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## AIMS AND SCOPE

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CASE REPORT

# Multiorgan dysfunction syndrome due to high-dose cantharidin poisoning: A case report

Wan-Ling Xu, Wen-Jing Tang, Wei-Ying Yang, Li-Chao Sun, Ze-Qun Zhang, Wei Li, Xiu-Xian Zang

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## Abstract

### *BACKGROUND*

This report delves into the diagnostic and therapeutic journey undertaken by a patient with high-dose cantharidin poisoning and multiorgan dysfunction syndrome (MODS). Particular emphasis is placed on the comprehensive elucidation of the clinical manifestations of high-dose cantharidin poisoning, the intricate path to diagnosis, and the exploration of potential underlying mechanisms.

### *CASE SUMMARY*

A patient taking 10 g of cantharidin powder orally subsequently developed MODS. The patient was treated with supportive care, fluid hydration and antibiotics, and hemoperfusion and hemofiltration therapy for 24 h and successfully recovered 8 d after hospital admission. Cantharidin poisoning can cause life-threatening MODS and is rare clinically. This case underscores the challenge in diagnosis and highlights the need for early clinical differentiation to facilitate accurate assessment and prompt intervention.

### *CONCLUSION*

This article has reported and analyzed the clinical data, diagnosis, treatment, and prognosis of a case of high-dose cantharidin poisoning resulting in MODS and reviewed the relevant literature to improve the clinical understanding of this rare condition.

**Key Words:** Cantharidin; Poisoning; Multiorgan dysfunction syndrome; Clinical treatment and management; Case report

**Core Tip:** A patient taking 10 g of cantharidin powder orally subsequently developed multiorgan dysfunction syndrome (MODS). Cantharidin poisoning can cause life-threatening MODS and is rare clinically. Currently, there is no special antidote for cantharidin poisoning. Treatments mostly involve supportive care. Fluid resuscitation is essential. Hemoperfusion and hemofiltration can be applied, especially in patients with acute renal failure. Complications such as infectious pneumonia should be managed appropriately.

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## INTRODUCTION

Cantharis is popularly known as the Spanish Fly. It can produce a colorless and odor-free substance, cantharidin, which is lipophilic and soluble in acetone, oil, ether, and chloroform but is insoluble in water[1]. Cantharidin is used to treat rabies, skin rash, infection, or even cancer[2-4]. It is also thought to act as an aphrodisiac[5]. However, cantharidin is also a potent toxin.

Most patients with cantharidin poisoning present clinically with irritative effects, particularly gastrointestinal discomfort, genitourinary bleeding, and renal dysfunction, but rarely with concurrent multiorgan system damage[6]. Here, we report on a patient with multiorgan dysfunction syndrome (MODS) after cantharidin ingestion. Her in-hospital clinical course was complicated by aspiration pneumonia. Finally, she was successfully treated with intravenous fluid resuscitation, antibiotics, hemoperfusion, and hemofiltration.

We discuss this case with the purpose of increasing awareness of the severity of cantharidin poisoning as well as potential treatment options.

## CASE PRESENTATION

### *Chief complaints*

A 36-year-old female presented to our hospital with a productive cough and a burning sensation in the esophagus.

### *History of present illness*

12 h earlier, she ingested 10 g of cantharidin powder after an argument with her family.

### *History of past illness*

She denied any past medical history.

### *Personal and family history*

The patient denied any family history of genetic diseases or tumors.

### *Physical examination*

Her vital signs were temperature 36.6 °C, respiration 27 breaths/min, heart rate 108 beats/min, and blood pressure 110/53 mmHg. The patient was awake and alert but in acute distress. Her mouth and throat were red and swollen. Lung auscultations revealed bilaterally diminished breath sounds and bibasilar crackles. On the first day after hospital admission, the patient developed hematuria, with a total of 600 mL of urine output over the next 24 h. On physical examination, her temperature was 38.1 °C, respirations 20 breaths/min, heart rate 135 beats/min, blood pressure 90/51 mmHg, and pulse oximetry 95% on 3 L/min oxygen provided through the nasal cannula. The patient looked lethargic; her mouth and throat showed erythema and ulcers, with yellow discharge. Cardiovascular and neurological examinations were unremarkable. On the third day following hospital admission, her vital signs improved to temperature 36.9 °C, respiration 20 breaths/min, heart rate 106 beats/min, blood pressure 119/84 mmHg, and pulse oximetry 99% on 6 L/min oxygen through the face mask. Moreover, she was awake and alert. There was improved erythema, swelling, and ulcers in the mouth and throat, with little exudate.

