

Ricin poisoning causing death after ingestion of herbal medicine

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Ricin intoxication is a fatal and an uncommon medical condition. We report a case of ricin poisoning in a 42-year-old Saudi male patient who ingested a herbal medicine mixture containing ricin bean powder, after which he presented with gastrointestinal symptoms followed by gastrointestinal bleeding and hypotension. The patient then passed into a state of shock with respiratory failure followed by cardiac arrest and death. Public health awareness of self-prescribed herbal medications is necessary.

Ricin is a natural toxic protein derived from the castor bean plant, *Ricinus communis* (Figures 1a and b).¹ Purified ricin is a white water-soluble powder that is inactivated by heating at 80°C in aqueous solution for 1 hour.² It was discovered by Stillmark in 1889 as the first plant lectin from the seeds of the castor plant.³ Ricin is composed of two polypeptide chains: an A-chain (30 kDa) and a B-chain (32 kDa), and the two chains are linked by a disulfide bond. The mechanism of toxicity has been explained as follows: the A-chain inhibits protein synthesis by modifying the 22S subunits of ribosomes, whereas the B-chain binds to the cell surface receptors containing terminal galactose and facilitates the transport of the toxic protein into the cell by binding to specific sugar residues of the glycoproteins or glycolipids on the cell membrane and then promoting internalization by endocytosis.

Ricin has been studied as a chemotherapeutic agent. Experimental evidence confirms that malignant cells are more susceptible to ricin toxicity because they express more carbohydrate-containing surface-lectin binding sites than do nonmalignant cells.⁴⁻⁹ The extreme toxicity of ricin and relative ease of its production render it as a potential chemical warfare agent and a terrorist weapon. It is included in schedule 1 of the chemical weapons convention. The Centers for Disease Control and Prevention (CDC) classifies ricin as a category B agent (second high priority) because it is moderately easy to disseminate, it causes low mortality and moderate to high morbidity, and it requires specific enhancement of the CDC's diagnostic and disease surveillance capacity.¹⁰

CASE

A 42-year-old male Saudi patient presented to the emergency department with a 12-hour history of epigastric pain, nausea, repeated attacks of vomiting, chest tightness, and mild nonproductive cough.

These symptoms were preceded by a 5-day history of constipation for which the patient ingested a large amount of a mixture of herbal medicine preparation 2 days prior to his admission. A review of systems was unremarkable. He had no history of any medical illnesses and medication use except for the herbal medicine. Initial examination showed a mild elevation of temperature (38°C), with generalized abdominal tenderness and hyperactive bowel sounds. His respiratory system examination showed equal bilateral air entry and no added sounds. The rest of his systemic examinations were unremarkable.

Laboratory investigations on admission showed mild leukocytosis of $14 \times 10^9/L$, a normal platelet count

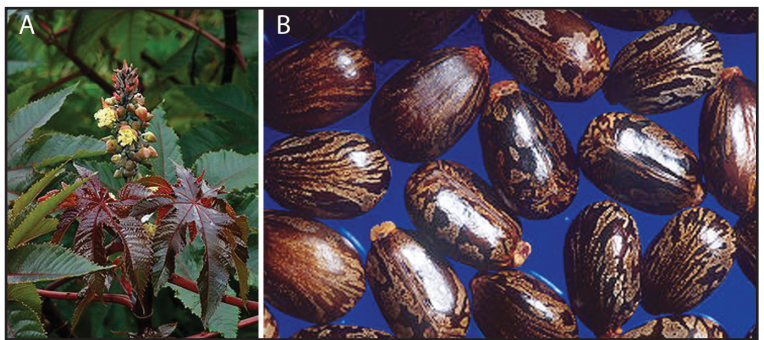


Figure 1. a. Castor bean plant (*Ricinus communis*), b. castor beans.

of $200 \times 10^9/L$, and normal hemoglobin level of 15.8 g/dL. Liver enzymes initially showed mild to moderate elevation of alanine transaminase (ALT) 86 U/L (normal range up to 37 U/L), aspartate transaminase (AST) 252 U/L (normal range up to 40 U/L), and serum lactate dehydrogenase 281 U/L (normal range 72-182 U/L), and the renal function was normal. The initial coagulation profile was impaired as documented by a prolonged prothrombin time (19 seconds, control 12 seconds) and a prolonged activated partial thromboplastin time (56 seconds, control 32 seconds). Electrocardiogram showed a right bundle branch block, and a chest radiograph was normal.

