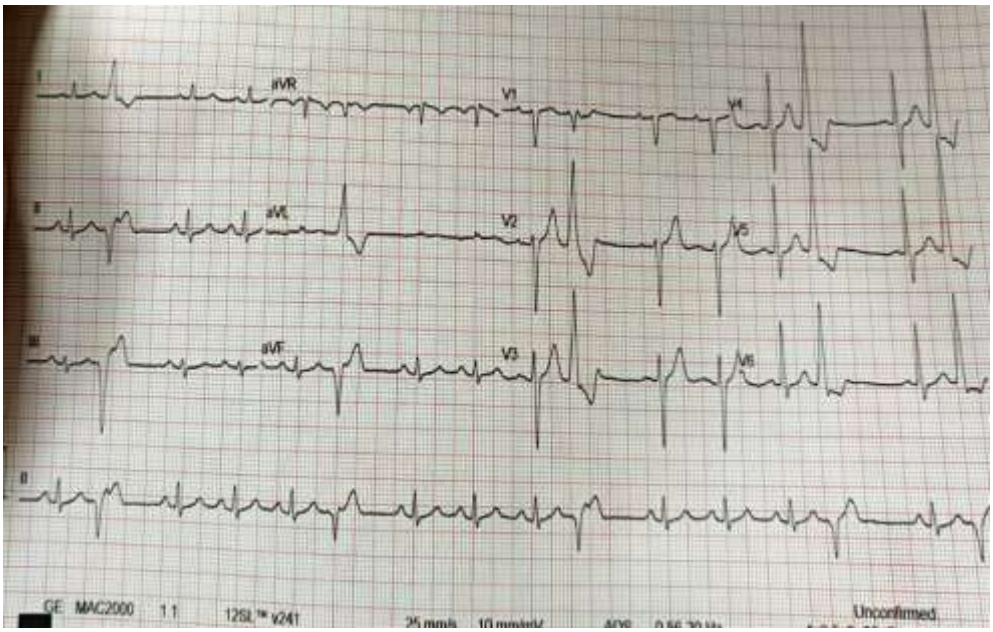

Fig 2.0 ECG post inotropic and chronotropic stabilisation

Findings of the imaging study revealed no evidence of a cerebrovascular accident of the hemorrhagic or ischaemic etiology. Results of the baseline pathological investigations were indicative of raised Troponin I, normal Creatine Kinase Myocardial Band (CK-MB), raised C-reactive protein (CRP) with all other tested parameters being within normal limits.
Upon detailed history taking, the patient revealed no new changes in dietary habits or lifestyle. However, on further probing narrated that she recently consumed an ayurvedic formulation meant for post natal wellbeing which was made by her own self at home after reading about it online in a blog written in a vernacular medium by a local wellness influencer. After sourcing the link of the same from the patient and verifying it with a translator, the formulation was confirmed to be composed of Aconitum roots - symptoms of its toxicity correlating with the patients' presentation.
Point-specific querying revealed that after procurement of the dried plant parts from a local ayurvedic dispensary, she skipped through the steps associated with its processing and consumed it after merely washing it with water and grinding it into a paste.

A Critical Care Medicine (CCM) consult was sought and the patient was admitted in the Intensive Care Unit (ICU) where the patient was treated with antibiotics, hydration and other supportive measures including but not limited to invasive monitoring of hemodynamics. The patient was weaned off of vasopressor support the following day, stepped down to wards and eventually discharged after 48 hours post presentation with instructions to avoid breastfeeding for a period of 7 days.

Category	Differential Diagnosis	Key Clinical Clues / Comments	Gold Standard Diagnostic Test
Cerebrovascular Events	Ischemic stroke	Sudden-onset focal weakness, dysarthria, and sensory loss	MRI Brain (DWI) — detects early ischemia
	Hemorrhagic stroke / Intracerebral bleed	Acute focal deficit, altered sensorium, hypertension	Non-contrast CT Brain — detects acute bleed
	Cerebral venous sinus thrombosis (CVST)	Postpartum setting, headache, seizures, focal deficits	MR Venography (MRV) — shows sinus occlusion
Cardiac Causes	Cardioembolic stroke (AF, endocarditis, PFO)	Sudden focal deficit, often multiple vascular territories	Echocardiography (TTE/TEE) + MRI Brain showing embolic pattern
	Arrhythmia with cerebral hypoperfusion	Syncope, transient deficits, hypotension	Continuous ECG / Holter monitoring
	Peripartum cardiomyopathy	Dyspnea, edema, low EF, cardiogenic shock; may mimic neurological deficit due to hypoperfusion	Echocardiography — global systolic dysfunction
	Myocardial infarction with secondary encephalopathy	Chest pain, hypotension, altered mentation	ECG + Cardiac biomarkers (Troponin I/T)
Neurometabolic / Toxic Causes	Toxic encephalopathy (e.g., aconitine)	History of ingestion; multisystem involvement	Toxin assay / LC-MS for toxin; clinical correlation
	Metabolic derangements	Confusion, altered sensorium, generalized weakness	Serum biochemistry — glucose, sodium, calcium, urea, creatinine
	Sepsis-associated encephalopathy	Hypotension, fever, infection, altered mentation	Blood cultures; diagnosis of exclusion
Neuromuscular Transmission Disorders	Guillain–Barré syndrome (GBS)	Areflexic paralysis, ascending pattern, autonomic dysfunction	Nerve conduction studies (NCS) + CSF albuminocytologic dissociation
	Myasthenic crisis	Bulbar weakness, fatigability, respiratory distress	Anti-AChR antibody assay / Repetitive nerve stimulation
	Botulism	Cranial nerve palsies, descending weakness	Toxin detection (serum/stool/food) — mouse bioassay / PCR
Postpartum-Specific Disorders	Eclampsia / PRES	Seizures, headache, hypertension, visual loss	MRI Brain (FLAIR) — posterior white matter edema
	Cerebral venous thrombosis (CVT)	Hypercoagulable postpartum state; headache, seizures	MR Venography (MRV) — confirms occlusion

Table 1: Differential Diagnoses for Undifferentiated Acute Neurological Deficits +/- Hemodynamic Instability in a Postpartum Patient.