### *Laboratory examinations*

Laboratory tests reported a blood white blood cell count of 12.2 × $10^9$/L, neutrophil percentage of 88%, and platelet count of 145 × $10^9$/L. Renal function test results were blood urea nitrogen (BUN) 3.8 mmol/L and creatinine 97.1 μmol/L. The

blood coagulation panel, hepatic function test, chemistry, and troponin results were with normal limits.

Urinalysis showed occult blood 3+, protein 1+, and a red blood cell count of 58.0 *per* high power field (HPF). Complete blood cell counts included a white blood cell (WBC) count of 30.9 × $10^9$/L and a platelet count of 100 × $10^9$/L.

Blood gas analysis showed pH 7.34, $pCO_2$ 29 mmHg, $pO_2$ 61 mmHg, lactate 5.8 mmol/L, base excess -8.8 mmol/L, and oxygen saturation 89%. Other blood test results were C-reactive protein 151.8 mg/L, aspartate aminotransferase 46.5 U/L, total protein 55.8 g/L, albumin 28.5 g/L, and procalcitonin 4.1 ng/mL. The coagulation panel was thrombin time 32.6 s, activated partial thromboplastin time 21 s, prothrombin time 13.9 s, international normalized ratio 1.2, and prothrombin activity 67%. Renal function tests showed an increased BUN of 10.4 mmol/L and creatinine 373.1 μmol/L.

On the third day following hospital admission, renal function also improved with BUN 4.6 mmol/L and creatinine 174.4 μmol/L. Blood tests reported a WBC count of 32.4 × $10^9$ /L, platelet count of 52 × $10^9$/L, B-type natriuretic peptide of 2590 pg/mL, myoglobin of 528.6 ng/mL, and troponin of 0.1 ng/mL. Blood gas analysis showed pH 7.48, $pCO_2$ 33 mmHg, $pO_2$ 123 mmHg, lactate 1.0 mmol/L, base excess 1.4 mmol/L, and oxygen saturation 99%. However, her hematuria persisted with the red blood cell count increasing to 493.2 *per* HPF in the urinalysis.

On the fourth day following hospital admission, her blood and urine cultures showed negative results, but a sputum culture grew *Klebsiella pneumoniae*.

On the sixth day, her repeat vital signs, blood cell counts, renal function, and lactate levels all returned to within normal limits.

### *Imaging examinations*

An abdominal computed tomography (CT) scan showed bilateral perinephric fascia thickening with infiltrative changes, generalized fat stranding in the abdominal cavity and retroperitoneal space, a small amount of pelvic fluid, and mild subcutaneous exudation in the lower back. A chest CT scan reported bilateral pulmonary infiltrations, opacities in the right upper lobe and bilateral lower lobes, and small left pleural effusion. Echocardiography was normal.

## FINAL DIAGNOSIS

Acute cantharidin poisoning, MODS.

## TREATMENT

On admission the patient was treated with rehydration, antibiotics and 24 h hemoperfusion and hemofiltration. On the third day of admission, a 1-unit platelet transfusion and recombinant human thrombopoietin were administered due to thrombocytopenia. On the fourth day of admission, meropenem was given for *Klebsiella pneumoniae* infection based on the drug sensitivity result.

## OUTCOME AND FOLLOW-UP

She was discharged from hospital on the eighth day after admission. Three months after the hospital discharge, the patient was followed up *via* telephone interview. She reported a complete recovery without any other treatment or clinical visit.

