Cryptostegia grandiflora Toxicity Manifesting as Hyperkalemia, Complete Heart Block and Thrombocytopenia

Shashikala A Sangle1, Sonali Inamdar2, Vikrant Deshmukh3

Abstract
Cardiac glycosides are widely available in botanic products and other naturally occurring substances worldwide. Accidental consumption of it leads to digitalis toxicity with varied systemic manifestations.1 We describe a case of consumption of extract of leaves of the Indian rubber vine plant (Cryptostegia grandiflora) which led to gastrointestinal, cardiac, electrolyte, and hematological disturbances.

Introduction
Digitalis or cardiac glycosides have been used for medicinal purposes for more than 200 years, ever since Sir William Withering suggested that digitalis may be beneficial in patients with heart complaints in 1785. Cardiac glycosides are widely available in some botanic products and other naturally occurring substances. Cryptostegia grandiflora, also known as the Indian rubber vine is said to contain cardiac glycosides responsible for producing a digitalis-like toxicity on consumption of its leaves. Digitalis toxicity produces a toxidrome characterized by gastrointestinal, neurologic, electrolyte, hematologic and cardiac manifestations.1

Case Report
A 16 year old male was brought to the casualty with complaints of repeated episodes of vomiting, breathlessness and disorientation after consumption of extract of leaves as Ayurvedic medication. They had been prescribed to him for the treatment of burning micturition and turbid urine. He had around 20 episodes of watery, non-bilious vomiting, with no history of hematemesis. There was also associated nausea.

On examination, he was found to be drowsy and disoriented with no focal neurological deficit. His pulse rate was 68/min, regular with a systolic BP of 60 mmHg. Respiratory rate was 24/min. Signs of dehydration were present on general examination. Other systemic examination was normal.

Lab investigations revealed a serum potassium level of 9 mmol/L with normal sodium levels (138 mmol/L) Renal function tests suggested a urea level of 13.3 mmol/L (80 mg/dl) and serum creatinine level of 194 μmol/L (2.2 mg/dl).

A central line was inserted for central venous pressure monitoring. CVP was 1 cm of water. He was given fluids and a dopamine drip for hypotension. Hyperkalemia was treated with intravenous sodium bicarbonate, glucose-insulin drip and ion-exchange resins. The potassium was corrected to 4.9 mmol/L after 12 hours of treatment.

His ECG was suggestive of a prolonged PR interval suggestive of a first degree heart block. Consequently, he developed a complete heart block, with the heart rate of 40 beats per minute (Figure 1). He was given IV Atropine for the same, after which the rate increased to 70/min although with a persistent first degree heart block. Temporary cardiac pacing was planned but was withheld after the response to atropine.

Later on, he developed three episodes of spontaneous epistaxis. There was no bleeding from any other site and no evidence of a rash. Blood pressure was maintained at 110/70 mmHg on fluid therapy alone. Laboratory investigations revealed a platelet count of 38,000/cmm. Four random donor platelet transfusions were given for thrombocytopenia. Subsequently, his platelet count was stabilized at 1,00,000/cmm.

In view of a possible digitalis intoxication, serum digoxin levels were measured which were 4 ng/ml (normal range : 0.8 to 2 ng/ml). His CPK-MB levels were normal.

1Ex. Associate Professor, 2Assistant Professor, 3Resident, Department of Medicine, B. J. Medical College and Sassoon General Hospitals, Station Road, Pune, Maharashtra
Received: 06.09.2013; Revised: 30.01.2014; Accepted: 13.02.2014
By the third day, the patient was fully conscious, his gastrointestinal disturbances had subsided and his pulse rate had improved to 80/min, regular with a BP of 120/80 mmHg. Serum potassium was 4.2 mmol/L. The renal parameters had normalized as well (serum urea: 3.32 mmol/L or 20 mg/dl, serum creatinine: 70 μmol/L or 0.8 mg/dl). A repeat ECG revealed the persistent first degree heart block.

On detailed examination of the leaves similar to the ones that the patient had consumed, it was identified to be the leaves of Cryptostegia Grandiflora also called as the Indian rubber wine which is the source of cardiac glycosides (Figure 2).

The patient was discharged on the 7th day of admission with no complaints and is on regular follow up.