DISCUSSION

Vatsanabha (A. ferox) is a well established ingredient in Ayurvedic formulations and its use is prevalent for purposes of antipyrexia, analgesia, appetite stimulation and digestive benefits. It is to be noted that Vatsanabha root is always used after thorough purification in these preparations. This process involves submerging the roots into the fresh urine of a healthy cow for 72 to 168 hours following which the outer covering of the root is peeled, cut into pieces and left to bask in sunlight for 24 hours. After this, it is boiled in fresh cow milk for a few hours and is ready for consumption after being dried and powdered.

Toxicity at therapeutic levels is a possibility, and safe dose is determined by processing. The lethal dose for humans is around 5 milligrams; however, a dose of 2 milligrams is typically sufficient to cause significant cardiac rhythm problems[6]. Aconitine is rapidly absorbed; metabolized primarily by esterases and partly by cytochrome P450. It is excreted in the urine and faeces.

Symptoms of intoxication are multi-system with paresthesias in any or all over the body, motor deficits in one or all limbs and gastrointestinal (GI) disturbances being the most commonly reported. Cardiovascular features include hypotension, chest pain, palpitations, bradycardia, sinus tachycardia, ventricular ectopics, ventricular tachycardia, and ventricular fibrillation.

The cardiotoxic and neurotoxic impact of Aconitine and its associated metabolite viz. Mesaconitine are exerted by their effect on the voltage sensitive sodium channels present in the cell membranes of excitable tissues in the body i.e. myocardia, neural pathways and musculature primarily. This high affinity binding of the toxic metabolites to the open state of the voltage sensitive sodium channels results in their persistent activation ultimately rendering them refractory to excitation.

The arrhythmogenic nature of aconitine is owed to its anticholinergic effects mediated by the vagus nerve whilst its hypotensive and bradycardic effects arise due to activation of the ventromedial nucleus of the hypothalamus.

Neurologically speaking, via its effect on voltage-sensitive sodium channels in the axons, aconitine blocks neuromuscular transmission by decreasing the evoked quantal release of acetylcholine.

GI involvement results from both Aconitine and Mesaconitine inducing strong contractions of the ileum through acetylcholine release from the postganglionic cholinergic nerves contributing to the myriad involvement of the body's different systems.

The most common cause of death associated with Aconitum poisoning are refractory ventricular arrhythmias with the overall in-hospital mortality being projected to range around 5.5% [7].

Management is primarily supportive with arrhythmias being dealt as per standard Advanced Cardiac Life Support (ACLS) algorithms [8].

In serious cases with debilitating arrhythmias, the use of Amiodarone, Flecainide, Procainamide, Lidocaine and Magnesium sulphate have all been investigated with varying degrees of efficacy [9, 10,11] of which Lidocaine has not proven to be effective in published case reports specifically involving ventricular tachyarrhythmias in particular[12]. This has established Amiodarone and Flecainide as first line therapies with Coulson et al. reporting the treatment of 65 cases of probable aconite poisoning culminating in ventricular dysrhythmias and concluding that Flecainide or Amiodarone appeared to be more beneficial towards reinstituting sinus rhythm as compared to lidocaine and/or cardioversion[13].

Beyond the primal resuscitative management of such toxicologies in the Emergency Department and subsequent continuum of care in the ICU, newer modalities of treatment along the lines of Extracorporeal Life Support (ECMO) have shown to improve outcomes [14].

CONCLUSION

Over 70% of the total sales of Ayurvedic drugs are over-the-counter (OTC) contributing to its misuse without prescription, guidance and oversight of trained and registered Ayurvedic physicians[15].

Analysis of Aconite poisonings in Asia particularly the subcontinent reveal that they were primarily caused by wrong dosing, inadequate or incomplete processing techniques(as observed in our patient), use of tinctures and crude roots and lack of standardisation in the supply chain by regulatory bodies [16].

When antecedent history is unclear, aconitine detection in serum might be useful via chromatographic procedures; however, they are normally unavailable in most laboratories, are time-consuming, and might result in diagnostic delays.

With masking and overlap of symptomatology, no known antidotes and significant time-sensitive mortality rates; it is imperative to diagnose, stabilise and treat this toxicity at the earliest - initiation of the treatment arc hingeing on timely recognition in the emergency department by the attending clinician.

In the bigger scheme of things, awareness drives about self-medication along with prudent research backed integrative efforts of ethnic medical practices with modern day medicine undoubtedly helps in preventing fatal, near-fatal and adverse presentations arising from its misuse and misinformation, thereby truncating the negative implications of alternative medicine in the community.

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[Fig 1] Aconitum napellus (Blauer Eisenhut). Chromolithographic botanical plate (Plate 72) from Köhler's Medizinal-Pflanzen in naturgetreuen Abbildungen (Vol. 1, 1887). Reproduced from Köhler (1887). Public domain. Image source: Biodiversity Heritage Library / Wikimedia Commons.