A Case Series of Patients with Mad Honey Poisoning from a Tertiary Care Center in Nepal

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Mad honey, which consists of grayanotoxins found in certain types of rhododendron nectar, is used in Nepal for both medicinal and recreational purposes. Grayanotoxins can increase vagal tone and result in cardiac problems, including bradycardia, arrhythmias, and hypotension. Patients experience symptoms like dizziness, nausea, vomiting, blurred vision, headache, sweating, convulsions, ataxia, and loss of consciousness. We presented two cases treated in a tertiary care center with a history of mad honey intoxication. Case 1, a 52-year-old male, presented with a pulse rate of 40 beats per minute and unrecordable blood pressure. Case 2, a 54-year-old female, presented with a pulse of 48 beats per minute, blood pressure of 85/50 mm of Hg, and bilateral diffuse wheeze. Diagnosis of mad honey poisoning was made through a history of recent consumption, physical examination, and lab tests. Both patients were treated with intravenous fluids, atropine administration in the Emergency Department, and subsequent admission to the Intensive Care Unit, where Case 1 was treated with adrenaline infusion and Case 2 with noradrenaline infusion. 24-hour electrocardiography monitoring was ensured to watch out for cardiac events. Early diagnosis and prompt management are key to good recovery and preventing severe cardiac complications.

Keywords: cardiac issues, grayanotoxin, mad honey poisoning.

Mad honey is frequently produced and consumed as a traditional medicine or recreational drug in Nepal. It is produced in a specific world region, notably Nepal and the Black Sea Region of Turkey.[1] The key component of mad honey, grayantoxon, is derived from Rhododendron species, Oleander, and Azalea. Himalayan giant honey bees derive nectar from these species of plants and hence, play a pivotal role in transferring grayanotoxin to the honey, which is responsible for poisoning and anaphylaxis, thus termed as 'mad honey'.[2] Ingestion of mad honey can lead to serious cardiovascular, gastrointestinal, and neurological symptoms requiring intravenous fluid therapy, antihistamines, and even ionotropes.[2,3] Here, the authors describe a case series of two patients initially presenting to the Emergency Department and subsequently requiring Intensive Care Unit admission in a tertiary healthcare center in Nepal.

Case Details

Case 1

A 52-year-old male with no known comorbidities presented to the Emergency Department with complaints of dizziness, vomiting, and an episode of loss of consciousness 30 minutes after consuming 2 tablespoons (30 ml) of wild honey. Loss of consciousness lasted for about 1 minute with no history of weakness, urinary/fecal incontinence, or confusion. On presentation, his blood pressure was unrecordable, and his pulse rate was 40 beats per minute. **Figure 1** shows the bradycardia in echocardiography. The laboratory investigations, including complete blood count, kidney function test, liver function test, and venous blood gas analysis, were within normal limits. In the Emergency Department, he was managed with intravenous fluids and Atropine 0.6 mg. His blood pressure initially rose to 130/70 mm of Hg. However, after admission to the Intensive Care Unit, it again dropped to 90/50 mm of Hg, and thus, Adrenaline infusion was started at 0.1 mcg/kg/min and titrated at 0.01 to 0.1 mcg/kg/min to maintain a mean arterial pressure (MAP) > 65 mm of Hg. He received the infusion for the next 19 hours. On the following day, he was shifted to the High Dependency Unit (HDU) and the next day to the general ward with 24-hour electrocardiography monitoring. His stay in the ward was uneventful; he was discharged on the fourth hospital day.

Case 2

A 54-year-old female, known patient of bipolar disorder, presented to the Emergency Department with complaints of multiple episodes of vomiting, loose stools,

