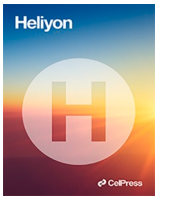
Heliyon 10 (2024) e32407

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Case report

Colchicine poisoning: Case report of three homicides in a family

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ARTICLE INFO

Keywords:
Colchicine poisoning
Septic shock
Procalcitonin
Homicides
Case report

ABSTRACT

Background: Colchicine is a common therapeutic agent for inflammatory conditions such as gout, yet its narrow therapeutic range frequently results in cases of overdose and subsequent poisoning. Acute colchicine poisoning can be difficult to identify due to its nonspecific clinical manifestations, posing a diagnostic challenge for emergency physicians without a clear history of colchicine ingestion.

Case presentation: This report describes a tragic case of acute colchicine poisoning that resulted in three familial homicides. The patients presented with fever, abdominal pain, and diarrhea, which rapidly escalated to shock during their emergency department visits. Laboratory tests revealed a marked leukocytosis, mild elevation in procalcitonin (PCT), significantly elevated creatine kinase (CK) and CK-MB levels, and liver function abnormalities. Despite treatment with carbapenem antibiotics and aggressive fluid resuscitation, the patients' condition deteriorated, marked by a progressive decline in leukocytes and neutrophils. Initially misdiagnosed as septic shock, the ineffectiveness of the standard treatment protocols led to a fatal outcome for all three individuals.

Conclusion: Emergency physicians should consider acute colchicine poisoning as a differential diagnosis in patients presenting with shock and the following clinical indicators: (1) pronounced increase in peripheral leukocytes with a disproportionate rise in neutrophils; (2) discordance between the level of serum procalcitonin and the severity of presumed septic shock; (3) early increase in serum creatine kinase (CK) and CK-MB; (4) poor response to antibiotics and resuscitative efforts, accompanied by a continuous decrease in white blood cells and neutrophils. This case underscores the critical need for awareness of colchicine toxicity in the emergency setting, particularly when the clinical presentation mimics septic shock but fails to respond to standard treatments.

1. Introduction

Colchicine, an alkaloid extracted from the autumn crocus, was first isolated and named in 1820. It has a wide range of clinical applications and is commonly used to treat conditions such as gouty arthritis, familial Mediterranean fever, and pericarditis [1]. Recent studies have shown that taking 0.5 mg of colchicine daily significantly reduces the risk of cardiovascular events in patients with chronic coronary disease, suggesting an increase in future usage of the drug [2].

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https://doi.org/10.1016/j.heliyon.2024.e32407
Received 10 January 2024; Received in revised form 3 June 2024; Accepted 3 June 2024
Available online 4 June 2024

Due to its narrow therapeutic window, colchicine poses a heightened risk of toxicity, particularly in the elderly and those with impaired renal function. There has been an increase in reported cases of acute colchicine poisoning, which are often associated with high mortality and disability rates [3,4]. Clinically, colchicine poisoning progresses through three stages: the initial phase involves gastrointestinal symptoms, including potential bleeding. The second phase is marked by metabolic acidosis, liver and kidney damage, multi-organ dysfunction, and a high mortality risk. The final stage primarily affects the bone marrow, leading to significant reductions in blood cell counts [5].

Diagnosing colchicine poisoning is relatively straightforward when there is a clear history of overdose. However, the diagnosis becomes challenging in the absence of such a history or when information is intentionally withheld. While accidental poisoning due to prolonged therapeutic use of colchicine is well-documented, deliberate poisoning with this substance is exceedingly rare [6]. In this report, we document a series of cases that involved the sequential fatalities of three family members due to colchicine-induced poisoning.