## DISCUSSION

The Cantharis beetle is commonly known as the Spanish fly or blister beetle (Figure 1). Once stimulated, young Cantharis beetles produce cantharidin in the form of a milky white oral fluid, and adult Cantharis secrete cantharidin from their leg joints[7]. Depending on the beetle species, 0.2–0.7 mg of cantharidin can be exudated from each beetle. Cantharidin has the chemical formula 3, 6-epoxy-1, 2-dimethylcyclohexane-1, 2-dicarboxylic anhydride[8]. It can cause injury to various organ systems.

The immediate effect of cantharidin is its direct chemical irritation. After direct contact with the human body, cantharidin can stimulate mucosal membranes and cause skin blisters[9]. Once in the bloodstream, cantharidin can bind to albumin, which is then excreted from the renal glomeruli to induce glomerular damage and acute tubular necrosis[10]. In the cells, cantharidin can bind and inhibit protein phosphatase types 1 and 2A, which cause cell cycle arrest at the G2/M phase[11,12]. In addition, cantharidin can suppress protein expression in the endoplasmic reticulum stress pathway, leading to cell autophagy and apoptosis[13].

Clinically, patients with cantharidin poisoning can present with various symptoms[14,15]. The Direct chemical irritation can result in mouth and oropharynx burning, blisters, and ulceration, as well as abdominal discomfort, cramping, nausea, vomiting, and even hematemesis. Renal glomerular damage and tubular necrosis can present as acute renal failure and hematuria. In addition, patients can suffer cardiovascular (sinus bradycardia, junctional escape rhythm, and hypotension); neurological (seizure, dizziness, headache, altered mental status, and hallucinations); and hemato-

**Figure 1 Cantharis beetles.** The cantharis beetle is commonly known as the Spanish fly or blister beetle.

logical (thrombocytopenia, polycythemia) system complaints[16-18].

Postmortem autopsy examinations reveal that the gastrointestinal tract and kidneys are most frequently affected[15]. Gastrointestinal tract effects include esophageal mucosal congestion, swelling, ulceration, gastrointestinal mucosal congestion, hemorrhage, focal superficial erosion, and acute splenitis. Renal pelvis and ureter effects include diffuse petechial hemorrhage. Microscopically, Bowman's capsules and basement membranes become edematous, causing glomerular capillary constriction. The sloughed epithelial cells accumulated in the Bowman's capsules, together with the cellular debris and edematous basement membranes, to finally lead to luminal occlusion. Pulmonary involvement may include bronchopneumonia and subpleural hemorrhage[19]. Deaths from cantharidin poisoning due to cerebral edema, meningeal petechiae, and cerebral petechiae have also been reported[17,20].

Most patients start to show clinical symptoms within 2–4 h after cantharidin ingestion[14]. Our patient presented to hospital 12 h after intentional ingestion of 10 g of cantharidin powder. In the next 24 h, she started to develop symptoms of multiorgan damage, including hematuria, decreased urinary output, acute renal failure, thrombocytopenia, respiratory distress, hypotension, and lethargy.

Currently, there is no special antidote for cantharidin poisoning. Treatments mostly involve supportive care. Fluid resuscitation is essential. Antibiotics are administered following signs of pneumonia. Considering that hemodialysis cannot effectively remove cantharidin, since it binds to albumin in the circulation and has poor solubility in water, we attempted hemoperfusion and hemofiltration to remove cantharidin, inflammatory cytokines, and metabolic products, as well as to correct the electrolyte and acid-base disturbances. In addition, we initiated enteric nutrition to avoid the absorption of lipid-soluble cantharidin through the gastrointestinal tract.

## CONCLUSION

Cantharidin poisoning can cause life-threatening MODS. Hence, prompt supportive care should be initiated. Hemoperfusion and hemofiltration can be applied, especially in patients with acute renal failure. Complications such as infectious pneumonia should be managed appropriately.

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## FOOTNOTES

**Co-first authors:** Wan-Ling Xu and Wen-Jing Tang.

**Author contributions:** Xu WL and Tang WJ drafted the manuscript, contributed equally to this work and share the first authorship; Yang WY, Sun LC, Zhang ZQ, Li W participated in the patient management; Zang XX designed the study. All authors made a significant contribution to the work reported and approved the final version of this manuscript for publication.

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