

Short communication

Fatal colchicine poisoning by accidental ingestion of meadow saffron-case report

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Abstract

A 62-year-old male died of colchicine poisoning after accidental ingestion of *Colchicum autumnale* (meadow saffron). He ate a salad of plant with green leaves regarded as wild garlic (*Allium ursinum*). A few hours later he developed symptoms of gastroenteritis and was admitted to hospital. In spite of gastric lavage, activated charcoal and supportive measures, multi-organ system failure developed over the next two days. Laboratory analysis showed highly elevated blood concentrations of hepatic enzymes, creatine kinase, lactate dehydrogenase and blood urea nitrogen, as well as leukocytopenia and thrombocytopenia. Mechanical ventilation, dopamine, noradrenaline, crystalloid solutions and fresh frozen plasma were applied but despite treatment the patient died five days after the ingestion. Post-mortem examination revealed hepatic centrilobular necrosis, nephrotoxic acute tubular necrosis, petechial bleeding in fatty tissue, blunt and shortened intestinal villi and cerebral toxic edema. Botanical identification of incriminated plant gave *Colchicum autumnale* which confirmed colchicine poisoning. Although the accidental ingestion of *Colchicum autumnale* is rare and to our knowledge only five such cases have been described in detail, this is the second fatal case in Croatia described in the last 3 years.

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1. Introduction

The species *Colchicum autumnale* (meadow saffron) is native to West, Central and East Europe and North Africa. It grows mostly in damp meadows from lowland to mountain districts. All parts of plant contain highly poisonous colchicine and 20 other alkaloids. Formerly, the crude corns or

seeds were used for medical purposes; nowadays, only pure isolated alkaloids are used, namely colchicine and more often the less toxic demelkocine. Therapeutic indications are acute gouty arthritis, Familial Mediterranean fever and amyloidosis [1].

Children and warm-blooded animals are the main victims of dangerous and even fatal plant poisoning. Colchicine intoxication due to accidental poisoning or suicide attempt is frequently reported [2–9]. Homicidal deaths in which colchicine is used are extremely rare [10]. Fatal intoxication by ingestion of *Colchicum autumnale* is rare and to our

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knowledge only five cases have been reported in detail [11–15]. The symptoms appear 2–5 h after consuming the plant and include burning sensation in the mouth, intense thirst, vomiting, severe diarrhea, hematuria, sudden lowering of body temperature, collapse and death about 30 h after ingestion. A fatal dose of colchicine for adults is 0.8 mm/kg, but lower doses have been reported to be fatal [2]. We present a case of a 62-year-old male who died after accidental poisoning by ingestion of *Colchicum autumnale*.

2. Case history

The 62-year-old, previously healthy male was admitted to a local hospital because of general weakness, abdominal cramps, nausea, vomiting and watery stools. The symptoms began several hours after consumption of a plant with green leaves, which he mistakenly collected on the meadow near his village beside Gračac, Croatia, instead of the wild garlic (*Allium ursinum*). His wife tasted a little bit of the prepared salad and complained about the bitter taste. She also experienced similar but less dramatic pain but her symptoms subsided in the following days.

On admission his body temperature was 37.4 °C and respiratory rate 16 min⁻¹. He was in relatively good condition with normal clinical findings except for slight epigastric pain and diarrhea and his laboratory findings were within normal ranges. Gastric lavage, activated charcoal and supportive measures were implemented. During the following two days progressive clinical deterioration began with confusion, fever, hypothermia, hypotension, tachycardia and tachypnea. He developed elevated blood concentrations of hepatic enzymes, creatine kinase, blood urea nitrogen, and presented with hyperbilirubinemia, prolonged prothrombin time, thrombocytopenia and leukocytopenia and finally multi-organ system failure (Table 1). The patient was sent

to the intensive care unit of the regional Clinical Hospital where mechanical ventilation, dopamine, noradrenaline, crystalloid solutions and fresh frozen plasma were administered. Five days after intoxication, patient died in oliguria and cardiopulmonary insufficiency.

3. Post-mortem examination

Autopsy findings revealed marked pulmonary edema and congestion. Liver and spleen were enlarged, small intestine and colon were distended and petechial bleeding was observed in all fatty and subserosal tissue. Left cardiac ventricle was hypertrophied and the brain edematous. Microscopically, significant haemorrhagic necrosis was found around central hepatic veins. Hepatocytes showed hydropic or microvesicular fatty change, and portal triads were sparsely infiltrated by mononuclei. Disruption of white pulp and congestion of red pulp was found in the spleen. Intestinal mucous was blunted and lamina propria infiltrated by lymphocytes. Acute tubular necrosis without myoglobin or other casts was presented in the kidneys.