2. Case report

Case 1. A 68-year-old female presented with a one-day history of vomiting and diarrhea, which worsened to include 3 h of confusion. She had no significant chronic health issues. Initial blood tests showed increased white blood cells and neutrophils, elevated procalcitonin (PCT), high arterial blood lactate, and elevated creatinine levels (Table 1). Head CT scans showed no abnormalities, while abdominal CT scans indicated pancreatic edema but no other issues. Initially suspected of sepsis, she was treated with carbapenem antibiotics for infection control and received fluid resuscitation. Despite these interventions, her condition progressed to shock. Endotracheal intubation and mechanical ventilation were initiated, along with norepinephrine at 0.5 μg/kg/min to maintain blood pressure (103/43 mmHg). Continuous renal replacement therapy (CRRT) was started to stabilize her internal environment. Despite these measures, there was no significant improvement, and norepinephrine dosage was gradually increased to 4 μg/kg/min. After 48 hours of hospitalization, the patient's family opted to discontinue treatment, and she subsequently died. Blood cultures remained negative after a seven-day incubation period.

Case 2. A 69-year-old male presented with a one-day history of vomiting and diarrhea. He had a past medical history of cerebral infarction but had no residual symptoms and denied any other health issues. His condition rapidly worsened, resulting in altered consciousness. On examination, his heart rate was 142 bpm, blood pressure was 70/40 mmHg, respiratory rate was 40 bpm, and his oxygen saturation (SpO_2) was 92 %. His abdomen was soft with active bowel sounds and exhibited no tenderness. Abdominal CT scans were unremarkable, and laboratory results are detailed in Table 2. Given his presentation, septic shock was suspected in the emergency department. The patient was treated with carbapenems and aggressive fluid resuscitation. However, the patient's family opted against further organ support measures, and he passed away 20 hours after admission.

Case 3. A 40-year-old male presented with two days of diarrhea and fever, accompanied by elevated creatinine levels, prompting him to seek emergency medical care. He had no significant medical history. Clinical examination revealed a temperature of 39.3 °C, heart rate of 116 bpm, blood pressure of 112/46 mmHg (supported by norepinephrine at 0.5 μg/kg/min and dopamine at 5 μg/kg/min), SpO_2 of 92 %, and a respiratory rate of 40 breaths per minute. His abdomen was soft with active bowel sounds and no tenderness. Laboratory tests (detailed in Table 3) and clinical indicators were suggestive of septic shock. In the emergency department, the patient

Table 1
Laboratory test results of Case 1.

	Normal range	Admission	24h	48h
WBC ($\times 10^9$/L)	3.5–9.5	24.50	16.80	4.59
N%	40~75	69.2	69.5	58.6
Plts ($\times 10^9$/L)	125~350	126	65	28
Hb (g/L)	115~150	169	121	90
PCT (ng/ml)	0.04–0.5	11.25	12.83	
CRP (mg/L)	0~10		>300	>300
CK (U/L)	20~200	401		
CK-MB (U/L)	0~30	20		
TNI (ng/ml)	0~0.4	0.09	0.16	10.1
Cr (umol/L)	44~115	347	304	204
Lac (mmol/L)	0.6–1.4	11.1	10.8	16.7
AST (U/L)	8~40	448	403	520
ALT(U/L)	5~40	103	112	107
LDH (U/L)	94~250	5018	3706	4163
AMY (U/L)	30~110	418	342	
LIPA (U/L)	23~300	1022	595	
TBIL (mmol/L)	3.4–20.0	14.9	12.8	17.2
PH	7.35–7.45	7.208	7.328	7.334
PO_2 (mmHg)	83~208	102.1	60	153.7
PCO_2 (mmHg)	32~48	22.3	23.3	20.4
HCO_3 (mmol/L)	22~27	11.5	11.9	10.6
BE (mmol/L)	−3~3	−17	−12.4	−14

Table 2
Laboratory test results of Case 2.

