

The Perils Of Grandma's Medication: Colchicine Toxicity causing Pneumomediastinum.

E Shuttleworth, R Sawyer, M Holland & T Cooksley

Abstract

A 19 year old male presented with a deliberate overdose of colchicine (50mg). He had no other significant medical history. 36 hours following admission he developed widespread surgical emphysema. An urgent CT scan of his chest and abdomen demonstrated mediastinal gas of lung origin. He also developed bone marrow suppression and disseminated intravascular coagulopathy. He was treated supportively with intravenous fluids, high flow oxygen and intravenous antibiotics and made a full recovery.

Colchicine toxicity is a rare, but important presentation with high levels of morbidity and mortality. Pneumomediastinum is a potentially important complication. It may be appropriate to monitor patients in the later stages of the condition through an ambulatory setting.

Keywords

Colchicine, Toxicity, Overdose, Pneumomediastinum, Marrow suppression

Learning Points

- Colchicine toxicity has high levels of morbidity and mortality with gastrointestinal disturbance, bone marrow suppression and multi-organ failure key features.
- Pneumomediastinum is an important potential complication of colchicine toxicity.
- Supportive management is the mainstay of therapy in patients with colchicine toxicity. Organ dysfunction and initial bone marrow toxicity needs inpatient monitoring but ambulatory care after day 7 can prevent prolonged inpatient admission.
- Literature searches and Specialist advice is important when a patient presents with an overdose of an unusual drug.

Case Report

A 19 year old male presented with a deliberate overdose of colchicine. He ingested 50mg (0.75mg/kg) and attended the Emergency Department within 2 hours. The tablets had belonged to his grandmother. He had no significant previous medical history and was not on any regular medications.

Initial assessment found him to be alert and oriented. He was afebrile, blood pressure was 120/70mmHg with a pulse 70/min. Respiratory and abdominal examination were unremarkable. He was transferred to the Acute Medical Unit for further monitoring.

During the next 24 hours he had significant gastrointestinal disturbance with refractory vomiting despite anti-emetic treatment. He was treated with intravenous fluid resuscitation.

36 hours after admission he was noted to have marked surgical emphysema to his face, arms, chest and upper abdomen. An urgent CT scan of his chest and abdomen demonstrated mediastinal gas of lung origin (see figure 1).

He remained haemodynamically stable throughout the admission. He was treated supportively with intravenous fluids, high flow oxygen and intravenous antibiotics.

48 hours after admission he developed bone marrow suppression and disseminated intravascular coagulopathy (DIC) (see table 1). He was managed supportively with regular monitoring of blood parameters.

1 week later, his clinical condition remained relatively stable and he was keen to go home. Following psychiatric assessment he was discharged with regular reviews in the ambulatory care unit and acute medicine clinic.

10 days after his original presentation he developed alopecia. He developed rebound bone marrow activity which resolved spontaneously. He had no long term sequelae following the overdose and after 8 weeks was discharged from clinic.

Discussion

Colchicine is an active alkaloid used in the treatment of gout and familial Mediterranean fever.¹ It has a narrow therapeutic index and toxicity is associated with significant morbidity and mortality. High fatality rates occur with acute ingestions greater than 0.5mg/kg.²

Colchicine toxicity occurs as a result of the interruption of mitosis by preventing polymerization

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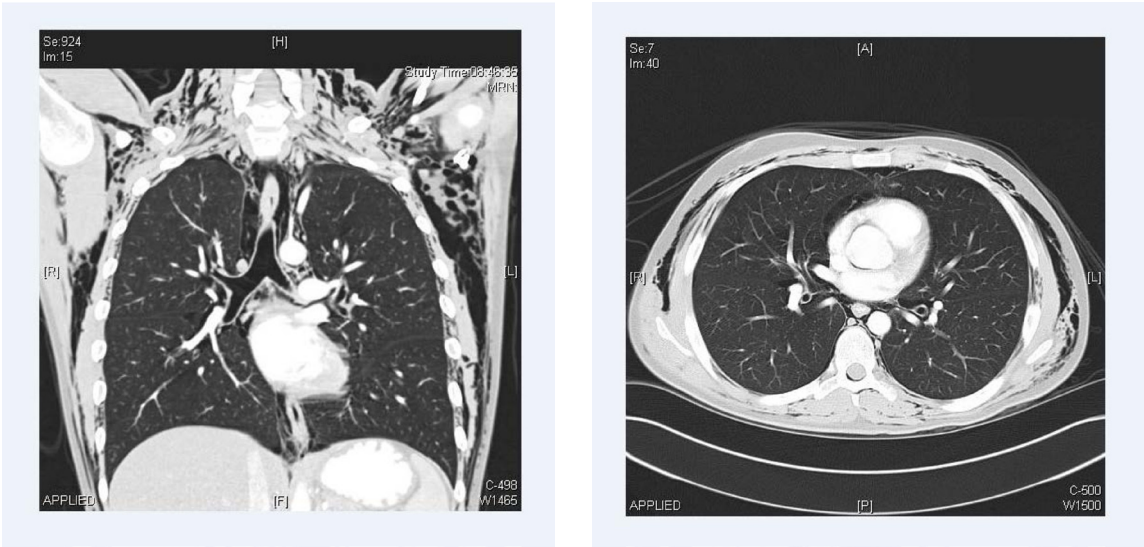


Figure 1. CT scan images showing pneumomediastinum from pulmonary origin as a result of colchicine toxicity. This is demonstrated by the presence of interstitial oedema which is tracking towards the mediastinum through the root of the lungs.

of tubulin into microtubules. Hence, although colchicine is absorbed by all cells of the body, its toxic effect is more marked in those with increased mitotic activity, such as the gastrointestinal tract and bone marrow.²

Colchicine poisoning classically has 3 distinct stages:²⁻⁴

Stage 1 – First 24 hours – This is characterized by gastrointestinal disturbance with vomiting and abdominal pain.

