Digitalis Toxicity Caused by Toad Venom*

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A case of toad venom-induced digitalis toxicity is presented. A pause of 13.5 s was noted in the patient taking a Chinese medication which contained toad venom. This is the first case report of clinical digitalis toxicity related to toad venom in Western society. ***(Chest 1992; 102:949-50)***

Digitalis is a commonly used medication in the United States. Its therapeutic efficacy and toxicity have been known for centuries.[1] The diagnosis of digitalis toxicity is easily made in patients known to be taking the drug. Digitalis toxicity is described in a patient not taking any prescription medication.

Case Report

A 90-year-old Chinese man with a history of glucose intolerance, was brought to the Emergency Department after suffering a syncopal episode while walking. The patient regained consciousness about 5 min later. He denied any chest pain, dyspnea, palpitation, or seizure activity. He felt nauseated, but there was no vomiting. The only "medication" the patient had been taking was Yixin Wan. He took one tablet daily for the past month "to strenghen his heart" (as recommended by a relative). Physical examination revealed a blood pressure of 110/70 mm Hg, and an abnormally irregular pulse of 50/min. Heart sounds were normal without gallops, rubs, or murmur. The lungs were clear. Abdominal and neurologic examination results were unremarkable. Laboratory data showed a normal white blood cell count and hematocrit value, sodium value of 139 mEq/L; potassium, 4.2 mEq/L; glucose, 179 mg/dl; calcium, 8.4 mg/dl; magnesium, 1.8 mg/dl and creatinine, 1.5 mEq/L. A 12-lead ECG showed atrial fibrillation with a ventricular response of approximately 55 beats/min and evidence of an old anteroseptal wall myocardial infarction. The patient was admitted to the coronary care unit immediately and was noted to have multiple pauses, the longest being 13.5 s (Fig 1). This episode was associated with transient loss of consciousness, from which the patient recovered spontaneously without sequelae. A temporary pacemaker was inserted promptly. Serial cardiac enzyme values were all within normal limits. A serum digoxin level by fluorescence immunoassay, drawn 36 h after the last ingestion of the Chinese medication, was 0.87 ng/ml (therapeutic range from 0.4 to 1.8 ng/ml). Cardiac monitoring was continued, and the patient received no medication including the Yixin Wan. The following day, the serum digoxin level was 0.49 ng/ml; two days later, it was less than 0.2 ng/ml. A 24-h ambulatory ECG recording revealed atrial fibrillation with a ventricular response of 60 to 90 beats/min. No significant pauses were noted. The patient was discharged without medication (he was instructed to avoid Yixin Wan) and has remained asymptomatic during follow-up in the outpatient clinic.

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Discussion

Cardiac glycosides are present in a large number of plant extracts and in the venom of toads. It was known by the ancient Egyptians and Romans, who used these as diuretics and cardiotonic agents. Cardiac glycosides were introduced to modern medicine more than 200 years ago. Since then, digitalis has become a widely used medication in the Western world.

Yixin Wan was the only medication that the patient was taking and a digitalis-like immunoreactive substance was found. This is a nonprescription Chinese medication which contains several ingredients including toad venom (Ch'an-Su), ginseng, pearl (Chen-Chu), and musk (She-Hsiang). According to the package insert, it has been shown to benefit patients with coronary artery disease and congestive heart failure. Previous studies have confirmed that toad venom contains a digitalis-like immunoreactive cardiotrophic substance.[2-9] There are several different types of substances in toad venom called bufotoxin.[9] The bufotalin, a major bufotoxin in the toad venom, has a chemical structure similar to digoxin (Fig 2). The exact mechanisms of the cardiotrophic activity of toad venom have not been well defined, but its clinical activity may be related to its digitalis-like structure.

Although the digoxin level was within therapeutic range, significant pauses were found. The overlap of serum digoxin levels between patients with or without clinical digitalis toxicity is well described.[10] Nevertheless, the patient probably had underlying atrioventricular node conduction disease as suggested by the ECG showing atrial fibrillation with slow ventricular response; even a small amount of an atrioventricular node blocking agent could cause significant toxicity. The pharmacokinetics of this Chinese medication