	Normal range	Admission
WBC ($\times 10^9$/L)	3.5–9.5	26.73
N%	40~75	88.7
Plts ($\times 10^9$/L)	125~350	157
Hb (g/L)	115~150	177
PCT (ng/ml)	0.04–0.5	8.46
CRP (mg/L)	0~10	>300
CK (U/L)	20~200	427
CK-MB (U/L)	0~30	40
TNI (ng/ml)	0~0.4	0.072
Cr (umol/L)	44~115	204
Lac (mmol/L)	0.6–1.4	5.7
AST (U/L)	8~40	370
ALT(U/L)	5~40	144
LDH (U/L)	94~250	3389
AMY (U/L)	30~110	419
LIPA (U/L)	23~300	1503
TBIL (mmol/L)	3.4–20.0	11.9
PH	7.35–7.45	7.282
PO_2 (mmHg)	83~208	66.5
PCO_2 (mmHg)	32~48	34.1
HCO_3 (mmol/L)	22~27	16.8
BE (mmol/L)	−3~3	−11

was treated with carbapenems for infection control, fluid resuscitation, and CRRT to support his renal function. Despite these interventions, there was no significant improvement in his clinical status. Blood pressure was maintained with norepinephrine and dopamine, and additional treatments including plasma and blood component transfusions were administered to support organ function. On the sixth day of hospitalization, the patient's organ functions continued to decline. Following the family's decision to discontinue further treatment, the patient succumbed to his condition.

Throughout the diagnostic and therapeutic journey of this patient, we made a significant discovery: he was a familial relative of the individuals previously discussed in Case 1 and Case 2, both of whom exhibited notably similar presenting symptoms. Owing to the persistent bone marrow suppression and multi-organ dysfunction observed, we undertook additional investigations, including serum and urine assessments for colchicine concentrations. These tests revealed elevated colchicine levels of 8.45 ng/ml in serum and 325 ng/ml in urine (on the fifth day of admission), definitively confirming colchicine toxicity. The samples were analyzed using LC-MS/MS. The patient received component transfusions and underwent CRRT for blood perfusion treatment, yet his organ function continued to decline, leading to his death. After these findings, a police investigation was initiated and uncovered a distressing truth: all three deceased patients had been intentionally poisoned with large doses of colchicine added to their food by another family member at different times, resulting in fatal colchicine toxicity. Figs. 1 and 2 depict the trajectory of key indicator changes and the course of

Table 3
Laboratory test results of Case 3.

	Normal range	Admission	8h	14h	42h	3d	4d	5d
WBC ($\times 10^9$/L)	3.5–9.5	41.18	26.85	20.33	11.02	4.16	2.59	0.78
N%	40~75	80.3	80.5	81.1	76.3	72.2	65.6	41.0
Plts ($\times 10^9$/L)	125~350	263	138	86	38	23	72	5
Hb (g/L)	115~150	197	177	170	138	121	116	116
PCT (ng/ml)	0.04–0.5	10.15						
CRP (mg/L)	0~10	93.89						
CK (U/L)	20~200	713	682	826	5420	33731	50082	42690
CK-MB (U/L)	0~30	94	17	23	152	1149	864	1852
Cr (umol/L)	44~115	228	320	365	270	204	210	187
Lac (mmol/L)	0.6–1.4	5.7	5.3	5.7	16.4	12.3	15.2	>20
AST (U/L)	8~40	463	582	641	6119	26125	15873	12313
ALT(U/L)	5~40	90	133	147	2705	6869	5148	4039
LDH (U/L)	94~250	4589	4584	5788	9934	26761	22562	18134
AMY (U/L)	30~110		299	365	274	338	292	
LIPA (U/L)	23~300		481	455	325	731	640	109
TBIL (mmol/L)	3.4–20.0	11.6	13		37.3	77.4	122.2	103.9
PH	7.35–7.45	7.343	7.35	7.37	7.44	7.46	7.42	7.39
PO_2 (mmHg)	83~208	74.7	109.8	101.9	96.6	109.4	171.6	80.9
PCO_2 (mmHg)	32~48	24.4	30.6	37.7	37.4	40.1	34.2	40.8
HCO_3 (mmol/L)	22~27	16.4	16.5	21.3	24.6	27.9	21.6	24.1
BE (mmol/L)	−3~3	−10	−7.48	−3.45	0.68	3.79	−2.28	−0.85

treatment across the three cases, respectively.

