Case Report

A Case of Accidental Ricin Poisoning

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Abstract

A case report of accidental, mild ricin poisoning by ingestion of ten Castor beans by a 70 year old man. The clinical presentation is followed by a discussion about the toxicity of ricin, its use and misuse and the contrast between the toxicity of pure ricin and the ingestion of castor beans. Management of castor bean poisoning is also discussed.

Case Presentation

A 70 year old man was admitted to St. Luke's Hospital Accident and Emergency department with persistent vomiting, profuse watery diarrhoea (up to eight times an hour) and diffuse colicky abdominal pain. Symptoms commenced about 6 hours after the ingestion of about ten beans of a plant found on the wayside. The patient brought a sample of ingested beans with him on presentation to hospital (Figure 1).

The patient had suffered a right middle cerebral artery embolic event a year earlier from which he had recovered completely. His only medication was Aspirin 150 mg daily and he had no documented allergies.

On admission, the patient looked unwell. He was dehydrated and tachycardic. He was hypotensive and showed a postural systolic drop of 30 mmHg. Examination of the abdomen showed diffuse tenderness with increased bowel sounds but was otherwise soft with no guarding. Rectal exam showed no bleeding or melaena and the stool was yellow and very loose. The rest of the physical examination was unremarkable.

Blood investigations revealed a white cell count of $20x10^9$/litre, urea 20 mmol/litre, creatinine 170 micromol/litre, potassium 3.0 mmol/litre, glucose 10.6mmol/litre, gamma glutaryl transferase 75 U/litre, alkaline phosphatase 119 IU/litre,

Key Words

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alanine aminotransferase 65 IU/l. The rest of the blood investigations, including clotting times were normal. Chest X-ray, abdominal X-rays and electrocardiogram were normal.

The provisional diagnosis was that of severe gastroenteritis secondary to ingested plant toxins. He was managed supportively with intravenous rehydration, strict fluid balance, potassium supplementation and monitoring of the electrolyte and renal function status. In the interim, the seeds that had been consumed were identified to be castor beans, coming from the plant *Ricinus comunis*. This identification led to the definitive diagnosis of accidental Ricin poisoning by ingestion.

Supportive management was continued and this led to full recovery, with relief of symptoms and normalization of the patient's biochemical status. The patient remained well and was discharged home after seven days of supportive care.

Discussion

The plant *Ricinus comunis*, commonly known as the Castor oil plant, is a spurge of the family Euphorbiaceae. Originally found in Africa, it is now ubiquitous in warm countries such as the Maltese Islands[1] (Figure 2). This plant is known to produce important biologically active substances; Castor Oil, (used as an industrial lubricant and as a laxative), ricinine (a weakly toxic alkaloid), and the toxalbumin ricin.[2] The plant itself and its pollen are also highly allergenic.

Ricin is one of the most potent naturally occurring toxins known to man. It is held among the top two or three deadliest poisons available namely plutonium and the phytotoxin abrin.[3] With a LD50 of 3 g/kg body weight (aerosol and parenteral) and 30 g/kg body weight (ingestion)[3] it is twice as poisonous as cobra venom.[4] Luckily ricin is immiscible with castor oil and this prevents contamination of the oil during its production.

Ricin belongs to a class of proteins known as ribosomal inactivating proteins (RIPs). As their name suggests, these proteins interfere with the function of ribosomes, halt protein synthesis and thus induce cellular death.[5]

Ricin is a type II RIP, as it can be internalized by cells. It is made up of two haemagglutinins and two toxins (RCL III and RCL IV). Each toxin, in turn is composed of two subunits; two smaller proteins bound together by a disulphide bridge. These two proteins are the A Chain (RTA) and the B Chain (RTB).[6] RTA is an N-glycosidase composed of 267 amino acid residues and is the toxically active component. RTB is composed of 262 amino acids and is classed as a lectin (sugar residue binding

Figure 1: Castor beans and seed pods

protein) with an affinity for binding to galactose and mannose containing glycoproteins at the cell surface.

