

Research

Case report: fatal poisoning with *Colchicum autumnale*

Miran Brvar¹, Tom Ploj², Gordana Kozelj³, Martin Mozina⁴, Marko Noc⁵ and Matjaz Bunc⁶

¹Physician, Poison Control Center, University Medical Center Ljubljana, Slovenia

²Physician, Center for Intensive Internal Medicine, University Medical Center Ljubljana, Slovenia

³Head, Institute of Forensic Medicine, Medical Faculty, Ljubljana, Slovenia

⁴Head, Poison Control Centre, University Medical Center Ljubljana, Slovenia

⁵Professor, Head, Center for Intensive Internal Medicine, University Medical Center Ljubljana, Slovenia

⁶Associated Professor, Institute for Pathophysiology, Medical Faculty and Department for Cardiology, University Medical Center Ljubljana, Slovenia

Correspondence: Miran Brvar, miran.brvar@kclj.si

Received: 28 September 2003

Revisions requested: 18 November 2003

Revisions received: 26 November 2003

Accepted: 17 December 2003

Published: 2 January 2004

Critical Care 2004, **8**:R56-R59 (DOI 10.1186/cc2427)

This article is online at <http://ccforum.com/content/8/1/R56>

© 2004 Brvar *et al.*, licensee BioMed Central Ltd

(Print ISSN 1364-8535; Online ISSN 1466-609X). This is an Open Access article: verbatim copying and redistribution of this article are permitted in all media for any purpose, provided this notice is preserved along with the article's original URL.

Abstract

Introduction *Colchicum autumnale*, commonly known as the autumn crocus, contains alkaloid colchicine with antimitotic properties.

Case report A 76-year-old man with a history of alcoholic liver disease and renal insufficiency, who mistakenly ingested *Colchicum autumnale* instead of wild garlic (*Aliium ursinum*), presented with nausea, vomiting and diarrhea 12 hours after ingestion. On admission the patient had laboratory signs of dehydration. On the second day the patient became somnolent and developed respiratory insufficiency. The echocardiogram showed heart dilatation with diffuse hypokinesia with positive troponin I. The respiratory insufficiency was further deteriorated by pneumonia, confirmed by chest X-ray and later on by autopsy. Laboratory tests also revealed rhabdomyolysis, coagulopathy and deterioration of renal function and hepatic function. The toxicological analysis disclosed colchicine in the patient's urine (6 µg/l) and serum (9 µg/l) on the second day. Therapy was supportive with hydration, vasopressors, mechanical ventilation and antibiotics. On the third day the patient died due to asystolic cardiac arrest.

Discussion and conclusion Colchicine poisoning should be considered in patients with gastroenterocolitis after a meal of wild plants. Management includes only intensive support therapy. A more severe clinical presentation should be expected in patients with pre-existing liver and renal diseases. The main reasons for death are cardiovascular collapse, respiratory failure and leukopenia with infection.

Keywords autumn crocus, colchicine, *Colchicum autumnale*, death, poisoning

Introduction

Colchicum autumnale, commonly known as the autumn crocus, wild saffron and naked lady, contains alkaloid colchicine that is antimitotic, blocking the mitosis by preventing DNA synthesis and tubulin polymerization [1].

The clinical manifestations of colchicine poisoning are present in three phases following a latent period of 4–12 hours. The first

phase is characterized by peripheral leukocytosis, gastrointestinal symptoms with fluid losses and hypovolemic shock. During 24–72 hours, the second stage of intoxication, life-threatening complications occur such as heart failure, arrhythmias, renal failure, hepatic injury, respiratory distress, coagulopathies, bone marrow depression and neuromuscular involvement. This second phase can last for 5–7 days and is followed by the third phase, characterized by leukocytosis and alopecia [2,3].

Figure 1

*Colchicum autumnale* (Emergency Department).

When ingested, colchicine is rapidly absorbed from the gastrointestinal tract and is primarily metabolized by the liver in a first-order process [4]. There is significant biliary excretion and enterohepatic recirculation [5,6]. Renal excretion is responsible for only about 20% of unchanged colchicine elimination, although this fraction may be increased in the presence of liver disease [7].

Colchicine has been responsible for numerous intoxications and deaths. Colchicine is used in the management of acute gouty arthritis, and a suicidal colchicine tablet overdose is the most common cause of colchicine poisoning [8,9]. Accidental poisoning with *Colchicum autumnale* is very rare. Searching Medline we found only four case reports of accidental poisoning with *Colchicum autumnale*, and in none of them were blood colchicine concentrations measured [10–12].