Toxicological analysis was not performed due to long interval from ingestion to death, during which colchicine would have been metabolized and eliminated [11].

4. Identification of the plant

Botanical examination of the plant was done in the Department of Agricultural Botany. The plant material was identified as meadow saffron (*Colchicum autumnale*).

5. Discussion

We reported a fatality due to accidental colchicine intoxication by ingestion of meadow saffron. In our case symptoms of intoxication after ingestion of unknown plant coupled with laboratory and morphological findings suggested colchicine poisoning even prior to the botanical identification. HPLC and UV detection in the blood can measure presence of drug or its metabolite, although often no substance is detectable [3]. In the fatal cases, bile appears to be the sample of choice for toxicological analysis [4]. In cases of possible colchicine poisoning, useful post-mortem histological characteristic is increased number of mitotic figure [5]. Colchicine is rapidly absorbed after oral administration and is metabolised on the body temperature to more poisonous oxydicolchicine. Hepatic excretion of colchicine and its metabolites by bile explains toxic effect on the labile intestinal epithelium and early onset of gastrointestinal symptoms. Half-life of colchicine in blood is twenty minutes, because of high affinity to tissues. Kidney, liver and spleen contain high concentrations of colchicine, but it is

Table 1
Laboratory findings on 3rd day after *Colchicum autumnale* intoxication

Analysis	Measured value	Unit	Normal range
Leukocytes	0.7	×10 ⁹ L ⁻¹	4–10
Platelets	10	×10 ⁹ L ⁻¹	130–400
Calcium, plasma	1.73	mmol/L	2.3–2.8
Urea nitrogen	18.1	mmol/L	2.5–8.3
Creatinine	295	μmol/L	54.2–116.0
Bilirubin, total	50.7	μmol/L	1.7–20.5
Amylase, serum	216	U/L	60–180
SGOT (AST)	4750	U/L	0–25
SGPT (ALT)	2240	U/L	0–29
Creatine kinase	10,120	U/L	15–130
Lactate dehydrogenase	13,080	U/L	160–320
Ammonia	73.5	μmol/L	26–48
Prothrombin time	21'	s	11'–15'
Lactate	4.5	mmol/L	0.5–2.2

apparently largely excluded from heart, skeletal muscle and brain [16].

Colchicine binds to cell protein tubulin and arrests mitosis in metaphase due to failure of spindle formation. It causes depolymerisation and disappearance of the fibrillar microtubules in granulocytes and other motile cells, inhibiting their migration to inflamed area as well as metabolic and phagocytic activity [1]. Colchicine is directly toxic to tissues with rapid turnover like intestinal mucous membrane and bone marrow, provoking diarrhea and decreasing absolute number of short-living blood cells granulocytes and thrombocytes. Congestion of red pulp is found in the spleen, but the reason for marked disruption of the white pulp is unclear, except possible antimetabolic colchicine influence on the lymphoid cells. Disseminated petechial bleeding in fatty tissues is related to thrombocytopenia and hepatic failure. Renal and hepatic deterioration were manifested by high blood concentrations of urea nitrogen, liver enzymes, ammonia and bilirubin. We found centrilobular liver necrosis typical for toxic hepatic injury, without specific “colchicine bodies” clumps of chromatin in nuclei of hepatocytes [11]. Highly elevated blood concentration of creatine kinase was presumably related to hypoxic brain and heart damage. According to known toxicological data, colchicine concentration in the brain is low [1,16]. We found histological signs of brain damage as marked pericellular and perivascular edema probably due to multiple system organ failure. Cardiac muscle showed left ventricular hypertrophy without myolysis and myoglobin casts in the renal tubules.

In this paper, we report an association between laboratory findings and pathological examination only on the 3rd day after *Colchicum autumnale* intoxication. On admission biochemical and haematological findings were also not markedly deviated from the range of normal standard parameters [11,14].

There is no antidote for colchicine and supportive treatment remains the only option. Aggressive primary decontamination with gastric lavage and activated charcoal is required as early as possible. Hemodialysis or hemoperfusion are not particularly effective due to the cell distribution of the drug [17]. Co-ingested opioid and anticholinergic compounds can affect colchicine absorption [18]. Use of colony stimulating factor improves the hematopoiesis [19]. In the future, monoclonal antibodies to colchicine will possibly improve the chance of survival [20].

Although the accidental ingestion of *Colchicum autumnale* is rare and, to our knowledge, only five such cases have been described in detail, this is the second fatal case in Republic Croatia, described in the last 3 years. To avoid the risk of confusion among the local population between highly poisonous *Colchicum autumnale* and edible plants like *Allium ursinum*, reliance on strong smell of the latter should be emphasized. Interestingly the elderly with a weaker sense of smell may not recognize the difference between the plants.

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