

Colchicine-Induced Cardiac Toxicity: Case Report

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Abstract

A 56-year-old woman with a medical history including hypertension, diabetes, depression, and gout was admitted to the emergency department after consuming 60 tablets of Colchicine, each containing 0.6 mg. The case involved significant deviations in vital signs, including an abnormally rapid heart rate and low blood pressure, indicating the widespread effects of Colchicine on the body. The patient's physical examination revealed restlessness, a decreased Glasgow Coma Scale score, chest and abdominal findings, and laboratory tests revealed acute kidney injury, elevated liver enzymes, and metabolic abnormalities. The patient's cardiac assessments revealed profound biventricular insufficiency. A point-of-care ultrasound revealed global left ventricle hypokinesia, providing crucial insights into cardiac function. The initial course of action involved intubation and administering activated charcoal to restrict colchicine absorption. The patient's hemodynamics were stabilized through empiric sepsis treatment, vasopressors, and crystalloid fluids. Despite vigorous interventions, the patient's condition worsened, resulting in unresponsive shock, failure of multiple organ systems, and slow heart rate arrest. Cardiopulmonary resuscitation attempts were unsuccessful, leading to the decision to stop resuscitative measures.

This case highlights the difficulties related to colchicine toxicity and emphasizes the importance of prompt identification and collaborative approaches involving multiple disciplines. The report contributes to the current literature by providing a deeper understanding of colchicine toxicity and its clinical challenges.

Key words: Colchicine, Colchicine overdose, Colchicine toxicity, Colchicine-induced cardiac toxicity, Case report.

INTRODUCTION

Colchicine, an alkaloid obtained from the autumn crocus (*Colchicum autumnale*), is renowned for its therapeutic application in treating gout and various inflammatory disorders [1,2]. Colchicine is a drug that disrupts cell microtubule assembly, affecting inflammation and making it a crucial component in treating gout and other inflammatory conditions [3]. Nevertheless, the narrow therapeutic index and potential for toxicity of Colchicine make an overdose of this medication a rare yet significant medical emergency [4].

Colchicine toxicity presents a significant clinical challenge, with toxicity often occurring due to deliberate ingestion or unintentional excessive use. It can have a wide range of

effects on various organ systems, including gastrointestinal symptoms such as nausea, vomiting, and abdominal pain [4,5]. Systemic toxicity can lead to cardiovascular impairment, myocardial depression, dysrhythmias, and cardiogenic shock. Myelosuppression can also increase vulnerability to infection due to the impact on the bone marrow. Neurological symptoms can complicate the clinical presentation [6].

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Factors contributing to colchicine toxicity include renal impairment, hepatic dysfunction, elderly individuals, drug interactions, genetic variations, gastrointestinal disorders, incorrect dosage, and concurrent conditions like cardiomyopathies [7–9]. Colchicine toxicity for suicide attempts is rare but has been previously reported. Two cases of colchicine toxicity reported had different outcomes. In the first case, the administration of a dose of 1 mg/kg directly resulted in mortality, whereas in the second case, the administration of a dose of 0.2 mg/kg was correlated with survival [10]. The margin between effective and harmful doses is minimal, and in certain instances, they may coincide. Exceeding a dosage of 0.5 mg/kg in an acute overdose is typically lethal, and even doses as low as 0.18 mg/kg have caused fatalities [5].

Diagnosis of colchicine toxicity is challenging due to the wide range of clinical manifestations and the lack of a specific antidote. Laboratory results may include increased white blood cells, elevated liver enzyme levels, and metabolic acidosis, but these markers lack specificity and may not correlate with the severity of colchicine toxicity [2,9].

To effectively manage colchicine toxicity, a comprehensive and multifaceted strategy is required. Early identification and decontamination, such as providing activated charcoal, are essential to restrict additional absorption [11]. Supportive care is essential, focusing on the involvement of specific organ systems. Treatment aims to alleviate symptoms and avert potential complications. In severe cases, extracorporeal elimination techniques, such as hemodialysis and hemoperfusion, may be considered to augment colchicine removal from the body [9].

In this case report, we present a case of a 56-year-old female with a history of comorbidities, including hypertension, diabetes, depression, and gout, who was admitted to the emergency department after attempting suicide by consuming an overdose of Colchicine. This case emphasizes the difficulties in handling patients of this nature, emphasizing the significance of promptly identifying the issue, intervening promptly, and utilizing a multidisciplinary approach to maximize results.

CASE DESCRIPTION

A 56-year-old female patient with a medical history of hypertension, diabetes, depression, and gout presented to the emergency department. The patient exhibited

symptoms of nausea, vomiting, abdominal pain, and agitation after attempting suicide by consuming 60 tablets of 0.6 mg of Colchicine. The precise moment of consumption was uncertain.

Physical examination findings showed that the patient had tachycardia, with a heart rate of 135 beats per minute, and hypotension, with a blood pressure reading of 77/40 mm Hg. The oxygen saturation level was between 95-97% when using a 4-litter-face mask. There was an absence of elevated body temperature.

