

## Clinical Report

# Acute kidney injury by cantharidin poisoning following a silly bet on an ugly beetle

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### Abstract

Cantharidin is a poisonous substance secreted by blister beetles, including the ‘Spanish fly’. Historically, cantharidin was used as an aphrodisiac, vesicant and abortifacient. Symptoms of poisoning include gastrointestinal and genitourinary mucosal irritation along with renal dysfunction. We present the case of a reckless 23-year-old soldier who accepted the challenge of eating a beetle (*Berberomeloe majalis*). Six hours later he was admitted to the emergency room with abdominal pain, dysuria, gross haematuria with clots, hypotension, fever and renal insufficiency. With intravenous fluid therapy, he recovered clinically. Laboratory parameters returned to normal within 1 week.

**Keywords:** acute kidney injury; cantharidin poisoning; haematuria

## Introduction

Cantharidin is a toxic substance secreted by beetles of the Meloidae family (Coleoptera order). The ‘Spanish fly’ (*Cantharis vesicatoria*) is the best known species and *Berberomeloe majalis* (Figure 1) is another member of the family [1]. They secrete cantharidin, the anhydride of cantharic acid with a chemical formula 3,6-epoxy-1,2-dimethylcyclohexane-1,2-dicarboxylic anhydride. Its odourless and colourless crystals are relatively insoluble in water but soluble in chloroform, acetone, ether and fixed oils [2].

Cantharidin has a long, infamous reputation for being an aphrodisiac. This record stems from cantharidin’s ability to cause pelvic congestion in women and priapism in men—a kind of old but dangerous precursor of sildenafil. Actually, in 1772, the Marquis de Sade had poisoned prostitutes with candies containing Spanish fly in the hope of increasing sexual pleasure [3]. There are two reports from the 19th century on soldiers suffering from—or enjoying—priapism after eating frog legs. On dissection of the frogs, it was found that their stomachs were filled with meloid beetles [4]. Spanish flies and other meloids have also been used medicinally as cutaneous irritants, vesicants and abortifacients [1]. Cantharidin toxic effects have caused it to fall into disgrace. Symptoms of poisoning include gastrointestinal and genitourinary mucosal irritation and bleeding, along with renal dysfunction [5].

We report a case of acute kidney injury (AKI) and haematuria due to cantharidin poisoning, following the foolish bet of swallowing a beetle.

## Case report

A healthy 23-year-old male soldier spent 3 days in a military training camp, a drill unwisely comprising water restriction (<600 mL/day) and hard physical exercise. By 5 p.m. of the third day, in a bet with fellow soldiers, he chewed and swallowed a beetle (*Berberomeloe majalis*). Within 15 min his mouth burned, he retched, vomited, complained of diffuse abdominal pain, dysuria and gross haematuria with clots. By 11 p.m. he was admitted to the emergency room of a district hospital. He was conscious, with normal breathing, dehydrated, hypotensive (BP 98/53 mmHg), mildly tachycardic (PR 96 ppm) and febrile (axillary temperature 37.8°C). The remaining cardiopulmonary and abdominal examination was normal. He had no signs of Murphy’s kidney.

Blood screening revealed neutrophil leukocytosis (27 300 leukocytes/ $\mu$ L; 24 800 neutrophils/ $\mu$ L), moderate azotemia [serum creatinine (SCr) 224  $\mu$ mol/L (59–104); urea (Ur) 8.1 mmol/L (2.8–7.2)] with normal electrolytes, high lactate dehydrogenase [LDH, 339 U/L (100–247)] and creatine kinase [CK, 1580 U/L (10–171)]. Urinalysis showed proteinuria (4+), glycosuria (2+), leukocyturia (75/ $\mu$ L) and haematuria (3+). Renal ultrasound was unremarkable.

He received saline infusion (NaCl 0.9% 166 mL/h), empiric antibiotic (IV ciprofloxacin 200 mg 12/12 h), antipyretic, antiemetic and antacid treatment. Twenty-four hours later his BP was normalized, but despite the sustained urine output (~100 mL/h), worsening azotaemia (SCr 430  $\mu$ mol/L, Ur 18.7 mmol/L) led to transferring him to our nephrology unit. He was doing well, but complained of dysuria and haematuria. Our laboratory work-up



**Fig. 1.** *Berberomeloe majalis*—should be firmly considered as not edible. Photo by “Siga”, reproduced from Wikimedia Commons.

confirmed the earlier findings, along with thrombocytopaenia (88 000/ $\mu$ L), elevated serum C-reactive protein [74 mg/L (<5)], CK [3289 U/L (30–170)] and myoglobin [152 ng/mL (10–92)].

