Case Report

Gastrointestinal histopathology of acute colchicine toxicity after lower dose treatment of pericarditis: A case report

Lisa Liu, Steven Tessier, Rodrigo Duarte-Chavez¹, Daniel Marino², Anish Kaza³, Santo Longo³, Sudip Nanda⁴

ABSTRACT

Colchicine is an anti-inflammatory alkaloid drug with anti-microtubule activity. Colchicine toxicity is a serious and potentially fatal complication associated with hallmark histopathological features most conspicuous in proliferative tissues such as the gastrointestinal tract. These features have only been reported in patients treated with high doses. We report a patient who experienced acute colchicine toxicity with gastrointestinal histologic changes after treatment with the lowest dose of colchicine. Knowledge of drug–drug interactions and the organs involved in colchicine metabolism is imperative when using colchicine, even when administered at its lowest dose.

Key Words: Colchicine toxicity, histopathology, pericarditis

INTRODUCTION

Colchicine is an anti-inflammatory alkaloid drug extracted from the plant Colchicum Autumnale. Its primary mechanism of action involves inhibition of microtubule polymerization and neutrophil adhesion to the endothelium.¹ The clinical indications of colchicine therapy include recurrent pericarditis, gout, and familial Mediterranean fever.² The recommended colchicine regimen for the treatment of recurrent pericarditis is 0.6 mg once daily (QD) or 0.6 mg twice daily (BID) for patients that weigh ≤70 kg or >70 kg, respectively.³ Colchicine is metabolized by the liver and cleared by the kidneys, making dosing particularly important in patients who have pathology in either or both these organs. The half-life of colchicine is increased two to three times in patients with renal failure and over 10 times in patients with combined cirrhosis and renal failure.² Symptoms of colchicine toxicity include diarrhea, vomiting, neuropathy, and hypotension.⁴ It is important to recognize the early signs of colchicine toxicity as toxic serum levels can cause an increased risk for diarrhea and gastrointestinal events.⁴ We report a patient treated with the lowest dose of colchicine who presented with acute gastrointestinal symptoms and characteristic histopathological features.

CASE

A 73-year-old female was admitted to the hospital for sharp, waxing, and waning chest pain. Myocardial infarction was less likely due to normal chest X-ray, electrocardiogram, arterial blood gas, and troponin levels. Two-dimensional echocardiogram revealed a pericardial effusion. The patient had a history of stage-3 chronic kidney disease, hypertension, and scleroderma. Labs included blood pressure 136/81, pulse 90/min, temperature 98°F, O₂ saturation 97%, white blood cell...
count 15.05 thousand/uL, and creatinine 1.28 mg/dL. Colchicine 0.6 mg BID was prescribed for suspected pericarditis. The next day, the patient developed diarrhea. Colchicine was thus switched to prednisone 40 mg to be tapered over 8 weeks and the diarrhea resolved.

At a 4-month follow-up, the patient presented with persistent chest pain and pericarditis. Since the pericarditis did not resolve with steroid therapy, the patient was restarted on colchicine at a low dose of 0.3 mg BID. Importantly, the patient was also on erythromycin and cyclosporin due to a recent cataract surgery. Two weeks later, the patient presented to the hospital with abdominal pain, vomiting, and diarrhea. Computed tomography scan showed inflammation around the pancreas and duodenum with duodenum thickening [Figure 1a]. Normal lipase levels made acute pancreatitis less likely. Esophagogastroduodenoscopy (EGD) revealed gastritis and diffuse inflammation and erythema of the second part of the duodenum consistent with duodenitis [Figure 1b]. The diagnosis of colchicine toxicity was supported by gastric biopsy, which ruled out *Helicobacter pylori*, and revealed ring mitosis, apoptotic bodies, and intestinal metaplasia of the gastric mucosa [Figure 1c and d]. The patient was advised to immediately discontinue colchicine. Three months later, a follow-up EGD was performed, and the gastric and duodenal mucosa were normal.

**DISCUSSION**

Colchicine binds to tubulin and inhibits its ability to polymerize into microtubules. Colchicine 0.6 mg BID was prescribed for suspected pericarditis. The next day, the patient developed diarrhea. Colchicine was thus switched to prednisone 40 mg to be tapered over 8 weeks and the diarrhea resolved.

Colchicine toxicity has been previously reported in patients treated with colchicine at doses of 0.6 mg and above, QD or BID. There are two factors that likely contributed to low-dose colchicine toxicity in our patient. The combination of stage-3 chronic kidney disease and concurrent use of erythromycin and cyclosporine. These drugs are known as cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitors. CYP3A4 metabolizes colchicine; P-gp pumps colchicine out of cells. Commonly used CYP3A4 inhibitors include clarithromycin, erythromycin, diltiazem, and grapefruit juice. Commonly used P-gp inhibitors include clarithromycin and cyclosporine. Inhibition of CYP3A4 or P-gp by any of the listed medications is expected to result in elevated serum colchicine levels and toxicity. An awareness of drug–drug interactions and the presence of renal and/or liver dysfunction is imperative when using colchicine. It is important to seek out options other than colchicine in these cases. Failure to adequately identify these factors can lead to serious, yet avoidable complications, even when colchicine is used at its lowest dose.

**Research quality and ethics statement**

This case report did not require approval by the Institutional Review Board/Ethics Committee. The authors followed applicable EQUATOR Network (http://www.equator-network.org/) guidelines, specifically the CARE guideline, during the conduct of this research project.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and

![Figure 1: (a) CT scan showing duodenitis (white arrow). (b) EGD showing diffuse inflammation of the duodenum (black arrowheads). Hematoxylin and eosin staining of gastric biopsy showing (c) ring mitoses (black arrowheads), and (d) apoptotic bodies (red arrowheads). CT: Computed tomography. EGD: Esophagogastroduodenoscopy](image-url)
due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Bhat A, Naguwa SM, Cheema GS, Gershwin ME. Colchicine revisited. Ann N Y Acad Sci 2009;1173:766-73.
2. Finkelstein Y, Aks SE, Hutson JR, Juurlink DN, Nguyen P, Dubnov-Raz G, et al. Colchicine poisoning: The dark side of an ancient drug. Clin Toxicol (Phila) 2010;48:407-14.
3. Imazio M, Belli R, Brucato A, Cemin R, Ferrua S, Beqaraj F, et al. Efficacy and safety of colchicine for treatment of multiple recurrences of pericarditis (CORP-2): A multicentre, double-blind, placebo-controlled, randomised trial. Lancet 2014;383:2232-7.
4. Cocco G, Chu DC, Pandolfi S. Colchicine in clinical medicine. A guide for internists. Eur J Intern Med 2010;21:503-8.
5. Stewart S, Yang KC, Atkins K, Dalbeth N, Robinson PC. Adverse events during oral colchicine use: A systematic review and meta-analysis of randomised controlled trials. Arthritis Res Ther 2020;22:28.
6. Iacobuzio-Donahue CA, Lee EL, Abraham SC, Yardley JH, Wu TT. Colchicine toxicity: Distinct morphologic findings in gastrointestinal biopsies. Am J Surg Pathol 2001;25:1067-73.