

Clinical Toxicology

Colchicine cardiotoxicity following ingestion of *Gloriosa superba* tubers

Shanthi Mendis

Department of Medicine, Faculty of Medicine, Peradeniya, Sri Lanka.

Summary: The clinical features of colchicine toxicity in a patient following ingestion of *Gloriosa superba* tubers are described. Gastroenteritis, acute renal failure, cardiotoxicity and haematological abnormalities were the main toxic manifestations. There was no hypotension and no neurological manifestations. Electrocardiographic changes were noteworthy and have not been reported previously.

Introduction

Gloriosa superba is a plant that grows wild in all parts of Sri Lanka. The tubers of this plant have been found to contain several alkaloids among which colchicine and gloriosine are the most important ones.¹ Acute intoxication associated with the ingestion of *Gloriosa superba* is indistinguishable from the clinical features of colchicine poisoning.

Case report

A 29 year old man who attempted suicide by ingesting tubers of *Gloriosa superba* was admitted 4 hours later to Teaching Hospital Peradeniya, complaining of burning in the mouth and throat, intense thirst, nausea, vomiting and abdominal colics. On examination he was restless, afebrile and dehydrated. Pulse rate was 90 beats/min. Blood pressure was 100/70 mmHg and respiratory rate was 20 per minute. Gastric lavage was performed and he was given intravenous fluids. Except for an elevated haematocrit (PCV = 0.54 l/l) his biochemical and haematological investigations were normal on admission.

He was oliguric for 24 hours. By the second day the blood urea increased to 10.3 mmol/l and urinalysis showed proteinuria and mild haematuria. He developed a watery diarrhoea, complained of severe body ache and generalized chest pain. An electrocardiogram done at this stage was normal. Serum aspartate transaminase was 10 IU/l (normal 0–12). Serum alanine transaminase was 20 IU/l (normal 0–11), serum bilirubin was 17 mmol/l, plasma potassium was 4.2 mmol/l and plasma sodium was 138 mmol/l. On the third day the patient complained of severe pain all over the chest associated with difficulty in breathing. His respiratory rate was 38/min, pulse was 100 beats/min regular, and blood pressure 110/70 mmHg. He had a triple rhythm and bilateral basal crepitations.

The electrocardiogram (Figure 1) showed ST elevation. Aspartate transaminase rose to over 60 IU/l (normal 0–12), creatine kinase was 40 IU/l (normal 0–12) and serum cholesterol was 5.0 mmol/l. He was treated with analgesics and frusemide. He continued to complain of chest pain on the fourth day. The electrocardiogram showed further T elevation (Figure 2). By the fifth day he developed bleeding gums and subconjunctival haemorrhages and haematuria. At this stage haematological investigations showed haemoglobin 9.5 g/dl, white cell count $2.8 \times 10^9/l$, platelet count $20 \times 10^9/l$, bleeding time 3 minutes, clotting time 11 minutes, prothrombin time 18 seconds (control 15 seconds).

He was transfused three pints of fresh blood in the next 48 hours. Serum aspartate transaminase and creatine kinase returned to normal by the ninth day. The electrocardiogram showed only inverted T waves in V5.

His condition gradually improved and 3 weeks after admission he was transferred to the Department of Psychiatry for further management. Biochemical and haematological investigations and the electrocardiogram (resting and in response to exercise) were normal.

Correspondence: S. Mendis, M.B., B.S., D.M., M.R.C.P. (UK), Department of Pathological Biochemistry, Queen Elizabeth's Building, Phase 1, 4th floor, Glasgow Royal Infirmary, Glasgow G4 0SF, UK.

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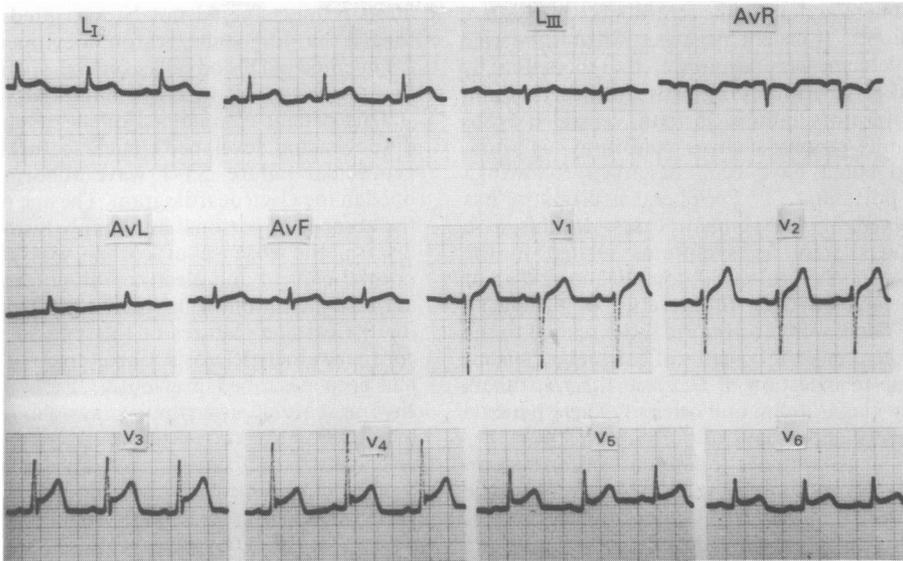


Figure 1 Electrocardiograph recording 3rd day after admission.