After 4 hours of admission, the abdominal pain became worse, and the patient started showing subcutaneous bleeding at the intravenous sites and upper gastrointestinal bleeding, manifested as hematemesis. The patient was managed by intravenous fluid therapy, fresh frozen plasma and platelet transfusion, and gastric decontamination with activated charcoal. A gastrointestinal consultation was requested in which endoscopy was planned after stabilization of the patient, but was not performed because of rapid deterioration of the patient.

In the second day after admission, his liver enzymes increased to a level of 5980 U/L for ALT and 7010 U/L for AST. Serum albumin was 31 g/L (normal range 38-50 g/L), total protein was 59 g/L (normal range 66-87 g/L), and the platelet count dropped to $85 \times 10^9/L$. His renal function also deteriorated, elevating the creatinine level to 150 $\mu\text{mol/L}$ (normal range up to 123 $\mu\text{mol/L}$), and urea to 110 mmol/L (normal range 1.7-83 mmol/L). His blood and sputum cultures and sensitivity were negative for bacterial pathogens, and an abdominal computerized tomography scan was normal. The patient was managed conservatively with supportive measures as maintained earlier; however, he remained persistently hypotensive necessitating inotropic support. On the 3rd day, he developed cardiopulmonary arrest and was resuscitated; however, he could not be revived. The sample of the herbal medicine powder was sent to the university lab. The chemical contents were extracted by the liquid chromatography/mass spectrometry technique, revealing the presence mainly of ricin powder,¹¹ which was further identified by the immuno-polymerase chain reaction assay¹² that confirmed the presence mainly of ricin with no other significant contaminants. This finding could be implicated as the cause for the patient's fulminant clinical course.

DISCUSSION

Ricin intoxication is a fatal clinical condition. Animals

showed variable responses to such toxic substances, for example, chickens and frogs are the least sensitive animals whereas horses are the most sensitive.¹³

The ricin content of castor beans varies between 1% and 5%. The degree of toxicity depends on the dose and the route of exposure.¹⁴ Ricin intoxication can occur via ingestion (like in our current case), inhalation, or injection. Person-to-person transmission does not occur. Recently a case of suicidal death after intravenous and subcutaneous injection of castor bean extract was reported with clinical presentation similar to our current case.¹⁵

Following ingestion of ricin, patients usually develop gastrointestinal symptoms, mainly nausea, vomiting, diarrhea, abdominal pain, and gastrointestinal bleeding. Repeated attacks of vomiting and diarrhea can lead to severe dehydration, especially in children, with a possible fatal outcome. Toxicity can also lead to hepatic and renal necrosis. Our patient was exposed to ricin through the oral route, and he developed the typical gastrointestinal manifestations that were complicated by gastrointestinal bleeding with multiple organ failure involving hepatic, renal, and hematological disorders.

Inhalation and injection routes are considered to be the most lethal routes of exposure. After inhalation, symptoms commence within 8 hours, manifesting as respiratory distress, dyspnea, cough, fever, nausea, and chest tightness, followed by profuse sweating, pulmonary edema, cyanosis, and hypotension. Eventually, the patient usually develops respiratory failure and shock. Time to death is usually between 36 to 72 hours after the initial exposure. Intramuscular intoxication may result in severe local pain, regional lymphadenitis, and moderate involvement of visceral organs. If patients do not die within 3 to 5 days, they usually recover. The laboratory investigations are usually nonspecific. Mild leukocytosis is a constant feature in most cases of human intoxication, which was a feature in the current case as well. Traditionally, enzyme-linked immunosorbent assays (ELISAs) of blood or other body fluids¹⁶ or immunohistochemical techniques are used to confirm ricin intoxication by identifying it in body fluids or tissues. A new laboratory technique for detection of ricin by an immuno-polymerase chain reaction assay was a very sensitive test, which was performed on the sample of herbal powder in the current case.¹² More recently, the technique of detecting ricin by comparative indirect ELISA using a fluorescence probe in blood and red blood cells proved to be a very sensitive method of testing with omission of the extraction step.¹⁷

The management is usually supportive and depends on the route of exposure. Patients who inhale ricin are managed by appropriate treatment for pulmonary

edema and respiratory support, while patients who ingest the toxins are managed by gastric decontamination with activated charcoal, followed by administering a cathartic agent-like magnesium citrate. Rehydration after gastrointestinal fluid loss is essential, and the patient may need vasopressor agents for circulatory support. The regional poison control center should be notified and cases should be reported.

Evidence from animal studies has shown that both active immunization and passive prophylaxis are very effective against intravenous and intraperitoneal intoxication with ricin, while the inhalation route is best prevented by active immunization or prophylactic admin-

istration of aerosolized-specific anti-ricin antibody.¹⁸ Nonetheless, effective immunization and prevention studies in humans are still lacking.