We report accidental lethal *Colchicum autumnale* poisoning where blood colchicine levels were obtained.

Case report

In spring 2003, a 76-year-old man ate two whole plants regarded as wild garlic (*Allium ursinum*). He believed wild

Table 1

Laboratory data after *Colchicum autumnale* ingestion

	Day 1	Day 2	Day 3	Normal value
White blood cells ($\times 10^9/l$)	18.5	15.5	6.9	4.3–10.8
Red blood cells ($\times 10^{12}/l$)	4.9	4.8	3.3	4.15–4.90
Platelets ($\times 10^9/l$)	150	115	51	130–400
Creatinine ($\mu\text{mol}/l$)	195	367	524	< 133
AST ($\mu\text{kat}/l$)	0.6	3.7	14.5	0–0.58
ALT ($\mu\text{kat}/l$)	0.4	0.6	2.4	0–0.58
LDH ($\mu\text{kat}/l$)	20.9	40.4	92.3	1.7–3.2
International Normalized Ratio	1.5	1.6	1.9	1.2
Lipase ($\mu\text{kat}/l$)	7.1	11.9	5.6	0–2.66
Myoglobin ($\mu\text{g}/l$)	304	755	3696	0–90
CK ($\mu\text{kat}/l$)	3.5	8.6	19.0	0.17–2.08
Troponin I ($\mu\text{g}/l$)	< 0.01	0.10	0.37	< 0.06
pH	7.38	7.24	7.26	7.38–7.44
Lactate (mmol/l)	7.9	8.0	9.7	0.6–1.7
D-dimer ($\mu\text{g}/l$)			3290	< 250
Colchicine				
Serum ($\mu\text{g}/l$)		9	14	
Urine ($\mu\text{g}/l$)		6		

AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; CK, creatine kinase.

garlic to be healthy for his alcoholic liver disease. He also had a history of chronic renal insufficiency and arterial hypertension, which he treated with verapamil and trandolopril. Two hours after the ingestion, he started complaining of nausea. Repeated vomiting and watery diarrhea appeared 4–5 hours after ingestion. Twelve hours later the man arrived at the Emergency Department. He brought with him the remaining plant that he had not yet eaten (Fig. 1). The plant was identified as a poisonous *Colchicum autumnale* by the toxicologist. The patient was treated with gastric lavage and 30 g oral activated charcoal and was transferred to the intensive care unit.

On arrival at the intensive care unit, the patient complained of diarrhea and abdominal pain. His vital signs were a Glasgow coma scale of 15, a tympanic temperature of 37.1°C, a respiratory rate of 22 counts/min, a pulse of 122 counts/min and a blood pressure of 125/80 mmHg in the supine position. The patient had clinical signs of dehydration and a tender abdomen on palpation. The remaining physical examination was unremarkable. The patient's laboratory test results are presented in Table 1. The electrocardiogram showed a sinus tachycardia, and the chest X-ray was normal. Abdominal ultrasound revealed hepatic steatosis. During day 1 the patient had only gastrointestinal symptoms and was treated with

3000 ml normal saline and repeated doses of activated charcoal. He was given 200 mmol sodium bicarbonate to treat lactic metabolic acidosis.

On day 2 the patient became somnolent. He developed acute respiratory failure, and assisted mechanical ventilation was started. The echocardiogram revealed heart dilatation with an ejection fraction of less than 30%. The electrocardiogram showed only diffuse nonspecific ST changes, yet with positive troponin I values indicating myocardial necrosis (Table 1).

On day 3 the patient developed a high-grade fever and became hypotensive and anuric despite hydration and norepinephrine infusion. Abdominal peristaltic sound could not be detected and abdominal X-ray showed a dilated intestine. Bilateral infiltrates appeared on the chest X-rays. Antibiotic cefuroxime was started. Blood cultures remained negative. Laboratory tests also revealed rhabdomyolysis, coagulopathy and deterioration of metabolic acidosis, renal function and hepatic function (Table 1). Profuse bleeding from the nose appeared and fresh frozen plasma and platelets were given. At the end of day 3 the patient went into asystolic cardiac arrest and cardiopulmonary resuscitation was unsuccessful. Subsequent toxicology analysis by gas chromatography coupled to mass spectrometry showed colchicine in the patient gastric lavage, urine and serum samples, which were stored in light-protected containers (Table 1) [13]. An autopsy showed a dilated heart with a transversal diameter of the left ventricle of around 65 mm, pulmonary edema, bilateral bronchopneumonia, liver and kidney necrosis, hypocellular bone marrow with diserythropoiesis, dismyeloeliosis and dismegacaryopoiesis.

