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Case Report

A Case Report on Wild Honey-Induced Grayanotoxin Poisoning from Nepal

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ABSTRACT

This case report presents an uncommon occurrence of grayanotoxin poisoning in a 52-year-old hypertensive individual from the Himalayan village of Chame, Nepal. Grayanotoxin, sourced from the *Rhododendron* plant, is extracted by bees to produce honey that contains this toxin, commonly known as mad honey. Consumption of mad honey can induce cholinergic symptoms such as hypotension, bradycardia, and dizziness. The patient presented with these symptoms and received immediate emergency treatment at Manang hospital. After 24 hours of observation, the patient returned to normal health.

Keywords: Wild honey; Grayanotoxin; Bradycardia; Poisoning; *Rhododendron*

INTRODUCTION

Honey is an intricate natural food produced by bees from the nectar of flower. Its composition varies based on factors such as the species of honeybees, flora, geographical origin, and climatic conditions. Predominantly, it is made up of sugars; honey also contains minerals, vitamins, proteins, organic acids, aromatic acids, and waxes [1]. However, the consumption of honey containing toxins can lead to intoxication. There are two types of honey intoxication: Mad honey poisoning, caused by grayanotoxins found in *Rhododendron* plants, primarily reported in Turkey, South Korea, and Nepal, and tutin honey poisoning, caused by tutin, a neurotoxin from Coraria shrubs, reported in New Zealand [2,3].

Grayanotoxin, extracted by bees from the nectar and pollens of *Rhododendron* flowers, has various forms, with Grayanotoxin I affecting cardiac manifestations, and Grayanotoxin II being less toxic, causing suppression of the sinoatrial node [4]. Mad honey, utilized as an alternative medicine, is reputed for treating conditions such as hypertension, diabetes, flu, gastrointestinal disorders, abdominal pain, arthritis, and various infections [4,5].

Grayanotoxin acts on sodium ion channels and muscarinic receptors, leading to vagal activation, resulting in symptoms like hypotension, rhythm disorders (bradycardia, atrial fibrillation, nodal rhythm, and atrioventricular block), respiratory depression, hypersalivation, nausea, vomiting, blurred vision, vertigo, headache, sweating, extremity paresthesia, impaired consciousness, and convulsions [6,7]. Intoxication occurs with the consumption of 15-30 g of mad honey, and symptoms manifest within half to 4 hours. The degree of intoxication depends on the amount of mad honey consumed, grayanotoxin concentration, and the season of production. Diagnosis is clinical, suspected in patients without prior heart conditions presenting with the mentioned symptoms after consumption of wild honey [4].

The treatment for mad honey poisoning involves symptomatic care and close patient monitoring. Dizziness and mild hypotension are managed with saline infusion, while atropine is preferred for severe hypotension and bradycardia. In exceptional cases where the patient does not respond to normal saline and atropine, temporary cardiac pacing may be considered. Symptoms typically last a day due to the rapid metabolism and excretion of grayanotoxins [4,8].

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CASE PRESENTATION

A 52-year-old baker and restaurant owner from the Himalayan village of Chame (2710 m) in the Manang district of Nepal visited the emergency department, reporting a sudden onset of dizziness, vomiting, profuse sweating, and hypersalivation. He attributed these symptoms to consuming 2 teaspoons of stored wild honey mixed with water and lemon, which occurred 30 minutes prior. The patient, a known case of hypertension, had been on Amlodipine 5 mg and Losartan 50 mg once daily for over 15 years.

Upon arrival, the patient experienced severe dizziness, making standing difficult and triggering an intense headache. His Blood Pressure (BP) was 65/45 mm Hg, Heart Rate (HR) was 54 beats per minute (bpm), and oxygen saturation (SpO_2) was 94% on room air. He denied taking an overdose of prescribed antihypertensive medication. A 12-lead electrocardiogram revealed sinus bradycardia at 54 bpm (Figure 1). Hematological parameters were mostly within normal limits, except for a total count of 18,500 cells per cubic millimeter and 80% neutrophils. Renal Function Tests (RFTs) showed elevated urea (65 mg/dl) and creatinine (1.8 mg/dl). Liver Function Tests (LFTs) indicated elevated Alanine Transaminase (ALT) at 72 U/L and Aspartate Aminotransferase (AST) at 62 U/L.

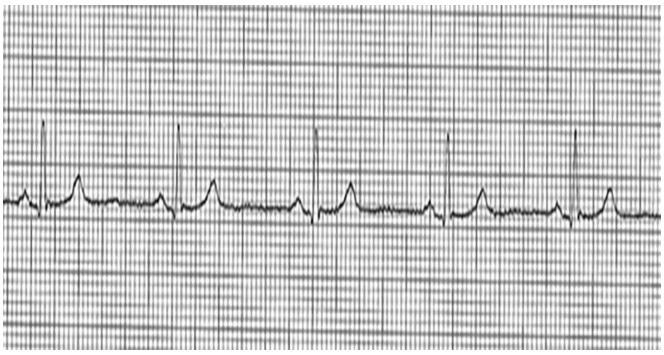

Figure 1: The Electrocardiogram (ECG), revealed sinus bradycardia at 54 bpm.

