

CASE REPORT

Toad venom poisoning: resemblance to digoxin toxicity and therapeutic implications

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Heart 2003;89:e14 (<http://www.heartjnl.com/cgi/content/full/89/4/e14>)

A healthy man developed gastrointestinal symptoms after ingesting purported aphrodisiac pills. He had severe unrelenting bradycardia, hyperkalaemia, and acidosis. He rapidly developed severe life threatening cardiac arrhythmias and died after a few hours. He was found to have positive serum digoxin concentrations, although he was not taking digoxin. Toad venom poisoning is similar to digitalis toxicity and carries a high mortality. Cardiac glycoside poisoning can occur from ingestion of various plants and animal toxins, and the venom gland of cane toad (*Bufo marinus*) contains large quantities of cardiac glycosides. Toad venom, a constituent of an aphrodisiac, was considered responsible for the development of clinical manifestations and death in this patient. Digoxin specific Fab fragment has been reported to be beneficial in the treatment of toad venom poisoning. This report alerts physicians to the need to be aware of a new community toxic exposure, as prompt treatment with digoxin specific Fab fragment may be life saving. The treatment approach to patients with suspected toad venom poisoning is described.

Toad venom poisoning is similar to digitalis toxicity and carries a high mortality.¹⁻⁷ Cardiac glycoside poisoning can occur from ingestion of various plant and animal toxins.¹ The venom gland of cane toad (*Bufo marinus*) contains large quantities of cardiac glycosides.¹ Dried toad venom is used in China as a traditional medicine known as chan su and is a major component of kyushin, another popular medication in Asia.⁴ Clinically, toad venom poisoning may predominantly manifest as gastrointestinal, mental, cardiac conduction, and arrhythmic disturbances. Digoxin specific Fab fragment has been reported to be beneficial in the treatment of toad venom poisoning.⁴ We describe a fatal case of ingestion of an aphrodisiac suspected to be toad venom, alerting physicians to a new community toxic exposure, and how prompt treatment with digoxin specific Fab fragment may be life saving.

CASE REPORT

A 40 year old man presented at 1 pm with nausea, vomiting, diaphoresis, and abdominal pain to the emergency department. He stated that earlier that morning at about 6 am he had ingested three pills of an unknown aphrodisiac (described by the patient as "sex pills"), suspected to be toad venom. The patient first developed pain in the throat and epigastric region and vomited yellow liquid twice. He had no chest pain or shortness of breath and no known underlying medical conditions or cardiac disease. He was not taking any medications. Vital signs were blood pressure of 115/44 mm Hg, pulse of 34 beats/minute, respiratory rate of 16 breaths/minute, and normal body temperature. The patient was disoriented and lethargic. His pupils were 4 mm bilaterally reactive to light.

There was no neck stiffness or focal neurological deficits. The cardiac and lung examination were grossly unremarkable. There was mild epigastric tenderness.

An ECG showed sinus bradycardia with first degree atrioventricular block. A chest x ray showed an early right basal infiltrate, possible secondary to aspiration during vomiting. There was heightened suspicion of glycoside toxicity. He was placed on an ECG monitor and admitted to the coronary care unit. Serum and urine toxicological screening were negative. The haematological investigation found a white cell count of $21.5 \times 10^9/l$, haemoglobin 172 g/l, haematocrit 49.4%, and platelet count $402 \times 10^9/l$. A comprehensive metabolic profile found the following concentrations: sodium 133 mmol/l, potassium 7.2 mmol/l (specimen haemolysed), bicarbonate 16 mmol/l, blood urea nitrogen 43 mmol/l, creatinine 114 $\mu\text{mol/l}$, calcium 2.8 mmol/l, and anion gap 16 mmol/l. The liver function test was grossly unremarkable. The repeat determinations were serum potassium 7.6 mmol/l, bicarbonate 11 mmol/l, and anion gap 12 mmol/l. The creatine kinase concentration was 215 u/l and lactate dehydrogenase was 544 u/l. The serum digoxin concentration was 0.9 nmol/l. Prophylactic digoxin specific Fab fragment was ordered at the recommendation of the poison control centre. The patient's condition deteriorated rapidly, with severe respiratory distress and lethargy, and he was intubated. His condition deteriorated progressively, with severe bradycardia and conduction abnormalities. He developed ventricular tachycardia, which rapidly degenerated to ventricular fibrillation. Cardiac resuscitation with standard advanced cardiac life support protocol was initiated, but despite all life supporting measures the patient died before administration of digoxin specific Fab fragment.