In conclusion, we reported a case of ricin intoxication after the ingestion of herbal medicine containing the powder of ricin beans. The patient presented with an aggressive clinical course of severe gastrointestinal manifestation and respiratory failure followed by death. A sample of the ingested herbal medicine was analyzed and reported to contain ricin bean powder. The management of such cases is mainly supportive, and human immunization is not yet available. Public health awareness of self-prescribed herbal medications is necessary.

REFERENCES

1. Audi J, Belson M, Patel M, Schier J, Osterloh J. Ricin poisoning. A comprehensive Review. *JAMA* 2005;294:2342-2351.
2. Lauren S, William H, Stuart J. Thermal Inactivation of Ricin Using Infant Formula as a Food Matrix. *J Agric Food Chem* 2006;54:7300-7304.
3. Stillmark, R. Ueber Ricin. *Arbeiten des Pharmakologischen Institutes zu Dorpat*, iii, 1889. Cited in: Flexner, J. The histological changes produced by ricin and abrin intoxications. *J Exp Med* 1897;2:197-216.
4. Bies C, Lehr CM, Woodley JF. Lectin-mediated drug targeting: history and applications. *Adv Drug Deliv Rev* 2004;56:425-435.
5. Chen ZK, Lin LW, Weng XH, Xue ES, Lin YH. Interstitial chemotherapy with ricin-loaded thermo-sensitive hydrogel in pancreatic cancer xenograft. *Hepatobiliary Pancreat Dis Int* 2009;8:418-423.
6. Longo DL, Duffey PL, Gribben JG, Jaffe ES, Curti BD, Gause BL, et al. Combination chemotherapy followed by an immunotoxin (anti-B4-blocked ricin) in patients with indolent lymphoma: Results of a phase II study. *Cancer J* 2000;6:146-150.
7. Tsimberidou AM, Giles FJ, Kantarjian HM, Keating MJ, O'Brien SM. Anti-B4 blocked ricin post chemotherapy in patients with chronic lymphocytic leukemia--long-term follow-up of a monoclonal antibody-based approach to residual disease. *Leuk Lymphoma* 2003;44:1719-1725.
8. Lord JM, Roberts LM, Robertus JD. Ricin: Structure, mode of action, and some current applications. *FASEB J* 1994;8:201-208.
9. Liu C, Lambert JM, Teicher BA, Blattler WA, O'Connor R. Cure of multidrug-resistant human B-cell lymphoma xenografts by combinations of anti-B4-blocked ricin and chemotherapeutic drugs. *Blood* 1996;87:3892-3898.
10. Centers for Disease Control and Prevention. Recommendations of the CDC Strategic Planning Workgroup Biological and Chemical Terrorism: Strategic plan for preparedness and response. *MMWR Morb Mortal Wkly Rep* 2000;49:1-14.
11. Darby SM, Miller ML, Allen RO. Forensic determination of ricin and the alkaloid marker ricinine from castor bean extracts. *J Forensic Sci* 2001;46:1033-4102.
12. Lubelli C, Chatgijialoglu A, Bolognesi A, Strocchi P, Colombatti M, Stirpe F. Detection of ricin and other ribosome-inactivating proteins by an immuno-polymerase chain reaction assay. *Anal Biochem* 2006;355:102-109.
13. Okorie AU, Anugwa FO. The feeding value of roasted castor oil bean (*Ricinus communis*) to growing chicks. *Plant Foods Hum Nutr* 1987;37:97-102.
14. Olsnes S. The history of ricin, abrin and related toxins. *Toxicon* 2004;44:361-370.
15. Vera Coopman a, Marc De Leeuw b,c, Jan Cordonnier a, Werner Jacobs c. Suicidal death after injection of a castor bean extract (*Ricinus communis* L.). *Forensic Sci Int* 2009;189:e13-20.
16. Poli MA, Rivera VR, Hewetson JF, Merrill GA. Detection of ricin by colorimetric and chemiluminescence ELISA. *Toxicon* 1994;32:1371-1377.
17. Pradhan S, Kumar OM, Jatav PC, Singh S. Detection Of Ricin By Comparative Indirect ELISA Using Fluorescence Probe In Blood And Red Blood Cells. *J Med CBR Def* 2009;7.[AUTHOR: Confirm the Journal Name and provide the Vol no]
18. Poli MA, Rivera VR, Pitt L, Voge P. Aerosolized specific antibody protects mice from lung injury associated with aerosolized ricin exposure. *Toxicon* 1996;34:1037-1044.