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Mad Honey Disease

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ABSTRACT

A 46-year-old woman presented to the emergency room with acute onset of nausea, vomiting and prostration. She appeared ill and was poorly responsive to verbal stimuli. Physical examination showed a systolic blood pressure of 60 mmHg and a pulse of 40 bpm. ECG was notable for slight ST-elevations in the inferior leads. Right ventricular myocardial infarction with cardiogenic shock and bradycardia was suspected. Supportive therapy with catecholamines was initiated and an emergency coronary angiography was arranged. However, laboratory results showed normal troponin levels and a subsequent echocardiogram showed the absence of abnormal wall motion. Thorough history taking with the spouse revealed that the patient had consumed Turkish honey approximately 1 h before the symptoms began. The patient made a full recovery within 24 h with only supportive therapy. In retrospect, the clinical presentation was highly indicative of poisoning with grayanotoxins from the rhododendron plant, which contaminate some types of honey in the Black Sea area. A pollen analysis confirmed the presence of rhododendron in a honey sample. Historically this poisoning is referred to as mad honey disease. The ST-elevations in the ECG were a sign of early repolarization, a non-pathological finding.

LEARNING POINTS

- ST-elevation in the inferior leads of an ECG in the context of hypotension and bradycardia does not always indicate right myocardial infarction.
- In the proper context, intoxication with grayanotoxins should be included in the differential diagnosis of hypotension and bradycardia.
- Study of diseases occurring in the past in a particular region offers the physician the chance to make a diagnosis otherwise missed.

KEYWORDS

Mad honey, poisoning with grayanotoxins, right ventricular myocardial infarction

CASE PRESENTATION

A 46-year-old woman of Turkish origin presented to our emergency room with acute onset of nausea, vomiting, profuse sweating and prostration. Her husband reported that she had just collapsed in the street. There was no mention of chest pain, dyspnoea, diarrhoea or abdominal pain. The patient's history was not notable for serious illness and she was not on any medication.

On admission the patient appeared very ill and was poorly responsive to verbal stimuli. Physical examination showed a slightly obese patient with profuse perspiration, a blood pressure of 60/40 mmHg and a pulse of 40 bpm, while the other vital parameters were normal. Heart auscultation revealed a regular rhythm and no cardiac murmurs or pathological heart sounds. In addition, there were no pulmonary crackles

or wheezing, the abdomen was soft, the peristaltic sounds were normal, and there was no jugular vein distension or leg oedema. Neurological examination showed a patient with slow undifferentiated reactions towards verbal stimuli (8 points on the Glasgow Coma Scale), normal-sized pupils with minimal response to light, and no focal neurological defects.

The ECG was notable for sinus bradycardia and slight (max. 1.5 mV) ST-elevations inferiorly (II, III, aVF). Due to the markedly low blood pressure and bradycardia, the patient was immediately transferred to the ICU. The preliminary diagnosis at this time was right ventricular myocardial infarction with cardiogenic shock and bradycardia. In addition to conservative treatment for acute coronary syndrome, supportive therapy with noradrenaline was initiated. An emergency coronary angiography was arranged.

However, within a few minutes the laboratory results revealed normal high-sensitive troponin T levels (5.2 pg/ml and 5.0 pg/ml approximately 1 hour later), mild lymphocytosis (3650/µl), eosinophilia (280/µl), a slightly elevated creatinine (1.2 mg/dl) and a blood glucose of 103 mg/dl. Echocardiography revealed no abnormal wall motion and a good systolic ejection fraction of both ventricles ('eyeballing'). The vena cava was also collapsing and not dilated. In view of these findings, an acute coronary syndrome could be ruled out. The ST-elevations in the ECG were therefore interpreted as a sign of early repolarization, which is mostly a non-pathological finding.