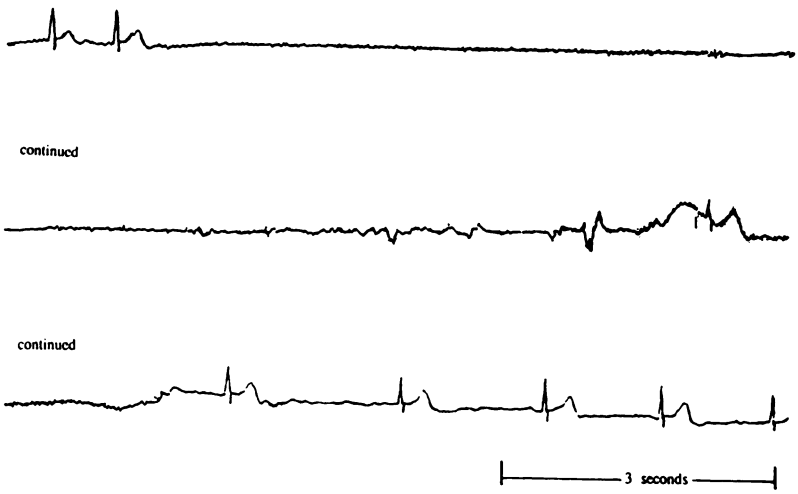

FIGURE 1. A continuous rhythm strip showing the 13.5 s pause.

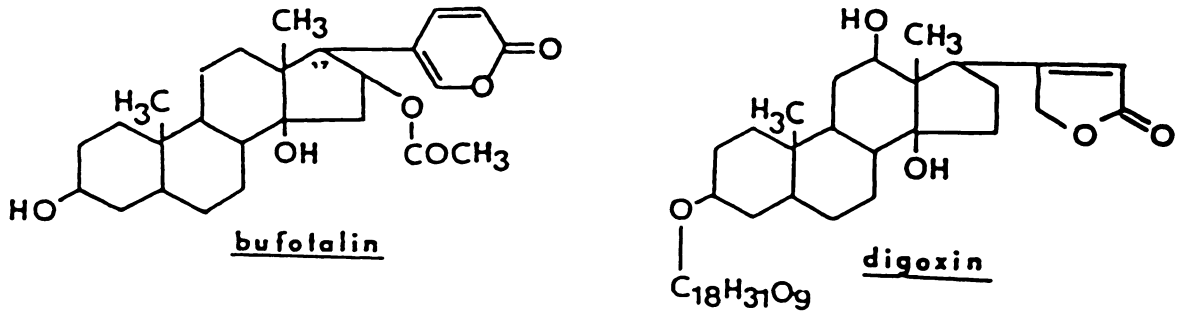

FIGURE 2. Chemical structures of bufotalin and digoxin.

is not clear; a creatinine level of 1.5 mEq/L was very high for this 90-year-old person and could contribute to the digitalis toxicity if the metabolism of this Chinese medication is similar to digoxin. The pauses seen during early hospitalization resolved as the serum digoxin level returned to zero after the medication was discontinued. We strongly believe that this medication not only caused a digitalis-like substance, but also was responsible for digitalis toxicity in our patient.

Although the clinical toxicity of toad venom has been described,[4,8] to our knowledge, this is the first case report in the Western literature. The use of nonprescription Chinese medication among the Chinese population in the United States is quite common. We believe the reason for this, especially in the elderly Chinese and the new immigrants, is their strong cultural belief in Chinese medicine and their lack of confidence in modern western medicine. Drugs such as Yixin Wan, are easily obtained in the United States, often in ethnic grocery stores and pharmacies. With a rapidly growing nonwestern immigrant population in the United States, physicians must be alert for the potential toxicity of nonstandard therapies these patients may be taking.

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Pulmonary Venous Infarction Secondary to Squamous Cell Carcinoma

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This type of pulmonary venous infarction has not been previously reported, namely: pulmonary vein obstruction from squamous cell carcinoma. Furthermore, this case is unique in that the characteristic pathologic vascular changes observed with pulmonary venous infarction were contrasted with a noninfarcted upper lobe that was removed from the same patient one year later.

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Pulmonary venous infarction is a rare clinical condition that is most commonly caused by sclerosing mediastinitis. Although other known causes exist, pulmonary venous infarction has not been reported secondary to carcinoma. We recently treated a patient with lobar pulmonary venous infarction secondary to extrinsic compression of the inferior pulmonary vein from a squamous cell carinoma.

CASE REPORT

A 47-year-old man presented with a ten-day history of intermittent chills, pleuritic chest pain, dry cough, fever to 38.8°C, and an episode of hemoptysis. Three years previously, Ivor Lewis esophagogastrectomy was performed for squamous cell carcinoma of the esophagus (stage IIA).[1]

Physical examination of the chest disclosed decreased breath sounds at the base of the left lung. Results of sputum Gram stain and culture were consistent with normal flora, and results of acid-fast bacilli stain were negative. Roentgenography of the thorax revealed consolidation in the left lower lobe with an air bronchogram and a left pleural effusion (Fig 1).

No endobronchial lesions were seen bronchoscopically; however, lavage of the anteromedial basal segment of the left lower lobe resulted in the return of bloody fluid. Transbronchial biopsy revealed parenchymal necrosis.

Computed tomography of the thorax revealed an extensive infiltrative process of the left lower lobe with an air bronchogram

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