We diagnosed a multifactorial AKI RIFLE class ‘F’, in the context of rhabdomyolysis, dehydration and cantharidin intoxication. Leptospirosis was also a possible aetiology of AKI in our minds (fever, acute phase inflammatory markers, LDH increase, thrombocytopaenia, AKI and epidemiologic data). Therefore, we asked for serology tests and changed the antibiotherapy to IV ceftriaxone, maintaining previous intensive parenteral fluid administration. During the subsequent days, we observed polyuria, resolution of haematuria (second day), with a progressive improvement of renal function. Leptospirosis serology and microbiological analysis of blood and urine were negative; immunological screening was also normal.

Seven days later, at the time of discharge, he was asymptomatic; renal function had recovered, as well as other laboratory parameters. This complete recovery was confirmed in a re-evaluation 15 days later.

## Discussion

This case illustrates a clinical presentation of cantharidin toxicity resulting from ingestion of a blister beetle.

The cantharidin content of one beetle ranges from 0.2 mg to 0.7 mg depending on the species [1]. The lethal dose in adults has been estimated to be from 10 to 80 mg, but most commonly is reported to be <60 mg [5]. Once disturbed, a larva produces cantharidin as a milky oral fluid, while an adult beetle secretes the toxin from leg joints [6].

Multiple organ systems have been reported to be affected by cantharidin. Many of its effects are attributable to direct chemical irritation. The mechanism of action may be related to binding at the cellular level, where it has been found to be a potent inhibitor of both protein phosphatases types 1 and 2A [5]. Cantharidin circulates bound to albumin and undergoes excretion by glomerular filtration, causing glomerular damage and acute tubular necrosis, as well as blister formation in the lower urinary tract. Death may occur from renal failure. The gross morbid anatomy in patients dying from cantharidin poisoning has shown renal engorgement with haemorrhage into the renal pelvis and ureter and diffuse petechial haemorrhages. Microscopy shows oedema of Bowman’s

capsule and basement membranes, causing constriction of glomerular capillaries. Sloughed epithelial cells pack into Bowman’s space. In renal tubules, epithelial disintegration and oedema of the basement membrane with resulting lumen occlusion are observed. Areas of complete tubular degeneration have been noted [5].

Symptoms of cantharidin intoxication typically begin within 2–4 h of ingestion, but delays of 10 min to 14 h have been described [1, 2, 7]. Initially, patient complaints include burning and blistering of the mouth, tongue, and oropharynx, dysphagia, abdominal cramping, vomiting and haematemesis. Symptoms related to the urinary tract include lumbar pain, dysuria and urinary frequency, which may persist for up to 15 days [5]. Gross or microscopic haematuria with granular casts is also a prominent feature which begins on the first or second day [1, 2, 8]. These symptoms are accompanied by renal function impairment with oliguria [5]. Serum electrolytes may be affected, manifesting as hyponatraemia, hyperkalaemia and hypocalcaemia [6]. Polycythaemia may be attributed to toxin-induced bone marrow hyperplasia or simply to volume loss and haemoconcentration. Priapism, seizures and cardiac abnormalities are less commonly seen [5].

There is no specific antidote for cantharidin. The management is supportive, including IV fluid at maintenance rate and correction of electrolyte and blood gas abnormalities. The use of IV proton pump inhibitors or H<sub>2</sub> blockers may enhance the healing of the ulcerations that result from the local effect of the toxin on the gastric mucosa [1]. Given cantharidin’s high-binding affinity for albumin, haemodialysis would be expected to have minimal, if any effect [5]. The ultimate prognosis is good with regard to renal function if the patient survives the acute phase [2].

In our case, the diagnosis was suggested by the abrupt onset of symptoms just after the beetle ingestion in an otherwise healthy young man. He presented with many of the reported typical features. Although there were other potential causes for AKI, the single explanation for gross haematuria with clots and gastrointestinal complaints was cantharidin intoxication. Yet, the occurrence of fever, leukocytosis and thrombocytopaenia, along with AKI raised suspicion of an infectious condition like leptospirosis. Actually, there are previous reports of these disorders in cases of cantharidin poisoning [1, 8]. With supportive management, the evolution of this case was very good.

There is no pathognomonic feature of cantharidin intoxication, but a careful history record combined with the sequence of events should alert for this rare event. Nowadays, cantharidin can be found in homeopathic dilutions in some ‘love potions’ available in sex shops. Therefore, educating both the general population and the medical community about Spanish fly’s toxicity may have some value in avoiding an epidemic of cantharidin poisoning.

The reckless soldier benefitted from recommendations to avoid foolish bets, even in a military setting.

*Conflict of interest statement.* None declared.

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Received for publication: 11.9.12; Accepted in revised form: 2.1.13