Stage 2 – Days 2-7 – This is characterized by multi-organ dysfunction, with classically bone marrow suppression, renal and liver failure and potentially the development of acute respiratory

distress syndrome (ARDS). Disseminated intravascular coagulation is common.³

Stage 3 – After day 7 – This is characterized by a renewal of bone marrow activity with rebound leucocytosis, improvement in organ dysfunction and the development of alopecia.

Delays in presentation and significant comorbidities, in particular renal and hepatic impairment, are associated with poorer outcomes.²

Pneumomediastinum has previously been reported in colchicine toxicity.⁵ It is probably related to raised intra-alveolar pressure as a result of the gastrointestinal disturbance. However, it has been postulated there may be direct damage to alveolar

Table 1. Patient’s laboratory results over a 3 month period of monitoring.

	Presentation	12hrs	24hrs	48hrs	72hrs	5 days	1week	2weeks	3weeks	4weeks	3months
WCC (x109/L)	15.3	17.9	20.3	17.2	1.7	1.1	3.3	28.5	19.1	8.4	8.3
Neutrophils (x109/L)	12.72	15.51	17.59	15.64	1.35	0.53	1.79	19.47	14.12	5.66	4.39
Haemoglobin (g/L)	181	196	179	156	137	132	161	126	12.6	129	149
Platelets (x109/L)	325	276	205	87	43	4	12	335	485	256	267
Creatinine (umol/L)	100	100	86	63	59	45	42	66	50	55	68
Albumin (g/L)	57	48	44	33	27	25	35	35	35	37	43
Prothrombin Time (secs)	11.4	12.0	12.0	17.9	16.9	12.1	13.4	12.4	9.3	10.0	10.7
Fibrinogen (g/L)				3.07			2.12				
D Dimer (ng FEU/ml)				87674	98565	5418	1086				
LDH (IU/L)	619		1447	5749							

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cells.⁵ It is a potentially important consequence of colchicine toxicity and patients should be examined regularly for signs of surgical emphysema.

The mainstay of treatment in colchicine toxicity is supportive management. The use of activated charcoal should be considered in patients with early presentation and large ingestions may benefit from gastric lavage. Granulocyte colony stimulating factor (G-CSF) may have a role in treating the bone marrow toxicity.^{2-4,6} However, its use may reflect the results in the neutropenic sepsis population in that it reduces the duration of leucopenia with no effect on mortality.⁷⁻⁸ This needs further study. A specific treatment (Fab fragment antibodies) for colchicine has been trialled but its use remains experimental and is not currently widely available.⁹

Patients presenting with massive colchicine overdose have prolonged inpatient hospital admissions of approximately 25 days.^{3,5} Our patient was discharged after 7 days and monitored weekly for the first month through the ambulatory care unit. He received a final review in the acute medicine clinic 3 months post overdose. At his weekly ambulatory care unit attendances he received Consultant review ensuring satisfactory clinical progress, confirming that his surgical emphysema continued to regress and monitoring for complications of his period of leucopenia and subsequent rebound marrow activity. His full blood count, clotting profile and U&Es were checked on each attendance.

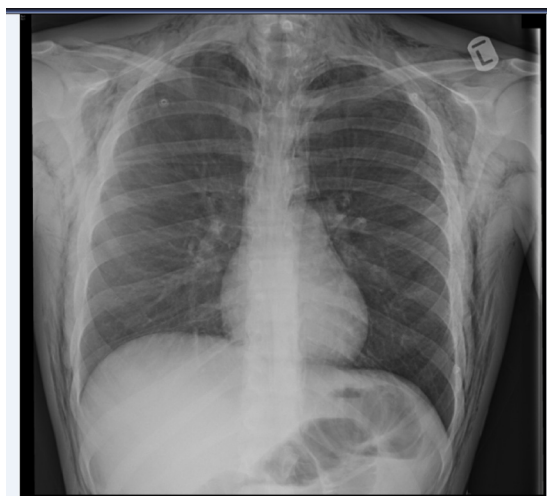


Figure 2. Chest X-ray showing extensive surgical emphysema with pneumopericardium.

Conclusion

Colchicine toxicity is a rare but important presentation with high levels of morbidity and mortality. It may be appropriate to monitor patients in the later stages of the condition, particularly bone marrow activity, through an ambulatory setting to reduce prolonged inpatient admission stays which are associated with this presentation.

Conflict of Interest

The authors have no conflict of interest in relation to this publication.

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