CASE REPORT

Fatal Honey Poisoning Caused by *Tripterygium wilfordii* Hook F in Southwest China: A Case Series

Qiang Zhang, MD, MPH; Xinguang Chen, PhD; Shunan Chen, MS; Zhitao Liu, MD, MPH; Rong Wan, MD; Juanjuan Li, MD, MPH

From the Yunnan Center for Disease Control and Prevention, Kunming, China (Drs Zhang, Liu, Wan, and Li); the Department of Epidemiology, University of Florida, Gainesville, FL (Drs Zhang and Chen); and the Yunnan Academy of Agricultural Science, Mengzi, China (Ms Chen).

Mad honey poisoning has been reported in many countries, and it seldom results in death. We describe a rare case series of fatal honey poisoning caused by *Tripterygium wilfordii* Hook F (TwHF) in Southwest China. Three male construction workers were delivered to the emergency department with symptoms of food poisoning after ingestion of wild raw honey. Laboratory results showed that the 3 patients were at different degrees of renal damage, and 1 patient with severe symptoms died of acute renal failure 1 day after admission. Pollen analysis indicated that the suspected honey was heavily contaminated with TwHF pollen. Early diagnosis and prompt treatment are crucial for such poisoning. Pollen analysis is a practical approach to help diagnosis in remote areas where such honey poisoning occurs.

Key words: honey poisoning, acute renal failure, pollen analysis

Introduction

Ingestion of wild honey made from poisonous nectar and plants may lead to acute poisoning. One of the best known examples of this is mad honey poisoning in the Black Sea coast of Turkey, which is caused by grayanotoxins from the nectar of the plant species *Rhododendron luteum* and *Rhododendron ponticum*.¹ In general, symptoms of mad honey poisoning are mild, and patients recover within 24 hours.² However, honey poisoning caused by *Tripterygium wilfordii* Hook F (TwHF) is usually fatal. Severely ill patients might die within days if not treated in time. As a widely used Chinese traditional herb, TwHF has caused many serious poisonings.³ Nevertheless, intoxication caused by honey ingestion is seldom reported. In this paper, we present a case series of honey poisoning caused by TwHF in Southwest China.

Case Report

Three male construction workers with an average age of 36.6 years were admitted to the emergency department

with nausea, vomiting, fever (37°C–38°C), and diarrhea. They had collected and eaten wild honey while working in the field 2 days prior. All 3 patients were otherwise healthy and had no trauma, food or drug allergy, or systemic disease. The initial symptoms began within 19 to 48 hours after ingesting approximately 50 g of wild honey. After symptoms began, 1 patient had sought medical care at a local clinic, without improvement. Within the next 2 days, the other 2 workers consecutively presented with different levels of poisoning symptoms and were delivered to the emergency department together (morbidity rate, 100%). The most dramatic symptoms among the patients were frequent vomiting (approximately 20 times a day) and back pain. Another 7 workers who drank boiled honey water were symptom free.

Laboratory results showed that these patients were suffering from different degrees of acute renal injury (Table 1). On admission, one 29-year-old severely ill patient presented with anuria and large ecchymosis in the skin. The patient died of acute renal failure and toxic myocarditis 1 day after admission. The other 2 patients improved after symptomatic treatment and were discharged 2 weeks later but still with back pain (mortality rate, 33.3%). The suspected honey was dark amber. The 2 patients recalled that the honey tasted a little bitter.

Corresponding author: Qiang Zhang, MD, MPH, Yunnan Center for Disease Control and Prevention, Kunming 650022, China (e-mail: zhangqiang_cs@aliyun.com).

Table 1. Laboratory values of the 3 patients

Number	Age	Sex	SCR	BUN	PLT	Outcome
1	29	Male	—	—	90	Died
2	40	Male	148	12.9	148	Recovered
3	41	Male	165	12.6	183	Recovered

SCR, serum creatinine (normal range: 53–106 $\mu\text{mol/L}$); BUN, blood urea nitrogen (normal range: 2.86–8.20 mmol/L); PLT, platelet count (normal range: $100\text{--}300 \times 10^9/\text{L}$); —, not examined.