3. Discussion

Colchicine is a pharmaceutical agent commonly used in the management of gout, with a recommended maximum daily dosage of 0.1 mg/kg. Toxicity is typically seen at doses ranging from 0.5 to 0.8 mg/kg, with doses exceeding 0.8 mg/kg often being lethal [7]. Diagnosing colchicine poisoning is straightforward when there is a known history of use. However, when no such history exists, and patients present with symptoms such as abdominal pain, diarrhea, fever, and shock, diagnosis can be challenging, as illustrated by our cases.

Colchicine toxicity inhibits mitosis by binding to microtubule subunits in cells, affecting rapidly dividing cells such as those in the gastrointestinal tract, bone marrow, and hair follicles [7,8]. The latency period of colchicine poisoning ranges from 1 to 3 hours [2], with the clinical course of acute poisoning divided into three stages: gastrointestinal dysfunction, multiple organ dysfunction, and potentially a recovery period [9]. Early symptoms typically include nausea, vomiting, abdominal pain, and diarrhea, frequently accompanied by fever. In cases of significant ingestion, refractory shock and multiple organ dysfunction can rapidly follow the onset of gastrointestinal symptoms. The cases discussed here shared several common features: acute onset, no history of underlying diseases or drug use, presentation with fever and gastrointestinal symptoms, significant elevation in peripheral blood white cell and neutrophil counts, and rapid progression to shock with multiple organ dysfunction. All three patients were treated at our medical center, and the time intervals between their visits were approximately three weeks. Due to the short duration of the second patient's visit (20 hours) and the rapid deterioration leading to death, comprehensive data could not be collected, making a comparative summary with the first patient impossible. It was only upon receiving the third patient that we recognized the similarities among the cases and noted that all three patients were from the same family.

Septic shock, a common type of shock in emergency departments, is mainly induced by Gram-negative bacterial infections and is often associated with infections in systems such as the liver-biliary and urinary systems. However, some patients may present with symptoms like diarrhea and fever without a clear site of infection, and blood cultures may indicate *Escherichia coli*, suggesting septic shock caused by translocation of intestinal flora due to disturbance of the intestinal flora. These patients exhibit refractory shock, elevated white blood cell and neutrophil counts, elevated PCT, and progressive shock. They share many similarities with patients experiencing acute colchicine poisoning, but four distinctive features can help differentiate colchicine poisoning: (1) a significant increase in peripheral blood white cells without a corresponding rise in neutrophil proportion; (2) a mismatch between the level of PCT elevation and the symptoms of septic shock; (3) early rise in creatine kinase and its isoenzymes; (4) difficulty in alleviating shock despite antibiotic use and resuscitation treatment, along with a progressive decrease in white blood cells and neutrophils, due to colchicine's inhibition of cell chemotaxis, adhesion, and phagocytosis, and its suppression of the bone marrow [10].

Furthermore, acute colchicine poisoning should be carefully differentiated from infectious diarrheal conditions such as bacterial dysentery. Infectious diarrhea can present similarly with symptoms such as fever, abdominal pain, diarrhea, elevated white blood cells, and neutrophils. In severe cases, it may lead to hypovolemic shock. However, most cases can be effectively managed with fluid resuscitation and rarely progress to intractable shock and multi-organ dysfunction.