Discussion

The presented patient mistakenly ingested autumn crocus instead of wild garlic, whose leaves are used as a spice or medical plant. Autumn crocus and wild garlic are quite similar, especially their leaves, and unfortunately they grow in the same areas at the same time [11].

We can only speculate about the colchicine amount ingested by the patient. The remaining plant that the patient brought to the Emergency Department weighed around 5 g. The colchicine content of autumn crocus is 0.1–0.6% [14]. The total colchicine dose ingested by the patient could be calculated as follows: 2 (plants) × 5 g (weight of the plant) × 0.1–0.6% (content of colchicine in the plant)/73 kg (patient's weight). The estimated colchicine dose ingested by the patient was between 0.14 mg/kg (10 mg) and 0.82 mg/kg (60 mg).

According to published data, gastrointestinal symptoms are usually observed at doses less than 0.5 mg/kg and doses greater than 0.8 mg/kg are almost invariably fatal [14,15]. Everything from mild gastroenterocolitis to multiorgan failure followed by death could therefore be expected in our patient. Serum colchicine levels were three to six times more than the upper therapeutic level on the second and third days [16]. We

can only speculate about the highest colchicine concentration because the colchicine blood half-life is very unpredictable, reported to be between 20 min [1] and 19 hours [17].

We can assume that the colchicine elimination and the blood half-life in our patient were prolonged because the patient had alcoholic liver disease, which reduces the hepatic colchicine metabolism and excretion through the bile system. The patient's liver function was further worsened by colchicine poisoning and later by the evolving shock. An excretion of colchicine could be reduced by verapamil, which is an inhibitor of P-glycoprotein, a protein responsible for colchicine transport from the hepatocyte into bile [9]. A compensatory increase of colchicine excretion through the kidneys was observed in cases of hepatic failure [7]. In our case the compensatory excretion was not possible since the patient's chronic renal insufficiency was additionally deteriorated by hypotension, hypoxia and rhabdomyolysis due to the colchicine effect on muscle cells. The higher colchicine concentration on the third day compared with on the second day observed in our patient corresponds to the two-compartment model of colchicine kinetic coupled with impaired elimination in the second phase, mainly due to liver and renal insufficiency.

On the first day the intoxication caused gastroenterocolitis and dehydration. Dehydration in combination with impaired cardiac function resulted in tissue hypoperfusion with lactic acid metabolic acidosis. The respiratory insufficiency was deteriorated by bilateral pneumonia, confirmed on autopsy. Acute heart failure was probably the result of a direct toxic effect of colchicine on myocardial cells [8,18,19].

Conclusion

Colchicine poisoning should be considered in patients with gastroenterocolitis after a wild plant meal. Blood and urine colchicine determination is useful for diagnostics in doubtful cases. Management includes early intensive support measures despite a relatively mild clinical picture at presentation. Specific therapy such as colchicine antibodies is reported in some case reports as well as in animal studies but it is not yet commercially available [20,21]. A more severe clinical presentation should be expected in patients with pre-existing liver and renal diseases. The main reasons for death are cardiovascular collapse, respiratory failure and leukopenia with infection. Hepatic and renal dysfunction as well as certain drugs could worsen the prognosis of poisoning with colchicine.

Key messages

- In patients with gastroenterocolitis after a wild plants meal, especially when wild garlic is mentioned, we should always consider poisoning with autumn crocus
- Prognosis of colchicine poisoning is worse in patients with pre-existing liver and renal diseases

Competing interests

None declared.