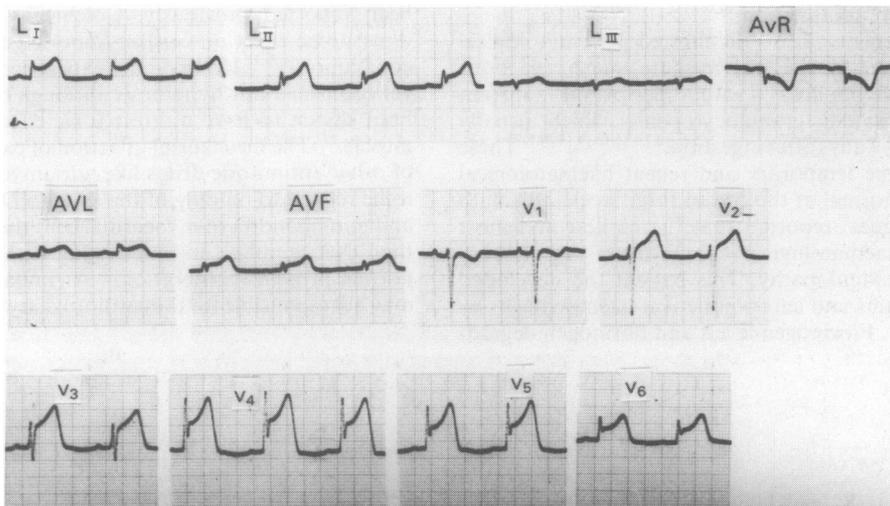


Figure 2 Electrocardiograph recording 4th day after admission.

Discussion

There does not appear to be a clear separation of non-toxic, toxic and lethal dosages of colchicine.²⁻⁵ This patient had ingested about 100 grams of tuber. Dunuville and others¹ have estimated that 10 g of fresh tuber contains approximately 6.0 mg of colchicine. Therefore the amount of colchicine ingested by this patient is in the region of 60 mg. Fatalities have been reported with doses as small as 7 mg.⁶ Bismuth

and colleagues⁷ reported that patients who ingested more than 0.8 mg/kg of colchicine died while those who ingested less than 0.5 mg/kg survived.

The commonest clinical presentation of poisoning with colchicine is one of severe gastroenteritis. Severe vomiting and diarrhoea causing fluid loss severe enough to produce hypotension has been reported.^{8,9} This patient, too, had nausea, vomiting and watery diarrhoea at the time of admission.

Colchicine has been shown by Ferguson¹⁰ to have its

most prominent action on the central nervous system. Rats developed transient paralysis when sub-lethal doses of colchicine were administered to them. Fatally intoxicated rats became progressively paralysed and died of respiratory failure. In man, central nervous system manifestations such as confusion, delirium, stupor and coma have been described following colchicine poisoning.¹¹⁻¹³ Peripheral neuropathy has been observed in four human cases. In this case however there were no symptoms related to the nervous system. Neurological complications do not appear to be related to the severity of colchicine poisoning. There were no abnormalities related to the nervous system in six fatal cases of colchicine poisoning also due to ingestion of *Gloriosa superba* tubers reported by Nagaratnam and others.¹⁶ These patients died between 1 and 8 days of poisoning.

Oliguric renal failure is a common occurrence in severe colchicine poisoning.^{3,6,9,11,12,14,17,18,19} Urine abnormalities such as proteinuria, myoglobinuria, haematuria and pyuria are described in the literature.^{3,9,17,18,20} This patient too was oliguric the first day and developed proteinuria and haematuria. The combined effects of hypotension, myoglobinuria and direct toxicity probably contribute to the abnormalities in renal function.^{20,21}

This patient also manifested haematological features seen in the intermediate stage, i.e. bone marrow hypoplasia with peripheral thrombocytopenia and granulocytopenia which usually manifest 4-7 days after ingestion.^{2,3,9,11,12,14,18,20,22} These changes were temporary and repeat haematological tests were normal at the end of three weeks. Bismuth and colleagues⁷ reported that the earliest and most common haematological complication was a consumption coagulopathy. This patient too developed bleeding gums and subconjunctival haemorrhages by the 5th day. Fibrinogen levels and fibrinogen degrad-

ation products could not be measured but the prolonged clotting time, thrombocytopenia and the fragmented red blood cells seen in the peripheral blood film are consistent with consumption coagulopathy.

This patient complained of severe chest pain and dyspnoea and developed clinical features of acute left ventricular failure. ST-T wave abnormalities developed in the electrocardiogram. The age of the patient, the absence of personal and family history of cardiac disease, the absence of coronary risk factors and normal clinical and electrocardiographic findings at admission and follow up, makes it extremely unlikely for the cardiac features of this patient to be due to coronary atherosclerosis. Cardiotoxicity of colchicine has been described previously. Tachycardia, gallop rhythm, cardiac arrhythmias, systolic murmurs and hypotension are known to occur.^{7,21,23} Sauder and his colleagues²⁴ performed haemodynamic studies in 8 cases of colchicine poisoning and reported that impairment of cardiac performance which can be detected in the initial stages of poisoning is an index of severity with a lethal outcome. Sub-pericardial haemorrhages and changes consistent with myocarditis have also been seen at autopsy.¹⁶ However, electrocardiographic changes as seen in this case have not been reported previously. Colchicine may have direct toxic effect on cardiac impulse generation and conduction.^{4,20,21} However, no experimental study has yet confirmed this hypothesis although colchicine has been shown to have a direct toxic effect on skeletal muscle.²⁵ The mechanism of action of cardiac toxicity of other antimitotic drugs like adriamycin is thought to be related to binding of the drug to DNA in nuclei and mitochondria of myocardial cells thereby altering the DNA template and interfering with processes of normal protein regeneration.²⁶ A similar mechanism may be responsible for the cardiotoxicity of colchicine.

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