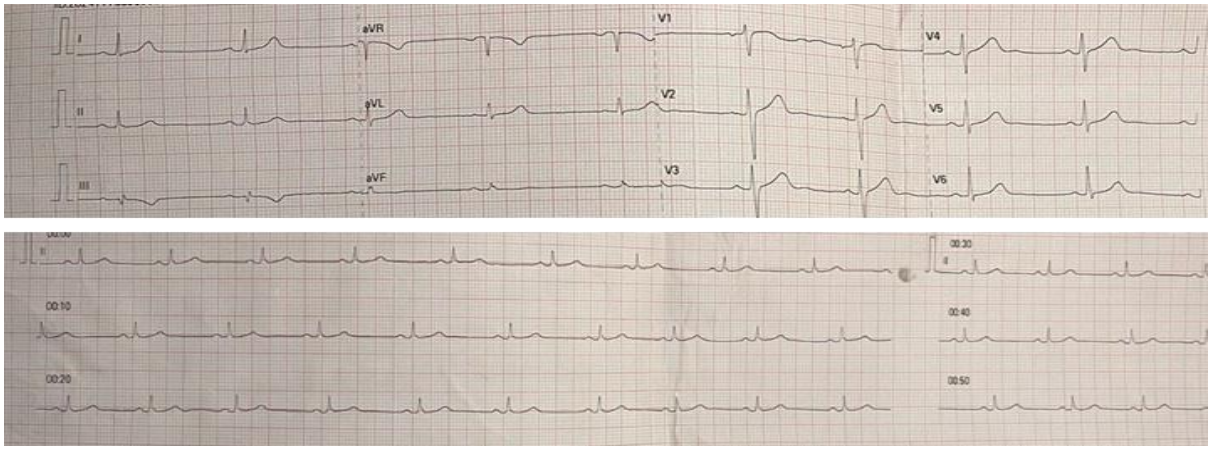

Figure 1: Echocardiography showing bradycardia in Case 1

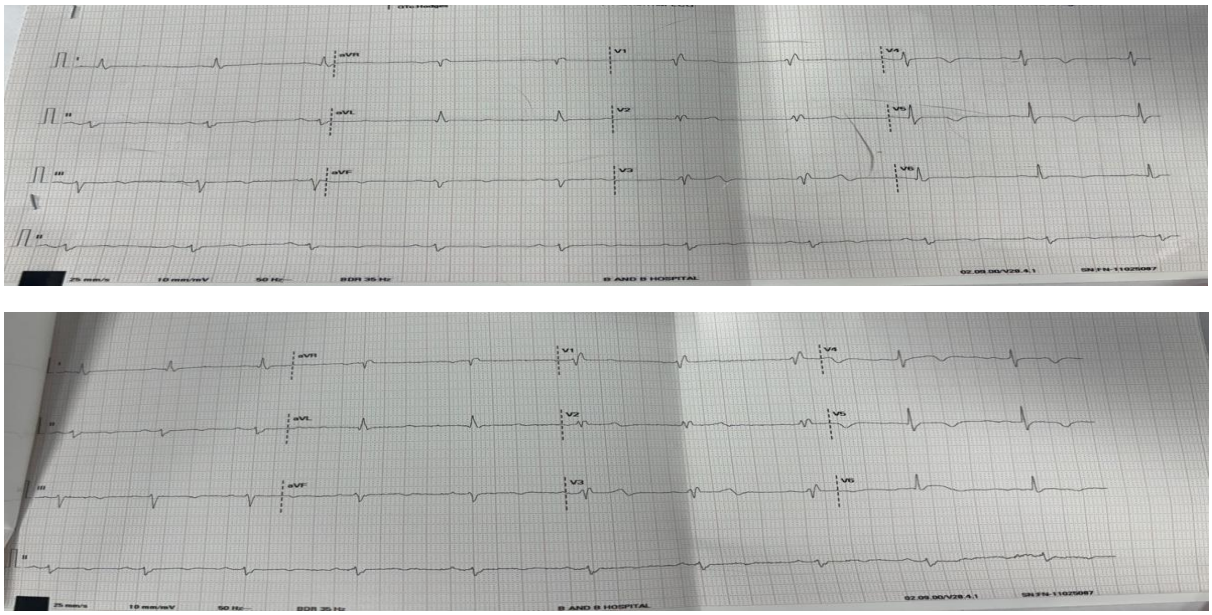

Figure 2: Echocardiography showing bradycardia and right bundle branch block in Case 2

headache, blurring of vision, and one episode of loss of consciousness 6 hours after consuming 2 tablespoons (30 ml) of wild honey. She, however, had a history of cough for 1 month, for which she had completed a 5-day course of oral antibiotics for a chest infection 5 days before presentation. On examination, her blood pressure was 85/50 mm of Hg, and her pulse rate was 48 beats per minute. Chest auscultation revealed bilateral wheeze, while laboratory investigations were within normal range. Echocardiography showed bradycardia and right bundle branch block, as shown in **Figure 2**. Chest X-ray showed ill-defined parenchymal opacity in the left upper and right lower zones. In the Emergency Department, she received intravenous fluids, Atropine 1.2 mg initially, followed by a second dose of Atropine 0.6 mg was administered along with antihistamine, steroid, and nebulization with salbutamol. She was admitted to the Intensive Care Unit and

