Case Report

Calotropis poisoning with severe cardiac toxicity A case report

Ramya Iyadurai[1], Karthik Gunasekaran[1], Arun Jose[2], Kishore Pitchaimuthu[3]

[1]Department of Medicine, [2]Biochemistry, and [3]Division of Critical Care, Christian Medical College, Vellore, Tamil Nadu, India

Abstract

Calotropis is a widely prevalent plant in the Indian Subcontinent. The extract and various parts of the plant are used by traditional healers for treating miscellaneous diseases. All parts of the plants are toxic; there are many case reports of gastrointestinal, cutaneous and ocular toxicity with Calotropis. The plant contains Cardenolide glycosides which have Digoxin like effects and can cause severe cardiotoxicity. We report a patient who developed cardiovascular collapse after oral ingestion and cutaneous application of Calotropis following snake bite by a traditional healer, this case thus highlights the potential cardiotoxicity of Calotropis.

Keywords: Calotropis poisoning, cardiotoxicity, traditional medicine

Background

Calotropis is a weed found throughout India. Due to the latex production the plant is called milkweed. The flowers are used to make floral tassels especially during festivals in India. Various parts of the plant are used to treat varied diseases such as cancer, arthritis, snake envenomation, and sepsis by traditional healers. The stem of the plant is commonly used for illegal abortions.

Case Report

Mrs. S is a 56-year-old lady who was brought to our hospital with history of alleged snake bite. Patient had been working in the fields when she was bitten by a snake. Patient was not able to identify the snake. She had informed her daughter-in-law who took her to a traditional medical practitioner. The practitioner had taken some leaves from a plant in his garden; he then crushed it and applied the crushed leaves to the bite site. The milky fluid which was obtained from crushing the leaves was given to the patient to drink by the healer. The patient on questioning later remembered that the fluid caused severe burning and irritation in the throat. After taking the medication the patient was taken home. At home the patient progressively worsened and became drowsy, so the relatives decided to take her to the District hospital a few kilometers away.

At the district hospital the doctors on arrival noticed that she was hypotensive and her blood pressure was not recordable. She was immediately intubated ventilated with ambu bag with oxygen initiated on ionotropes and referred to a tertiary care center for further management.

Patient was brought to our accident and emergency department, at this time her blood pressure was 90/60 mmHg, heart rate: 112/min, cardiovascular system there were normal heart sounds and no murmurs or gallop, respiratory system there were bibasal

Address for correspondence: Dr. Ramya Iyadurai, Professor in Medicine, Department of Medicine 5, Christian Medical College, Vellore - 632 004, Tamil Nadu, India.
E-mail: iramya@cmcvellore.ac.in

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crackles up to the angle of scapula. Central nervous system the Glasgow coma scale was 2T/15, pupils were equal and reacting to light, dolls eye movement was present, deep tendon reflexes were present the plantars were mute. The patient was admitted to the intensive care unit, mechanical ventilation, and ionotropes were continued. Local examination revealed fang marks over the dorsum of the right hand.

The patient was admitted and investigations revealed that her sugars were high at admission [Table 1] and potassium was slightly low otherwise all investigations were normal. But her echocardiogram done after admission into the medical intensive care unit showed global hypokinesia with a low ejection fraction 30%.

At this point the diagnosis we considered was that of cardiogenic shock due to plant toxin with cardiotoxicity, secondary ton antidote for the snake bite given by the traditional practitioner. We requested the patient's relatives to bring the plant, this was identified as calotropis. We sent the patients serum and urine for toxicological analysis.

Table 1 at admission

Biochemistry	Patient results	Normal ranges
Serum creatinine	0.59 g/l	0.4 - 1.4 g/l
CPK MB	38.5 ng/ ml	3.8 ng/ml
Troponin I	599.3 pg/ml	14 pg/ ml
CPK	368 IU/L	45 - 195 IU/L
Sodium	138 mmol/L	135 - 145 IU/L
Potassium	3 mmol /L	3.5 - 5 IU/L
Magnesium	2 mmol/L	1.8 - 2.4 mmol/L
Serum Lactate	5.6 mmol/l	< 1 mmol/L
Hematology	Patient results	Normal ranges
Heamoglobin	8.8 g/l	11 - 15 g/l
Total count	11,000 cu/mm	4000 = 12000 cu/mm
(White blood cell)	2,84,000 cu /mm	1,50,000 - 4,50,000
Platelets	11.4 secs	9.8 - 12 secs
Prothrombin time	1.04	
INR	28.1 secs	26.5 - 35.3 secs
Activated Partial Thromboplastin time		

The toxidrome of our patient did not fit into the clinical presentation of any of the big four snakes associated with snake envenomation in our country. There was no neurological weakness, bleeding diathesis, or renal failure [Table 1] ruling out snake envenomation related illness.

The patient was diagnosed to have severe calotropis poisoning with cardiovascular collapse. The patient was managed with ionotropes and she improved rapidly she was weaned off the ventilator and shifted to the ward, but she developed severe irritant cellulitis [Figure 1] at the site of the application of the calotropis it improved with debridement and regular dressings. At discharge the repeat echocardiogram showed left ventricular hypertrophy with normal ejection fraction 56.7%

Toxicological Analysis

The leaf of plant bought by patient relative were dried and extracted with water and filtered. Filtrate 5 ml was taken in a test tube and 2.5 ml of water is added and shaken after which 2 drops of oil was added and shaken vigorously. Froth was produced and emulsion was produced after adding oil which confirms the presence of Saponin.