DISCUSSION

Toads have toxic substances in the skin and parotid glands.^{1-3,4} Ingestion of toad or toad cake can lead to intoxication. Most toxic compounds of this venom are steroids similar to digoxin. Most patients have gastrointestinal symptoms consisting of nausea, vomiting, and abdominal discomfort. Toad toxin poisoning is manifest primarily by digitalis toxicity-like cardiac effects, including bradycardia, atrioventricular conduction block, ventricular tachycardia, ventricular fibrillation, and sudden death.¹⁻⁷ Patients usually have unexplained bradycardia, possibly with a normal blood pressure. Laboratory studies may show hyperkalaemia and a detectable digoxin concentration. Serum immunoassays for digoxin may cross react with the toad venom resulting in increased digoxin concentrations. But unlike digoxin, the concentration by itself is not important or predictive of the clinical outcome. Table 1 outlines a suggested approach to treating patients with toad venom poisoning.

The majority of patients with toad venom poisoning have detectable digoxin concentrations. Initial treatment principles address life support measures. Prevention of gastrointestinal absorption is recommended with emesis, gastric lavage, activated charcoal, and cathartics. Bradyarrhythmias can

Table 1 Suggested approach to treating patients with suspected toad venom poisoning

- Brief rapid triage with history taking and clinical assessment
- Basic laboratory investigations including measurement of serum potassium and digoxin concentrations
- Surface ECG and telemetry monitoring
- Reporting to and consult with the local poison control centre
- General life supportive measures
- Treatment with digoxin specific Fab fragments
- No calcium administration for hyperkalaemia
- Retention of any samples of ingested substances for further investigations and confirmation

respond to atropine or may require pacemaker placement. Antiarrhythmic drugs may be considered for ventricular arrhythmias. The majority of patients with toad poisoning have increased serum potassium concentrations.^{4,5} Serum potassium concentration has prognostic implications in alleged toad poisoning.⁵ If hyperkalaemia develops, treatment must be more aggressive to prevent mortality but calcium should not be administered for the treatment of hyperkalaemia. Immediate administration of digoxin specific Fab antibody (initial dose of ≥ 380 mg) has been reported to be life saving.^{4,8} Dosing of digoxin specific Fab should not be based on the concentration because of partial cross reactivity. If there is no clinical response in 30 minutes to one hour, dosing with 190–380 mg should be repeated.

Blood specimens should be rapidly screened for cardiac glycosides in suspected poisoning cases. In one report, analysed samples of the purported aphrodisiac substance were found to be identical to chan su, a Chinese medication made of toad venom.⁴ A heightened awareness is required of the existence of plant and animal toxins to prevent their consumption, to prevent poisoning, and to manage the poisoned patient.¹ Chan su is made of Chinese toad venom and contains a bufadienolide, a cardiac glycoside that causes clinical toxicity similar to that of digoxin. After several fatal cases of toad venom poisoning were reported by the New York City Poison Control Center, the Food and Drug Administration appropriately

banned the importation and sale in the USA of the material, which is sold as an aphrodisiac called “Rockhard”, “Love Stone”, or “chan su”.^{4,7-9}

Toad venom poisoning is rare but life threatening. Awareness of its clinical toxicity, leading to digoxin-like cardiovascular and gastrointestinal effects, is necessary. Increased vigilance and prompt initiation of life supportive measures with definite treatment with digoxin specific Fab fragments can be life saving.

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No financial support was received for this paper.

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Accepted 19 December 2002

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