The patient exhibited restlessness and had a Glasgow Coma Scale score of E2V2M5. The pupillary examination showed symmetrical size and responsiveness to light. There was an absence of neck rigidity or any focal neurological signs. The chest examination revealed bilateral air entry with basal crepitation, while the abdomen was found to be soft and lax. Primary laboratory examinations showed that the glucose level in the blood was 87 milligrams per deciliter, the concentration of sodium in the serum was 140 milliequivalents per liter, and the serum potassium level was 4.7 milliequivalents per liter.

The serum creatinine level was 250 micromoles per liter, which suggests the presence of acute kidney injury, and the lactate concentration was 7 millimoles per liter.

The liver enzymes alanine aminotransferase and aspartate aminotransferase were significantly elevated, with levels of 1500 IU/L and 3500 IU/L, respectively. Serum troponin was within the expected range. Blood and urine samples were sent for laboratory analysis, and no toxic substances were detected in the toxicology screen. A colchicine level test was requested, but management continued while waiting for blood colchicine levels.

Medical imaging was performed, and an electrocardiogram showed a normal sinus rhythm with no signs of ischemic changes. Chest X-ray showed a normal CT scan of the brain, with no signs of ischemic or hemorrhagic incidents.

The heart's point-of-care ultrasound showed significant global left ventricle hypokinesia, ranging from moderate to severe. There was no presence of pericardial effusion, and no signs of right ventricular strain were observed. The cardiology consultation resulted in transthoracic echocardiography, which revealed significant biventricular failure (with a left ventricular ejection fraction [LVEF] of 15-20%), with no evidence of valvular disease or pericardial effusion.

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The management approach involved multiple steps. First, considering the risk of airway obstruction, the patient was intubated, and a nasogastric tube was inserted due to two instances of vomiting along with a low Glasgow Coma Scale. Additionally, 50 grams of activated charcoal were administered. Second, to address shock, the medical team started empirical treatment for sepsis using Piperacillin/Tazobactam and vancomycin. The patient was administered hydrocortisone, along with 1 liter of crystalloid fluid. Infusions of norepinephrine and vasopressin were initiated in order to sustain a mean arterial pressure (MAP) of 65 mm Hg or higher.

During a period of more than 12 hours in the intensive care unit (ICU), the patient's need for pressor medications escalated, which was accompanied by a deterioration in kidney function and liver function. The central venous/mixed oxygen saturation was measured at 44%. Initiation of dobutamine at a dosage of 2.5 mcg/kg/minute and continuous renal replacement therapy (CRRT) was implemented to address hyperk

alemia and metabolic acidosis. The indication for pulmonary artery catheter insertion was the presence of cardiogenic shock characterized by elevated filling pressures, reduced cardiac output, and increased systemic vascular resistance. The infusion of dobutamine was gradually increased to a dosage of 5 mcg/kg/minute. Twenty-four hours after admission, the patient continued to experience refractory shock accompanied by severe multisystem organ failure, which involved acute kidney injury, acute liver failure, and severe coagulopathy. The patient suffered from bradycardic arrest, which necessitated the administration of cardiopulmonary resuscitation (CPR). Following approximately 45 minutes of CPR without any signs of Return of Spontaneous Circulation (ROSC), it was determined to cease CPR and officially declare the time of death.

The blood colchicine concentration was measured six days after admission, revealing a concentration of 14 ng/mL at 6 hours after admission.

DISCUSSION

Although the therapeutic use of Colchicine is well-established, it is important to exercise caution when administering it due to its narrow therapeutic index and potential for toxicity. The case of colchicine toxicity presented in this case report provides a thorough

understanding of the difficulties involved in treating this uncommon yet potentially lethal condition.

The patient's initial symptoms correspond to the documented findings on colchicine toxicity, wherein gastrointestinal discomfort, such as nausea and vomiting, is a characteristic indication [8,11]. The presence of restlessness, increased heart rate, and low blood pressure are indicative of cardiovascular involvement, a well-known complication of an excessive amount of Colchicine in the body [12]. Colchicine toxicity may present without fever and a relaxed, flaccid abdomen, which helps differentiate it from infectious and other comorbid causes. Fever and an increased white blood cell count may not be dependable indicators of sepsis when confronted with colchicine toxicity, as a continuously high fever is frequently observed in cases of colchicine toxicity, even in the absence of bacterial infection [13]. Additionally, after taking Colchicine, there is an initial increase in the number of white blood cells in the peripheral blood (peripheral leukocytosis). This is followed by leucopenia during the second stage of intoxication, which, during the resolution phase, is followed by a rebound leukocytosis [14]. The neurological manifestation, as evidenced by a diminished Glasgow Coma Scale score, corresponds to profound colchicine toxicity, underscoring its influence on the central nervous system. The presence of bilateral air entry with basal crepitation on chest examination indicates pulmonary involvement, which is a well-known outcome of colchicine poisoning [2,15]. Alveolar pulmonary edema is the most common histopathological finding observed in autopsies of individuals who have been intoxicated with colchicine [16].