For identification of Cardiac Glycosides 5 ml of the filtered extract 2 ml of glacial Acetic Acid and 1 drop Ferric Chloride solution was added. Then 1 ml conc. Sulphuric acid was slowly added from the side of test tube without disturbing the solution. A brown ring at the junction of the two layers proves presence of Cardiac Glycosides in the plant extract. Calotropis plant extract contain saponin and glycosides. With the chemical tests and (morphological, visual) examination conforms the plant is Calotropis procera. Above test was performed on the urine sample of the patient for detection of cardiac glycosides in the lab gave a positive result for the same

Figure 1: Calotropis procera

Figure 2: Calotropis gigantea

Discussion

Calotropis is a common weed in India. There are two species Calotropis gigantea and Calotropis procera. Calotropis procera [Figure 1] is the more toxic of the two species and is identified easily by the presence of larger flowers. Luckily for our patient she was given the extract of Calotropis gigantea [Figuer 2] the less toxic plant.

All parts of the plant are toxic, the stems and roots being more toxic than the leaves. The toxic component of the plant is Uscharin, Calotoxin, Calotropin, Calactin, and Calotropage.

Calotropin, like calactin, calotoxin, and uscharin are derived from calotropogenin. These chemicals are called Cardenolides. Cardenolides are glycosides; cardiac active steroids which contain a 5 member lactone ring.[1]

Cardenolides like Calotropin act on the $Na^+/K+$ ATPase pump, this enzyme is responsible for the active transport of sodium and potassium across the membrane. The inhibition of this pump affects the resting membrane potential and is the suggested mechanism for toxicity of Cardenolides cardiac toxicity.[2]

The toxicity of Cardenolides is due to their ability in inhibiting the Na^+ K^+ ATPase pump. Cardenolides are toxic to most animals and insects. Insects that are resistant to Cardenolides have developed cardenolide insensitive Na^+ K^+ ATPase (e.g., the caterpillar of the monarch butterfly which feeds exclusively on the leaves of Calotropis).[3] Our current understanding is that the Calotropin biosynthesis is similar to that of Digoxin. Other commonly used plant toxin for deliberate self-harm Oleander also contains Cardenolides.

A study done in rats and sheep has shown that Calotropis ingestion is associated with cardiotoxicity. The sheep developed tachycardia and arrhythmias within 4 h of ingestion of the leaves. This is similar to the time period within which our patient developed cardiogenic shock. The same study on rats that were given escalating doses of Calotropis latex revealed that; rats given 1 ml/kg of latex expired within 2 h of ingestion and necropsy of these animal models showed that there was sub-endocardial hemorrhages, multifocal coagulation, and necrosis cardiac muscle fibers. Hence the study concluded that Calotropis procera is a cardiotoxic plant, similar to oleander.[4]

There are many case reports of cutaneous and ocular toxicity with calotropis. Ocular toxicity due to calotropis is thought to be due to the direct acid injury in the early stages and toxin mediated ocular injury in later stages.[5,6]

When the calotropis extract is taken for deliberate self-harm patents presented with epigastric burning, vomiting, salivation, tetanic convulsions, collapse and death. In humans estimated fatal period is within 30 min up to 8 h.[7]

In a case series from Nalgonda in South India among 60 patients with Calotropis poisoning the most common clinical presentation was abdominal pain, there was no mortality in this case series.[8]

Primary Care Management of Poisonings and Snake Envenomation

Community-based studies from India have shown that the snake bite and poisoning are common in rural India where most often the primary care physician is the first point of contact for these patients.[9,10] Early diagnosis, with simple first aid measures initiated in primary care can reduce the mortality due to theses illnesses.[11]

There is an increase in the use of alternative medicines around the world. Primary care physicians should be aware about alternative medication use among local population, their indications and side effects this will help us in timely management of these patients.[12]

Why was Our Patient Given Calotropis?

Medicinal use of Calotropis

Calotropis is extensively used in Indian system of medicine for treatment as an analgesic, in the treatment of asthma, diabetes, malignancies, arthritis, and antoxidant.[13]

Recent studies have shown that the peptidases present in Calotropis procera have anti-fungal properties.[14] But there are no studies for the use of Calotropis in snake envenomation.[15]

Native medicine and snake envenomation

The plant is so toxic that snakes cannot stand its smell and snake charmers use it to ward away the snakes. Hence the assumption is that it will cure snake envenomation also, so traditional healers use Calotropis to treat snake envenomation.[12]

Conclusions

Calotropis can cause severe cardiotoxicity, calotropis poisoning should be considered when patients with snake bite present with sudden cardiovascular collapse especially when there is history of treatment with native medications.

Key points

1. Snake envenomation can be complicated by the use of native medications
2. Calotropis ingestion can cause cardiovascular collapse.

Ethics declaration

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting, and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that appropriate permissions were taken from the

institution and the patient. We also certify that we have not plagiarized the contents in this submission and have done a Plagiarism Check with standard plagiarism tools.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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