Pollen analysis indicated that the suspected honey was heavily contaminated with TwHF pollen, which accounted for 12% of all pollen in the honey (Figure 1).

Discussion

TwHF is a plant in the genus *Tripterygium* of the Celastraceae family, which mainly is distributed in mountains across East Asia (Figure 2).⁴ TwHF blooms from June to September each year, and its root has been used for the treatment of rheumatoid arthritis and autoimmune disease in Chinese traditional medicine. TwHF often results in serious poisoning because of its narrow therapeutic window. The most active component of TwHF is triptolide, a diterpenoid triepoxide, which can be found in the leaf, root, and pollen.

Triptolide is a highly toxic substance, and it has a median lethal dose of 0.83 mg/kg when administered intravenously in mice.⁵ As the main pathway for drug metabolism and excretion, the kidney is the major target organ of triptolide-induced toxicity. Acute renal dysfunction or failure is the main cause of death. However, the mechanism of renal injury caused by triptolide is not

entirely clear. Previous studies indicated that triptolide could induce oxidative stress by suppressing renal superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and result in the apoptosis of tubular cells.^{6,7}

TwHF is a major cause of honey poisoning in China. As a result of prolonged dry weather or other conditions in which regular nectar plants are less available, honeybees (*Apis cerana*) may forage on poisonous plants such as TwHF.⁸ This is true not only for wild honeybee colonies but also for cultivated colonies as well. Because of this, honey may be contaminated with toxic pollen. Thus, honey poisoning usually occurs during the blooming period of TwHF (from June to September). In mountain areas, honey is regarded as a delicacy, and is consumed by families and friends together. As a result, honey poisonings are usually clustered.

In contrast with mad honey poisoning in Turkey and other places, honey poisoning caused by TwHF is more serious and may be fatal.² In the early stage (the first 1 to 2 days of poisoning), most patients present with nausea, vomiting, diarrhea, and dizziness. If not properly treated in time, severely ill patients progress to multiorgan damage and present with oliguria, anuria, hematuria, and bleeding tendency within the next 2 to 3 days. Previous reports showed that the fatality rate of honey poisoning caused by TwHF was approximately 25%, and acute renal failure was the leading cause of death.⁹ Even if successfully rescued, renal function of severely ill patients may be permanently damaged. Moreover, TwHF poisoning caused by honey ingestion is somewhat different from that caused by Chinese herb intoxication. First, the incubation period of herb intoxication is relatively shorter (usually several hours) and the symptoms are more remarkable because of a

Figure 1. Photomicrographs of *Tripterygium wilfordii* Hook F pollen grains (photo by Shunan Chen).

Figure 2. *Tripterygium wilfordii* Hook F (Plant Photo Bank of China).

higher intake of triptolide. But the incubation period of honey poisoning can be more than 10 hours and without specific symptoms. Second, exposure to TwHF is explicit for herb poisoning cases, so a timely diagnosis and treatment is usually available. But for cases of honey poisoning, diagnosis is difficult as it is an unusual kind of poisoning.

Therefore, early diagnosis of TwHF honey poisoning is crucial for successful rescue. If emetic, gastric lavage, catharsis, and symptomatic treatment are conducted before severe organ damage, the prognosis is usually better. Blood purification therapies have been proposed to treat critically ill patients. By circulating the blood through an extracorporeal apparatus for selective removal of pathogenic factors, patient outcomes can effectively be improved. In the clinic, combined hemodialysis-hemoperfusion treatment is mostly used in such poisoning cases (hemodialysis to remove metabolic waste and hemoperfusion to eliminate toxic substances).¹⁰ In remote areas, pollen analysis is a practical approach to help diagnosis when chromatography is unavailable. It is also a possible approach for monitoring honey safety in places where poisoning often occurs. TwHF toxic honey is usually dark and tastes bitter. In this case, we found that TwHF pollen was concentrated in some spots of the hive. This might explain why a dose-response relationship was not significant among the 3 patients.

Conclusions

The possibility of TwHF poisoning should be considered for patients with honey consumption history during June to September in the distribution areas of TwHF. Early

diagnosis and prompt treatment is essential to prevent serious consequences, and pollen analysis offers a practical way to examine honey in remote areas.

References

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