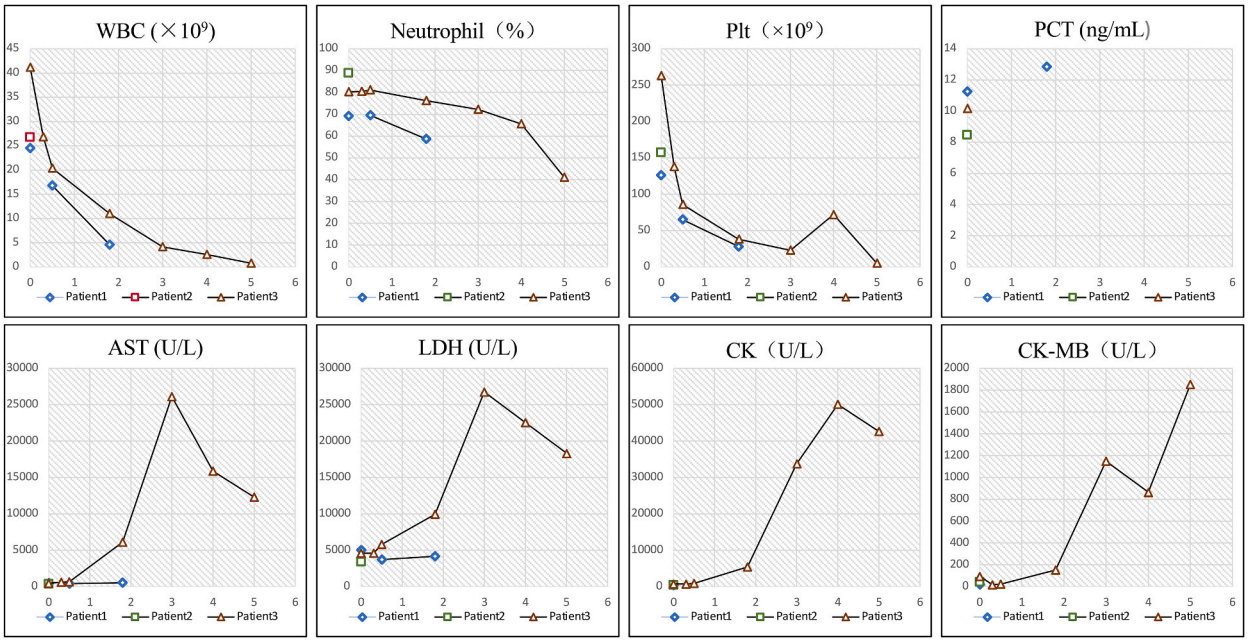

Fig. 1. The trajectory of key indicator changes observed in three cases.