Discussion

Cryptostegia grandiflora (Indian rubber vine, Kauli) is a perennial climber widely distributed in India, Madagascar, Australia and Florida. Its medicinal uses are as purgative, analgesic, wound healing remedies, antioxidant, antiviral, and for treatment of schistosomiasis. It is known in India by several local names like Vilayti-vakundi (Marathi), Garudappalai, Kauli (Marathi), Rubber vine, Chabuk-chhuree, Purple allamanda, Palai (Tamil), Palay Rubbervine, Rubber ki bel (Hindi). Our patient had consumed the local Kauli plant which was accidently prescribed by an Ayurvedic doctor for symptoms of urinary tract infection. Leaves of Cryptostegia grandiflora, contain many cardiac glycosides (oleandrigenin, cryptostigmin I-IV) along with two cardelonides. Powdered leaves, mixed with water, when swallowed can cause persistent vomiting after half an hour; death in 15 hours. It is a poisonous plant causing death in cattle, sheep, goats and horses and hence is unpalatable and rarely eaten by them. Other plant sources of cardiac glycosides include foxglove, yellow oleander, lily of the valley, wallflower and frangipani.

Cardiac glycosides reversibly inhibit the sodium-potassium adenosine triphosphatase exchanger (Na-K-ATPase) in cardiac myocytes resulting in higher than normal intracellular concentrations of sodium and subsequently calcium, leading to positive inotropy. In toxicity, the influx of sodium increases phase IV depolarization, lowers the resting membrane potential threshold, and increases automaticity leading to its proarrhythmic potential. Although AV block and extrasystoles are the most common dysrhythmias seen, almost any dysrhythmia is possible. Our patient manifested with a complete heart block, followed by a residual first degree heart block.

Hyperkalemia is a major manifestation of cardiac glycoside toxicity and is a result of the inhibition of Na-K-ATPase and the subsequent increase in extracellular potassium. In acute toxicity, there is a strong correlation between degree of hyperkalemia and mortality from digoxin overdose. Hyperkalemia was seen in our patient, which responded to treatment with sodium bicarbonate, glucose-insulin drip and ion-exchange resins without necessitating the need to resort to hemodialysis.

Na-K-ATPase exchangers are not limited to cardiac myocytes, and systemic toxicity is commonly observed in addition to cardiac toxicity. Neurologic symptoms (independent of those caused by circulatory collapse) include confusion, weakness, lethargy, delirium, and disorientation. Gastrointestinal problems, such as nausea, vomiting, and anorexia, are also common. Our patient presented with circulatory collapse with nausea, vomiting, lethargy and disorientation.

Intravenous calcium has traditionally been considered contraindicated in digoxin overdose because hypercalcemia potentiates digoxin toxicity since theoretically, a noncontractile
state is produced due to a failure of diastolic relaxation. Digoxin-specific antibody fragments (DSFab) is the treatment of choice and rapidly reverses cardiac manifestations of toxicity. Beta-blockers may be considered for supraventricular tachyarrhythmias with rapid ventricular response but may potentiate AV blockade, so short-acting agents, such as esmolol, are best. Atropine may be considered a temporary adjunct to treatment with DSBF, as is cardiac pacing.1 Our patient did not receive digoxin-specific antibodies due to financial reasons, however he responded well to symptomatic treatment, without the need of a pacemaker.

There is evidence of thrombin and plasmin-like activities present in the latices of Cryptostegia grandiflora leading to its fibrinogenolytic and procoagulant action.4 These properties could be responsible for the bleeding manifestation (epistaxis) seen in our patient. However, there are no reports of Cryptostegia grandiflora being responsible for the thrombocytopenia which was seen in our patient. The likely cause could be an immune thrombocytopenia secondary to its ingestion.

Similar case of digitalis toxicity being produced by Cryptostegia grandiflora consumption has been documented by Mathur et al.5 Severe cardiac arrhythmias have been described in poisoning of ruminants by plants containing cardiac glycosides. Necropsy findings include evidence of congestive heart failure, epicardial and endocardial haemorrhages and focal myocardial necrosis with mononuclear inflammatory cell infiltrates and evidence of early fibroplasias.6 Evidence of thrombocytopenia however, has not been documented in any other study, as was seen in our patient.

Thus, in a patient of unknown poisoning presenting with circulatory collapse, GI disturbances, dysrhythmias and hyperkalemia, one should suspect cardiac glycoside containing plant poisoning which needs to be treated promptly to reduce the high mortality rates associated with it.

References