The laboratory findings in our case, which show increased levels of liver enzymes, acute kidney damage, and metabolic abnormalities, align with previous studies that indicate the systemic impact of colchicine toxicity on various organ systems [5,17,18]. The systemic involvement of colchicine toxicity was confirmed by the medical imaging results of our patients. The ultrasound results showed a global left ventricle hypokinesia, which is consistent with the documented effects of septic shock. Global left ventricular hypokinesia is a common occurrence in adult patients with septic shock, and its correction typically involves the administration of an inotropic agent to enhance hemodynamic support [19]. The subsequent transthoracic echocardiography showed severe biventricular failure,

which is a recognized outcome of colchicine toxicity [20]. It is worth noting that the reported range of LVEF of 15-20% indicates severe ventricular failure, aligning with previous research [20]. The absence of toxic substances in the toxicology screen highlights the significance of conducting specific toxicological tests, especially considering the absence of a colchicine antidote.

The management strategy employed in this instance closely adheres to established protocols for addressing colchicine toxicity, with a particular focus on safeguarding the airway, employing activated charcoal for gastrointestinal decontamination, and providing supportive care [10,11,21]. The main goal of early identification and decontamination, such as providing activated charcoal, is to limit further absorption. However, the patient's clinical status did not favor the use of activated charcoal. It is crucial to provide supportive care that specifically targets the involvement of particular organ systems, and given the lack of a specific antidote, the primary objective of the treatment is to alleviate symptoms and prevent potential complications.

The utilization of vasopressors, inotropic agents such as dobutamine, and renal replacement therapy is consistent with the literature regarding the management of severe cases of colchicine toxicity with cardiovascular and renal failure [2,11]. The choice to increase the dosage of dobutamine and initiate continuous renal replacement therapy (CRRT) aligns with the aim of managing persistent shock and renal dysfunction as our patient persistently had cardiovascular and renal failure. We inserted a pulmonary artery catheter for hemodynamic monitoring, identifying cardiogenic shock, and directing therapeutic interventions. The effectiveness of extracorporeal elimination techniques, such as hemodialysis and hemoperfusion, is restricted due to the wide distribution volume of Colchicine [9]. Plasma exchange therapy has been previously used in cases of colchicine overdose that has led to fatal outcomes [9,18].

The regrettable development of refractory shock and multisystem organ failure is a well-acknowledged difficulty in severe cases of colchicine toxicity, frequently resulting in a poor prognosis [2,15], especially among patients with rapidly developing hemodynamic failure [17], similar to our patient, who eventually died.

There might be distinctive factors that influenced this outcome. The lack of clarity regarding the timing of

colchicine ingestion is a significant factor in this case, adding to the intricacy of its management. The evidence established the significance of early intervention [17,22], and the uncertainty in our case may have been an obstacle to successful management. Apart from the dose ingested, another important parameter, which defines the chance of survival, is the arrival time to the hospital after ingestion [10]. A report of two cases of colchicine toxicity showed that the time of arrival to the hospital was twice as long for the patient who died compared to the patient who survived (1 hour vs 2 hours). Delaying treatment beyond 2 hours after consuming Colchicine can greatly hinder its effectiveness, as Colchicine is typically absorbed within 30-120 minutes after being ingested [10,22].

The blood colchicine concentration report became available six days after admission, which is another limitation. Prompt reporting of hazardous levels can inform ongoing administration, but the delay in this instance may have influenced the immediate decision-making procedure.

Another factor of poor prognosis for our patient may be her advanced age and associated comorbidities. Colchicine toxicity is influenced by various factors, including renal impairment and hepatic dysfunction. Our patient was hypertensive and diabetic, with comorbidities known to also affect other organs, such as the liver and kidneys [23-25]. Elderly age, drug interactions, genetic variations, gastrointestinal disorders, polypharmacy, incorrect dosage and administration, and concurrent conditions like cardiomyopathies [7-9]. Patients with renal impairment are at a higher risk due to reduced drug elimination, necessitating dosage adjustments [8]. Hepatic dysfunction affects colchicine metabolism, requiring close monitoring. Elderly individuals are more susceptible due to advanced age, necessitating careful administration, and genetic variations also impact the response to Colchicine, necessitating personalized strategies [7-9]. Our patient had depression, which could have led to a suicide attempt, and the use of Colchicine as a suicide drug was influenced by the possession of this medication for her gout disease. Similar reports of colchicine use in suicide were reported in the literature [10]; however, rarely among elderly patients.

CONCLUSION

The toxicity of Colchicine presents a significant clinical difficulty, necessitating a detailed comprehension of

its mechanisms and varied clinical presentations. We presented the clinical course of an elderly patient with comorbidities who ingested 60 tablets of 0.6 mg colchicine in a suicide attempt. The difficulties faced in handling this presented case emphasize the necessity for heightened recognition of colchicine toxicity and its life-threatening outcomes. The infrequency of such cases underscores the significance of ongoing research and education in order to augment healthcare providers' capacity to identify early and handle colchicine toxicity. This case report provides valuable insights and elucidates the complexities of colchicine overdose and the clinical difficulties it poses, the significance of promptly identifying it, and adopting a collaborative approach involving multiple disciplines.

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