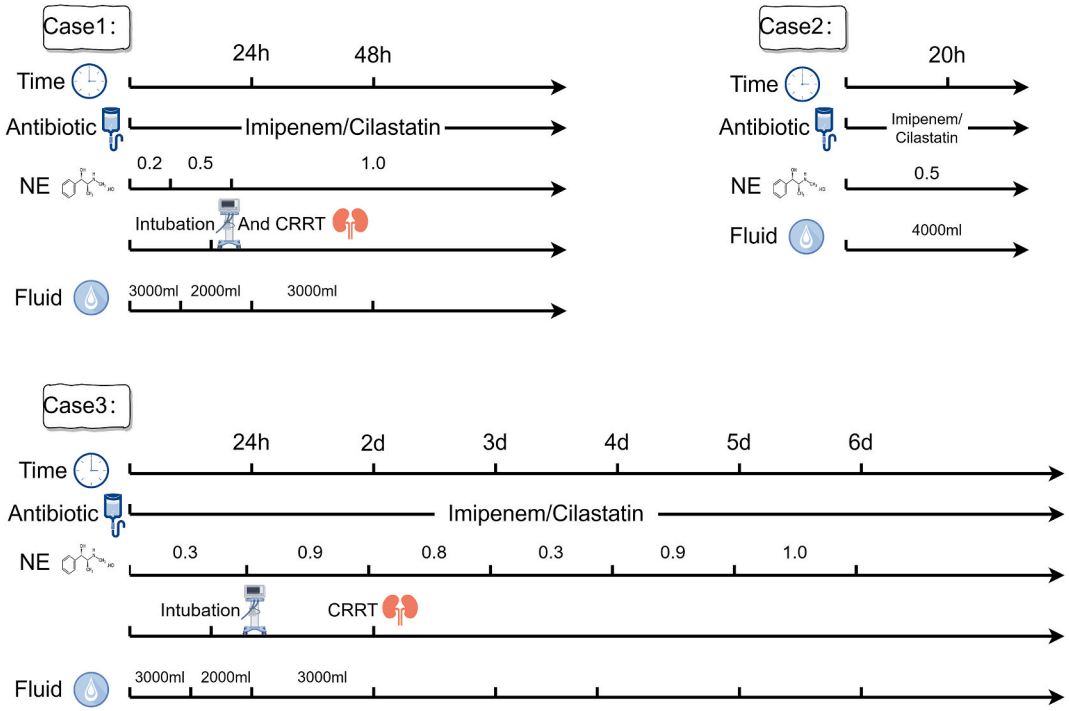

Fig. 2. The time courses of interventions of three cases.

Management strategies for colchicine poisoning include: (1) Prompt initiation of gastric lavage within the first hour, coupled with the administration of activated charcoal to reduce further drug absorption. (2) Early implementation of fluid resuscitation and robust organ support interventions. (3) Considering colchicine's substantial distribution volume and rapid peak blood concentrations within 0.5–3 hours, the effectiveness of blood purification methods is limited. (4) Vigilant monitoring for complications such as pneumonia and bone marrow suppression. The therapeutic approach to colchicine toxicity may also include the use of specific Fab fragments [11]. In cases of colchicine-induced cardiogenic shock leading to multi-organ failure, transfusion of packed red blood cells may be considered [12]. Clinical reports support the effectiveness of Extracorporeal Membrane Oxygenation (ECMO) for treating colchicine-induced cardiogenic shock [13]. Additionally, plasma exchange and blood purification interventions may improve patient outcomes [14,15].

Colchicine is widely used, but our case series suggests it can also serve as a potent tool for homicide. The consecutive occurrence of identical symptoms and deaths in three patients from the same family raised suspicions. Without multiple cases, it would be challenging to associate a single death with colchicine poisoning. Thus, in addition to emergency physicians being vigilant based on the clinical features of patients, there should also be careful prescription management of colchicine to prevent its misuse.

4. Conclusion

Severe acute colchicine poisoning can lead to refractory shock, multiple organ dysfunction, and even death. In cases where there is no known history of colchicine use, emergency physicians may find it challenging to connect the presentation of shock with colchicine poisoning. Our series of cases has shown that when patients present with suspected septic shock possibly induced by bacterial translocation from the gut, and exhibit the following characteristics, acute colchicine poisoning should be considered: (1) a significant increase in peripheral blood leukocytes with a relatively modest rise in neutrophil count; (2) a mismatch between the elevation of serum PCT and the severity of septic shock; (3) early elevation of serum CK and CK-MB levels; (4) a poor response to antibiotic treatment and resuscitation efforts, accompanied by progressive decreases in white blood cells and neutrophils. These features suggest that emergency physicians should consider acute colchicine poisoning as a potential diagnosis in such complex clinical scenarios.

Funding

This work was supported by the National Natural Science Foundation of China (No. 82172120), Natural Science Foundation of Tianjin, China (No. 22JCYBJC00530), and Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-007A).

Ethics approval and consent to participate

Not applicable.

Data availability statement

The data of the current study are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Yan-Cun Liu: Writing – original draft, Conceptualization. **Zi-Kang Zhou:** Visualization, Software. **Mu-Ming Yu:** Data curation. **Li-Jun Wang:** Data curation. **Song-Tao Shou:** Conceptualization. **Yan-Fen Chai:** Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank Professor Shu-Zhang Cui of Emergency Department of Tianjin Medical University General Hospital for the guidance of case presentation.

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