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## Case report

### A case of acute hepatitis following mad honey ingestion



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#### ABSTRACT

Acute hepatitis is characterized by liver inflammation and liver cell necrosis. The most frequently observed underlying cause thereof is viruses, but various other causes, such as alcohol, medication, or toxins may also lead thereto.

In this paper, a case of acute hepatitis presenting with bradycardia, hypotension, and a prominent increase in liver enzymes following mad honey ingestion is discussed. Since there are only few cases of acute hepatitis following mad honey ingestion in the literature, we want to present this subject matter.

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## 1. Introduction

Acute hepatitis is characterized by liver inflammation and liver cell necrosis. Many different causes, such as viruses, alcohol, medications, toxins, or infectious diseases, may result in acute hepatitis. Ischemic hepatitis that may develop as a result of disrupted hemodynamics is also among the causes of acute hepatitis.<sup>1</sup>

Grayanotoxin-containing flowers of the Rhododendron species from the family Ericaceae are found in Turkey, especially in the Eastern Black Sea Region. The honey derived from these flowers is colloquially known as mad honey, bitter honey, or wad honey. Following mad honey ingestion, many symptoms from mild gastrointestinal irritation to life-threatening bradyarrhythmias and hypotension may occur.<sup>2,3</sup>

In this paper, a case of acute hepatitis following an intake of mad honey is presented.

## 2. Case

An 89-year-old woman presented to the emergency service with complaints of nausea, weakness, and faintness. On admission, she was conscious and cooperative, and her body temperature, blood

pressure, and peak heart rate were 36 °C, 90/60 mmHg, and 50 beats per minute, respectively. On physical examination, her peak heart rate was 48 beats per minute, and no additional voice or murmur was detected. On ECG (electrocardiography), a sinus bradycardia corresponding to 48 beats per minute was observed. There was no finding of ischemia. When she was questioned for a more detailed medical history, it was revealed that she had heart failure, but currently takes neither medication specifically, nor any other substance or medicine with a potential for toxic effects; it was also discovered that she had eaten 2–3 spoons of honey 2 h before admission. Therefore, the possibility of mad honey poisoning was taken into consideration, and thus, the vascular access of patient was opened and monitored, and hydration was initiated. On laboratory analyses, various elevated values were detected for liver function tests (AST: 1025 IU/L, ALT: 817 IU/L, ALP: 177 IU/L, GGT: 298 IU/L, LDH: 799 IU/L). PT was 35, and INR was 2. Cardiac enzymes were negative. Hepatitis markers were also negative. Patient was pre-diagnosed with bradycardia-hypotension and acute hepatitis associated with mad honey poisoning following a consultation with internal medicine, and hospitalized for further monitoring and treatment. Fluid replacement was continued during monitoring. On transthoracic echocardiography, left ventricular ejection fraction was 65%, and left ventricular systolic function was normal. On abdominal ultrasonography, a liver size corresponding to the physiological upper limit and normal liver contours were found. Hepatic and portal vein diameters were normal. Intrahepatic

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bile ducts were also normal, and no calculus was detected. By the 12th hour of treatment, pulse and tension had returned to normal levels. Upon observations of decreased values of liver function tests and a recovered general health condition, patient was discharged to be followed through future polyclinic checks.

### 3. Discussion

Mad honey, also named bitter honey in our country, is a type of honey that is comprised of the nectar of grayanotoxin-containing flowers of a specific plant species called *Rhododendron*. Mad honey is generally consumed as food, but is also used as an alternative medicine element for stomachache, digestive disorders, hypertension and sexual stimulation among the general public.<sup>3–5</sup> Grayanotoxins have several sub-groups. Mad honey poisoning is essentially caused by the first and second sub-groups, which increase permeability of sodium channels in cell membranes and result in peripheral vagal stimulation.<sup>2,3</sup> Hypotension, bradycardia, atrioventricular block, vertigo, nausea, vomiting, diplopia, hypersalivation, and syncope may be seen in mad honey poisoning.<sup>2,3</sup> A recovery from complications is usually achieved through intravenous fluid support. In bradycardia cases that cannot be ameliorated with fluid supplementation, atropine is used.<sup>2</sup> In cases unresponsive to atropine, treatment should be planned in accordance with a bradyarrhythmia treatment algorithm; in the literature, there are reports of atropine-unresponsive cases requiring pacemaker implantation.<sup>2</sup> In the case reported by Gündüz et al,<sup>4</sup> the patient was brought to the emergency service with dizziness and syncope following honey ingestion, followed by cardiac arrest during initial examinations, and accordingly, cardiac pacemaker implantation was carried out. In our case, the patient was admitted to the emergency service with nausea and faintness; hypotension and bradycardia were successfully treated via hydration, and thus neither atropine nor pacemaker was required for treatment of bradycardia.

Acute hepatitis is characterized by liver inflammation and liver cell necrosis. Many different causes, such as viruses, alcohol, medications, toxins, infectious diseases, or hemodynamic disorders, may result in acute hepatitis.<sup>1</sup> In the differential diagnosis of acute hepatitis, liver biopsy may also be used in addition to laboratory tests. However, it may not always be possible to perform a surgical biopsy.