Table 1: Summary of clinical features, management, and outcomes of both cases

Details	**Case 1**	**Case 2**
Age	52 years	54 years
Sex	Male	Female
Amount of honey consumed	30 gm	30 gm
Origin of honey	Solukhumbu, Nepal (monsoon season)	Solukhumbu, Nepal (monsoon season)
Comorbidity	None.	Bipolar disorder
Reason for consumption	To improve general health	To relieve a cough
Onset of symptoms	30 minutes	6 hours
ECG finding	Sinus bradycardia	Bradycardia and right bundle branch block
Laboratory investigations	Normal	Normal
Atropine received	0.6 mg	0.6 mg + 1.2 mg
Ionotrope support	Adrenaline infusion	Nor adrenaline infusion
ICU stay	1 day	1 day
HDU stay	1 day	2 days
Ward stay	1 day	-
Complications	None	Complicated by a coexisting chest infection

treated with noradrenaline infusion at 0.01-0.03 mcg/kg/min for a total of 7 hours, intravenous fluid at 40 ml/hour, intravenous antibiotics (cefoperazone + sulbactam), and oral antibiotic (azithromycin). Her blood pressure then reached 120/70 mm of Hg, and a Mean Arterial Pressure of >65 mm of Hg could be achieved with the help of noradrenaline infusion and intravenous fluids. She was shifted to the High Dependency Unit the next day. Her stay was complicated as sputum culture showed growth of *Serratia marcescens,* High-Resolution Computed Tomography (HRCT) chest revealed findings likely of active/reactivation of tuberculosis. She was discharged on request on the 4th day of admission with antibiotics and to follow up with the sputum GeneXpert report. During follow-up, she showed improvement, and GeneXpert showed no evidence of tuberculosis. The summary of clinical

features, management, and outcomes of both cases is illustrated in **Table 1.**

Discussion

Worldwide, Nepal does hold several cases of mad honey poisoning, as mentioned in a 900-case-complied study conducted by Gunduz et al., where the majority of poisoning cases (91.44%) were reported from mad honey produced in Turkey, and Nepal (4.67%) came second.[1]

Grayanotoxins are responsible for various cardiovascular and neurological symptoms that appear after consuming mad honey.[2] 20 different types of Grayanotoxin (GTX) have been discovered so far. Among these types, GTX 1 and GTX 2 are found more frequently in Nepalese-derived honey. GTX1 is present in the highest quantity.[3] The amount of honey that leads to intoxication is about 15-30 grams, and the onset of symptoms is 30 minutes to 4 hours, as evidenced by a study conducted by Ullah S. et al.[2] The amount of honey is in conjunction with this case series, but the onset of symptoms showed a variability of 30 minutes in Case 1, and 6 hours in Case 2. The quantity of mad honey consumed, the concentration of Grayanotoxin in the honey, time of the year it is produced influence the degree of intoxication.[4,5]

The key component of mad honey is Grayanotoxin, which binds to the GTX site on Group II receptor sites of Na channels. It causes persistent depolarization of sodium channels in muscles and neurons.[3] Its agonist action on the M_2 receptor and vagus nerve further explains the occurrence of bradycardia.[3] Commonly encountered symptoms and signs include dizziness, nausea, vomiting, syncope, hypotension, and the commonest ECG finding being bradycardia,[2] atrioventricular block,[6] atrial fibrillation,[7] myocardial infarction,[8] and asystole[9] rarely occurs. Overall, the most common signs are hypotension and bradycardia.[3,5]

Most cases respond well when treated in response to anaphylactic shock with IV fluids, Atropine, ionotropes, steroids, and antihistamines. Case 1 was treated with Adrenaline infusion, Case 2 with nor adrenaline infusion, and both with Atropine, which shows that sympathomimetic effect of ionotropes and anticholinergic action of Atropine are of prime importance. Similarly, a systematic review conducted in 1199 cases by Silici et al. reported no mortality, which is analogous to this case series.[10]

Conclusion

Even though mad honey consumption is a common practice in Nepal, poisoning and anaphylaxis caused by it are rare. Diagnosis should be made clinically and promptly, as serum analysis of Grayanotoxin is a lesser-explored spectrum and can be challenging

in resource-limited settings. Patients must be admitted and treated with Atropine, intravenous fluids, and, if required, inotropes, antihistamines, and steroids. Adrenaline and noradrenaline both show a good response, as evidenced by this case series.

Conflict of Interest: All the authors declare to have no conflicts of interest relevant to this study.

Consent to Participate: Written informed consent was taken from the patient and the patient's party for publication of this case series.

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