Being an N-glycosidase, RTA acts by depurinating adenine in specific RNA sequences on the 28S ribosomal subunit. A single RTA molecule is capable of deactivating every ribosome in the cell, thus halting protein synthesis and enzymatic function, culminating in cell death. On its own, RTA cannot enter the cell to get access to ribosomes so it is classified as a type I RIP.[5] RTB, being a lectin with an affinity for galactose and mannose residues at the cell surface, works as a cell binding protein carrier for RTA, thus facilitating its cellular internalization; so by attaching RTA to RTB, castor oil plants have created a ribosome inactivator that can be carried into the cell where it is highly cytotoxic. This is the same strategy used by certain other toxins e.g. Choleratoxin and Shigatoxin among others; in each case the toxin is linked to a cell binding protein to enable internalization into the cell.[7]

Once internalized into endosomes, the ricin molecule is capable of prevention of acidification of its environment, which would otherwise render it less effective. At this stage, RTB facilitates the crossing of RTA into the cytosol. After cleavage from its partner subunit, RTA is taken up by the Golgi apparatus and makes its way to wreak havoc in the ribosomes of the rough endoplasmic reticulum.[8]

Although the toxicity of Castor beans has long been known, the actual poison was only discovered in the 1880s.[4] Awareness about ricin's high toxicity increased dramatically in 1978 due to the Bulgarian Umbrella murder, when Georgi Markov, a Bulgarian defector and political activist was murdered in London. He had been jabbed by a specially manufactured umbrella which shot a microscopic pellet containing Ricin into his leg. Markov died 3 days later.[9]

The ubiquitous nature of the Castor bean plant, the relative ease of extraction of ricin from castor beans and the deadly toxicity of pure ricin have raised serious worries about its use in bioterrorism for the contamination of water supplies or spread via the aerosol route.[3,6] These worries have led to intensive awareness campaigns[10,11,12] and research into the

Figure 2: Castor bean plants in Malta

development of vaccines of antiricin[13] and methods of rapid serological diagnosis by EIA.[14]

The toxicity of Ricin however has also been harnessed for use in medicine. In combination with monoclonal antibodies directed at cell surface receptors of tumourous cells, it fulfills the role of Erlich's *magic bullet* in the treatment of certain malignancies.[15] These immunotoxins have recently been improved by means of pegylation.[16] Ricin is also used in the research of neurological degenerative disorders and in the treatment of intractable painful neuropathies by use of *suicide transport* in neurons.[17]

Despite the impressive toxicity of pure ricin, particularly if administered via the parenteral or aerosol routes, one must not extrapolate this toxicity to the ingestion of castor beans, as numerous case reports in the literature have shown this route to be far less toxic than presumed[1,18,19,20] , with mortality rates of 8.1% (untreated) and 0.4% (treated).[18] The case presented above, exemplifies this point; however, castor bean ingestion, particularly if the husk has been broken by chewing, can indeed be fatal if numerous seeds are consumed and can also be responsible for severe morbidity. The greatest risk is posed to children who may be lured by the attractive patterns on the beans.[22] Figures about the number of seeds needed to cause a fatality are rather unreliable and very dependent on whether the seeds were chewed prior to ingestion.[18,19,20]

The ingestion of beans where the husk has been broken[18] is usually followed by a severe gastroenteritis characterized by the passage of large volumes of very loose stool and intractable vomiting. Subsequently patients may develop renal failure secondary to hypovolaemia and the direct toxicity of ricin. Patients may move into multiorgan failure as Ricin is also hepatotoxic, neurotoxic and cardiotoxic. Coagulation disturbances leading on to Disseminated Intravascular Coagulation (DIC) can also occur.[4,6,9,21]

The mainstay of treatment has not changed much over the decades, and remains supportive care. If presentation occurs within an hour of ingestion, gastric lavage may be attempted. The role of activated charcoal is very important if presentation is early. Careful attention to fluid balance is paramount, as hypovolaemia should be treated at all times. Patients should be observed in hospital until all biochemical disturbances settle. Such measures are usually sufficient to allow full recovery.[18,19,20] The early identification of the ingested substance by liaison with toxicology is essential. In this case the diagnosis was made using the clear evidence provided but in other scenarios where suspicion is strong but other corroborative evidence is lacking, the toxin can be detected by Enzyme Immuno Assay (EIA), as ricin is very immunogenic.

The above case clearly shows that castor bean poisoning is still a reality today and illustrates the need for general education about locally occurring poisonous plants. Prevention of ingestion can be promoted by education and providing awareness of the potential toxicity of castor beans and avoidance of planting the castor bean plant in domestic gardens.[18,20] Debris from the plant or the beans can be decontaminated by the use of dilute sodium hypochlorite as this denatures and inactivates ricin permanently.[23]

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