Viral markers in our patient were negative. There was neither alcohol consumption nor use of any herbal product or medicine that might lead to toxic hepatitis, other than honey. The focal infection could not be detected. Leukocytosis was not found. C-reactive protein (CRP) was negative. Therefore, viral hepatitis, alcoholic hepatitis, and infectious causes were excluded. In the light of this information, we concluded that the cause of acute hepatitis was ischemic hepatitis associated with hypotension or toxic hepatitis associated with mad honey ingestion.

Toxic hepatitis may occur months, days, or even hours after exposure to a toxic agent. The corresponding clinical picture involves various elements from asymptomatic enzyme elevations to fulminant hepatitis. Generally, symptoms are treated by preventing the toxin exposure. In some cases, however, irreversible scarring of the liver and hepatic insufficiency may develop. In diagnosis, the presence of toxic exposure is considered together with laboratory findings.<sup>5</sup>

In a study carried out on rats,<sup>6</sup> hepatitis and renal failure following mad honey ingestion were reported, and Çetin et al<sup>7</sup> also reported a case that they associated with mad honey ingestion.

Ischemic hepatitis, also referred to as shock liver or hypoxic hepatitis, is characterized by centrilobular liver cell necrosis and sharply increasing serum transaminase levels following a hypotensive episode, and in most cases, is ameliorated by treating the hypotensive status.<sup>8,9</sup> Serum transaminase and lactate dehydrogenase (LDH) levels frequently rise to at least twenty times the normal values, and return to normal in a short span of time. Generally, three basic criteria are used in diagnosis: 1 – acute cardiac, circulatory or respiratory failure; 2 – a temporary elevation in aminotransferases, which corresponds to at least twenty times the normal level; 3 – exclusion of a potential viral or medication-related hepatitis that may cause liver cell necrosis.<sup>8</sup> The ratio of ALT/LDH in ischemic hepatitis is usually <1.5. On the other hand, this ratio is much higher in acute viral hepatitis. A prothrombin time prolongation of 2–3 s may be seen. Serum transaminase levels may increase in viral hepatitis, ischemic hepatitis and toxic hepatitis, but lactate dehydrogenase levels rise to high values only in ischemic hepatitis.<sup>10,11</sup> In our case, laboratory values increased within 2 h of toxic substance ingestion, and, consistent with ischemic hepatitis, the ratio of ALT/LDH was 1.02 and the prothrombin time was 35 s. The patient, in whom tension and pulse values were returned to normal by hydration, had normal AST, ALT, and LDH levels by the 4th day. In conclusion, although we have considered the presence of ischemic hepatitis in the foreground, we could not exclude the possibility of toxic hepatitis because of toxic substance exposure.

### 4. Conclusion

In this paper, a case of acute hepatitis presenting with bradycardia, hypotension, and a prominent increase in liver enzymes following mad honey ingestion is discussed. Since there are only few cases of acute hepatitis following mad honey ingestion in the literature, we herein want to point out at the importance of medical history and anamnesis in hepatitis cases presented to the emergency service, and contribute to the literature thereby.

### References

1. Tabak F, Akut Hepatitler İÜ. In: . *Cerrahpaşa Tıp Fakültesi Sürekli Tıp Eğitimi Etkinlikleri Hepato-Bilier Sistem ve Pankreas Hastalıkları Sempozyum Dizisi*. 28. 2002:43–55.
2. Gündüz A, Tatlı Ö, Türedi S. Mad honey poisoning from the past to the present. *Turk J Emerg Med*. 2008;8:46–49.
3. Koca I, Koca A. Poisoning by mad honey: a brief review. *Food Chem Toxicol*. 2007;45:1315–1317.
4. Gündüz A, Durmuş I, Türedi S, Nuhuğlu I, Öztürk S. Mad honey poisoning-related asystole. *Emerg Med J*. 2007;24:592–593.
5. Goodman Z, Ihsak K. Medical diseases of the liver. In: *Silverberg's Principles and Practice of Surgical Pathology and Cytopathology*. 4th ed. Churchill Livingstone: Elsevier; 2006:1475–1500.
6. Aşçıoğlu M, Özemesi Ç, Doğan P, Öztürk F. Effects of acute grayanotoxin-i administration on hepatic and renal functions in rats. *Turk J Med Sci*. 2000;30:23–27.
7. Çetin NG, Marçal E, Kıldırım M, Ögüt S. Deli bal ile hepatotoksitesite. *Türkiye Acil Tıp Dergisi*. 2009;9:84–86.
8. Fuhrmann V, Jäger B, Zubkova A, Drolz A. Hypoxic hepatitis - epidemiology, pathophysiology and clinical management. *Wien Klin Wochenschr*. 2010;122:129–139.
9. Seeto RK, Fenn B, Rockey DC. Ischemic hepatitis: clinical presentation and pathogenesis. *Am J Med*. 2000;109:109–113.
10. Akar H, Şentürk T, Yükselen V, et al. Hipotansiyonun yol açtığı bir iskemik hepatit olgusu. *ADÜ Tıp Fakültesi Dergisi*. 2001;2:27–30.
11. Cassidy WM, Reynolds TB. Serum lactic dehydrogenase in the differential diagnosis of acute hepatocellular injury. *J Clin Gastroenterol*. 1994;19:118–121.