References

- Folpini A, Furfori P: **Colchicine toxicity-clinical features and treatment. Massive overdose case report.** *J Toxicol Clin Toxicol* 1995, **33**:71-77.
- Donovan JW: **Nonsteroidal anti-inflammatory drugs and colchicine.** In *Clinical Management of Poisoning and Drug Overdose*, 3rd edition. Edited by Haddad LM, Shannon MW, Winchester JE. Philadelphia, PA: WB Saunders Company; 1999:687-699.
- Stapczynski JS, Rothstein RJ, Gaye WA, Niemann JT: **Colchicine overdose: report of two cases and review of the literature.** *Ann Emerg Med* 1981, **10**:364-369.
- Sabouraud A, Rochdi M, Urtizberea M, Christen MO, Achtert G, Scherrmann JM: **Pharmacokinetics of colchicine: a review of experimental and clinical data.** *Z Gastroenterol* 1992, **30**:35-39.
- Rudi J, Raedsch R, Gerteis C, Schlenker T, Plachky J, Walter-Sack I, Sabouraud A, Scherrmann JM, Kommerell B: **Plasma kinetics and biliary excretion of colchicine in patients with chronic liver disease after oral administration of a single dose and after long-term treatment.** *Scand J Gastroenterol* 1994, **29**:346-351.
- Bain L, Galloway D, Petrie J, Wood R: **Gout.** *Br Med J* 1974, **1**:446-448.
- Wallace SL, Omokoku B, Ertel NH: **Colchicine plasma levels. Implications as to pharmacology and mechanism of action.** *Am J Med* 1970, **48**:443-448.
- Mullins ME, Carrico EA, Horowitz BZ: **Fatal cardiovascular collapse following acute colchicine ingestion.** *J Toxicol Clin Toxicol* 2000, **38**:51-54.
- Borron SW, Scherrmann JM, Baud FJ: **Markedly altered colchicine kinetics in a fatal intoxication: examination of contributing factors.** *Hum Exp Toxicol* 1996, **15**:885-890.
- Sannohe S, Makino Y, Kita T, Kuroda N, Shinozuka T: **Colchicine poisoning resulting from accidental ingestion of meadow saffron (*Colchicum autumnale*).** *J Forensic Sci* 2002, **47**:1391-1396.
- Klintschar M, Beham-Schmidt C, Radner H, Henning G, Roll P: **Colchicine poisoning by accidental ingestion of meadow saffron (*Colchicum autumnale*): pathological and medicolegal aspects.** *Forensic Sci Int* 1999, **106**:191-200.
- Brncic N, Viskovic I, Peric R, Dirlic A, Vitezic D, Cuculic D: **Accidental plant poisoning with *Colchicum autumnale*: report of two cases.** *Croat Med J* 2001, **42**:673-675.
- Kintz P, Jamey C, Tracqui A, Mangin P: **Colchicine poisoning: report of fatal case and presentation of an HPLC procedure for body fluid and tissue analyses.** *J Anal Toxicol* 1997, **21**:70-72.
- Danel VC, Wiart JF, Hardy GA, Vincent FH, Houdret NM: **Self-poisoning with *Colchicum autumnale* L. flowers.** *J Toxicol Clin Toxicol* 2001, **39**:409-411.
- Bismuth C, Baud F, Dally S: **Standardized prognosis evaluation in acute toxicology: its benefit in colchicine, paraquat, and digitalis poisonings.** *J Toxicol Clin Exp* 1986, **6**:33-38.
- Halkin H, Dany S, Greenwald M, Shnaps Y, Tirosh M: **Colchicine kinetics in patients with familial Mediterranean fever.** *Clin Pharmacol Ther* 1980, **28**:82-87.
- Girre C, Thomas G, Scherrmann JM, Crouzette J, Fournier PE: **Model-independent pharmacokinetics of colchicine after oral administration to healthy volunteers.** *Fundam Clin Pharmacol* 1989, **3**:537-543.
- Mery P, Riou B, Chemla D, Lecarpentier Y: **Cardiotoxicity of colchicine in the rat.** *Intensive Care Med* 1994, **20**:119-123.
- Putterman C, Ben-Chetrit E, Caraco Y, Levy M: **Colchicine intoxication: clinical pharmacology, risk factors, features, and management.** *Semin Arthritis Rheum* 1991, **21**:143-155.
- Eddleston M, Persson H: **Acute plant poisoning and antitoxin antibodies.** *J Toxicol Clin Toxicol* 2003, **41**:309-315.
- Baud FJ, Sabouraud A, Vicaute E, Taboulet P, Lang J, Bismuth C, Rouzioux JM, Scherrmann JM: **Brief report: treatment of severe colchicine overdose with colchicine-specific Fab fragments.** *N Engl J Med* 1995, **332**:642-645.