Hence a thorough history was taken from the spouse, which showed that the patient had consumed a bit more Turkish honey than usual approximately 1 h before the symptoms began and that the husband in the past had seen 'strong men' who fainted and were 'almost dead' after eating the same honey. At this point the differential diagnosis included intoxication or anaphylactic shock. Anaphylactic shock was deemed improbable because of the persistent bradycardia despite catecholamine administration; however, to be on the safe side, 250 mg prednisolone was administrated intravenously.

The more logical cause for this presentation was poisoning with a parasympathomimetic substance. A sample of the Turkish honey was collected with the aid of the husband. After numerous telephone calls all over Germany, a 'honey specialist' was found in a German institute for consumer protection. This official suggested the cause could be grayanotoxin from the rhododendron plant, which can be found in some types of honey in the eastern Black Sea area. The technique to measure grayanotoxins in patient serum was not routinely available in Germany, so we tried to determine the presence of grayanotoxins in the honey, but the sample was too small. The last possibility was microscopic analysis of the honey for pollen, which was carried out in the above institute. The results were positive for rhododendron.

The patient made a full recovery within 24 h with only supportive therapy. However, we were unable to convince the husband that this Turkish honey should no longer be consumed as he strongly believed in its therapeutic properties.

DISCUSSION

What is already known

Mad honey is made from the nectar of various species of the rhododendron plant, most commonly Rhododendron ponticum and Rhododendron luteum, which is mainly found in the eastern Black Sea area and has long been used for its supposed therapeutic properties in gastroduodenal disease, diabetes, hypertension and sexual dysfunction[1].

Historically, such poisoning over the millennia has been referred to as 'mad honey disease', first of all in antiquity by Xenophon, who was a leader of the March of the Ten Thousand against the Persian Empire in 401 BC and described the Greek mercenaries as 'intoxicated madmen' after they had consumed honey from beehives in the territory of Colchis. Strabo likewise mentioned the defeat suffered by Pompey's soldiers following the consumption of honey from toxic honeycombs, intentionally left behind by the Pontic armies during the Third Mithridatic War in 67 BC. There is also speculation that mad honey was the active compound of the potion which inspired the Delphic Oracle and also the Maenads, Dionysus' female followers, who were mentioned by Euripides [2].

What is new

We described intoxication with grayanotoxins, confirmed by pollen analysis, which at first sight mimicked a right ventricular myocardial infarction with cardiogenic shock and bradycardia. Only after acute coronary syndrome was ruled out by normal troponin levels and a non-dynamic ECG, was intoxication (i.e. cholinergic toxidrome) considered.

Why it is significant

The poisoning with grayanotoxins after honey consumption has been described mostly in Turkey[1], but due to global travel[3] is also being seen in other countries. Its main symptoms are nausea, vomiting, somnolence and syncope, the latter as a result of bradycardia and hypotension. Sinoatrial and atrioventricular blocks[4] and even ST-changes mimicking an acute coronary syndrome[5] have been described. The chief mechanisms are dysregulation of a sodium channel and the effect on the M2 receptors[1]. Although the symptoms may partially resemble the cholinergic toxidrome, a biochemical study found no data to suggest that mad honey caused this condition[6].

There was room for improvement in clinical reasoning. First, at admission the patient had no jugular vein distension, which argued against

massive right ventricular failure. Second, despite the strong suspicion of right myocardial infarction, additional right ECG chest leads (V3R, V4R), which are very specific in this setting, were not utilized. Third, a potential relationship with what the patient had consumed an hour previously was not considered. Lastly, in retrospect the patient could have been treated easily by administering atropine[3], which could also have served as a diagnostic test.

Mad honey poisoning is a rare, but emerging condition in the western world and should be included in the differential diagnosis of an acute presentation of bradycardia with hypotension.

Physicians are encouraged to always search for the primary cause and physiopathological mechanisms of diseases they encounter and be familiar with their place in the history of mankind. This could lead to better understanding of some illnesses and to reflection on the precarious condition of humans faced with disease over the millennia.

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