Immediate resuscitation involved intravenous fluids (0.9% normal saline), followed by intravenous administration of hydrocortisone (100 mg) and diazepam (5 mg) to control agitation. After receiving 1000 ml of normal saline, the patient's BP improved to 95/70 mm Hg, HR increased to 70 bpm, and he reported symptomatic improvement. Continuous monitoring ensued and anti-hypertensive medication was temporarily withheld. An additional 500 ml of normal saline resulted in a BP of 130/90 mm Hg, eliminating the need for vasopressor support or atropine.

After 24 hours of observation and the administration of 1.5 liters of normal saline, the patient was discharged with instructions for a follow-up the next day. Repeat Liver Function Tests (LFT) and Renal Function Test (RFT) results were within normal limits (Table 1). During the follow-up, the patient had returned to his usual state of health, experiencing only a mild headache. Anti-hypertensive medication was resumed, and he was advised against consuming wild honey or *Rhododendron* to prevent a recurrence of similar symptoms.

Blood tests	Values	
	At time of presentation	At time of discharge
Total cell count (4000-11000/ cu mm)	18500	10600
Blood glucose level (60-200 mg/dl)	65	76
Urea (5-20 mg/dl)	65	28
Serum creatinine (0.3-1.1 mg/dl)	1.8	1.1
AST (8-48 U/L)	62	40
ALT (7-55 U/L)	72	51

Table 1: some of the lab values at the time of presentation and at the time of discharge. **Note:** AST: Aspartate aminotransferase and ALT: Alanine transaminase.

RESULTS AND DISCUSSION

Grayanotoxins, a group of cyclic hydrocarbons lacking nitrogen, are well-known for their presence in honey derived from the nectar of *Rhododendron* flowers [9]. Common genera like *Agarista* and *Kalmia* in regions such as Manang, along with other hilly areas of Nepal, contribute to the availability of these toxins [10]. The traditional practice of hunting and consuming wild honey in the Himalayan regions, including Manang, raises the risk of exposure to grayanotoxins [9].

Of the 18 identified grayanotoxins, Grayanotoxin I and II, found in *Rhododendron* honey, leaves, and flowers, are recognized as the most potent variants [4,9]. Clinical studies have established that the minimum blood concentration of grayanotoxin capable of inducing hypotension ranges from 2.52 to 4.55 ng/ml [11]. Grayanotoxin I, specifically, is implicated in cardiac manifestations affecting atrioventricular conduction and the sinoatrial node. It binds to voltage-gated sodium channels, preventing their inactivation and increasing membrane permeability, leading to hyperpolarization [2,3]. Symptoms associated with grayanotoxin poisoning include dizziness, weakness, perspiration, salivation, syncope, hypotension, blurred vision, diplopia, nausea, vomiting, complete heart blocks, and, rarely, asystole [3,4,10]. Our patient exhibited similar signs and symptoms, aligning with the effects of grayanotoxin.

This case report highlights a distinct occurrence of mad honey intoxication in a hypertensive individual, emphasizing the severity of cardiovascular manifestations, particularly bradycardia and hypotension. The observed hypotension can be linked to the vagal activation induced by grayanotoxins affecting sodium ion channels and muscarinic receptors [6,7].

The patient's positive response to emergency management, including appropriate fluids, hydrocortisone, and diazepam, resulted in the rapid improvement of, hypotension, dizziness and bradycardia. The transient nature of mad honey intoxication symptoms, as evidenced by the patient's return to baseline health within 24 hours, supports the notion that with proper management, these symptoms are reversible over time [4,8].

It is important to distinguish mad honey intoxication from conditions with similar clinical presentations, such as acute coronary syndromes and organophosphate poisoning. Unlike the acute coronary syndromes, mad honey intoxication lacks ischemic changes in the ECG, positive serum markers for cardiac injury, or abnormalities in coronary vessels as seen in angiography. To rule out organophosphate poisoning, an estimation of cholinesterase enzyme levels in serum can be performed, as organophosphate poisoning shares similar manifestations of cholinergic excess [4,10].

CONCLUSION

We presented a rare case of wild honey poisoning from Nepal. Grayanotoxin, extracted by bees from the nectar and pollen of *Rhododendron* flowers, is present in wild honey. Grayanotoxin induces vagal activation, leading to symptoms such as hypotension, bradycardia, dizziness, and other cholinergic manifestations. The treatment for mad honey poisoning comprises symptomatic care with IV fluid and atropine. This case report helps better understanding of the clinical implications and treatment modalities for cases of grayanotoxin-induced intoxication, particularly in regions where wild honey consumption is prevalent.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

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