COLCHICINE-INDUCED PANCREATITIS IN AN ELDERLY PATIENT WITH RENAL IMPAIRMENT: A CASE REPORT

Shakil A Chohan, Diraviyam Balasubramaniam, Thet Thet Soe

Changi General Hospital, Geriatric Medicine, Singapore, Singapore.

Abstract

Colchicine is widely used in the treatment of acute gout. It has a narrow therapeutic window and can be extremely toxic in vulnerable older patients especially those with renal impairment. The most common side effects are gastrointestinal related, such as nausea, vomiting, diarrhea and abdominal pain. Colchicine-induced acute pancreatitis is very rare, especially within the therapeutic dose range. We report an atypical presentation of acute pancreatitis caused by a therapeutic dose of colchicine in an elderly patient with preexisting chronic renal disease.

Keywords: acute pancreatitis, atypical presentation, older person, colchicine-induced, renal impairment

Introduction

Drugs are a relatively uncommon cause of pancreatitis in adult patients, but should be considered when other reasonable causes of pancreatitis are not present. Definite proof that a drug causes pancreatitis requires that pancreatitis develops during treatment with the drug, that other likely causes of pancreatitis are not present, that pancreatitis resolves upon discontinuing the drug, and that pancreatitis usually recurs upon readministration of the drug. For ethical reasons, re-challenge with the suspect drug in this case cannot be done: thus this highly convincing piece of evidence relating the drug to pancreatitis may not be available. Acute pancreatitis due to colchicine has rarely been reported, and only in association with severe overdose accompanied by multi-organ failure. Colchicine possesses a narrow therapeutic window, frequently resulting in dose-limiting gastrointestinal side-effects such as diarrhoea and emesis. As colchicine is a cellular anti-mitotic agent, the most serious side effects include myelosuppression, myoneuropathy and multiple organ failure. This occurs with intentional overdose or with therapeutic dosing in patients with reduced clearance of colchicine due to pre-existing renal or hepatic impairment. We report an atypical presentation of acute pancreatitis caused by a therapeutic dose of colchicine in an elderly patient with pre-existing renal impairment.

Case report

An eighty-four-year-old Malay woman with a past history of gout, hypertension, and chronic kidney disease presented with generalized joint pains, consistent with a clinical diagnosis of acute severe polyarticular gout. Prior to admission, she had received one short course of colchicine from GP for five days. She was on regular colchicine 500 mcg once daily as prophylaxis.

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Blood tests showed very high inflammatory markers with a creatinine clearance (CrCl) of 17ml/min. She was treated with paracetamol 1gm QDS, colchicine 500mcg OD for five days together with prednisolone 20mg OD for the first three days. As there was an inadequate clinical and biochemical response, the second course of colchicine was given for another five days. On day 11 of admission, clinical and laboratory response were still unsatisfactory, and computed tomography of abdomen and pelvis (CTAP) was performed to rule out occult infection/inflammation. This was suggestive of acute pancreatitis but she had no clinical symptoms or signs. However, we started on maximal medical therapy following surgical review. Unfortunately, she succumbed to her illness five days after diagnosis despite maximum medical management.

Discussion

Colchicine induced pancreatitis is rare and a thorough review of the literature shows up only one prior reported case where a patient experienced typical features of pancreatitis after two days of initiating of 1mg of colchicine once daily [1]. The initial dose prescribed in our case is lower but her reduced renal function may have precipitated the toxicity. However, given her eGFR level, she's still eligible for a lower dose of colchicine as per British National Formulary (BNF) guidelines. It is also noted in the BNF that colchicine should not be repeated within three days, and in our case, the 2nd course is only after four days. (BNF 74 2018)

According to Bandalov et al. classification system [2], class I and II have the most considerable evidence to cause acute pancreatitis, followed by III and IV. Our patient was administered several drugs (colchicine, paracetamol, prednisolone, and ceftriaxone) which have known to cause acute pancreatitis. paracetamol class II, prednisolone class III, ceftriaxone class III and colchicine in class IV [2].

Correspondence: Shakil Ahmed Chohan, Changi General Hospital, Geriatric Medicine, Singapore, Singapore.
Email: chohanshakil@gmail.com.

Table 1. Naranjo Algorithm – ADR Probability scale

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1			1
2. Did the adverse event appear after the suspected drug was administered?	+2			2
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?				0
4. Did the adverse event reappear when the drug was readministered?			0	0
5. Are there alternative causes that could on their own have caused the reaction?		+ 2		2
6. Did the reaction reappear when a placebo was given?			0	0
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?			0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?			0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?			0	0
10. Was the adverse event confirmed by any objective evidence?	0			0
	Total Score: 5			

Naranjo CA et al. "A method for estimating the probability of adverse drug reactions". Clin.Pharmacol. Ther. August 1981[6]

Most cases of paracetamol-induced pancreatitis are due to overdose ranging from 9.75 to 50 g per day [3,4] except one case reported with approximately 5g of paracetamol every day for about 1 month. Schmidt and Dalhoff reported that most cases of paracetamol overdoses are associated with hepatotoxicity. In our patient, she'd been taking paracetamol 4g daily for 22 days but there were no signs of hepatotoxicity. Prednisolone less than 25 mg is suggested to be below the threshold to effect on the pancreatic enzyme level [5]. The doses she was prescribed is low (20mg/day) and given for a short duration (3 days).

Furthermore, the findings of pancreatitis on CT were found several days after taking prednisolone. Ceftriaxone can cause biliary sludge, hyperbilirubinemia and acute pancreatitis but usually associated with high bilirubin and elevated liver enzyme. In our patient, all were normal except marginally raised ALP which later returned back normal.

According to the "Naranjo adverse drug reaction probability scale" shown in Table 1, colchicine is the most probable etiological agent of acute pancreatitis in our patient.

Conclusion

Though a rare side effect, awareness of colchicine induced pancreatitis is necessary for doctors caring for older persons. A high level of suspicion and an awareness of this possibility is required for early diagnosis and management as it may be completely reversible in the early stages after discontinuation of the offending drug.

Key Points

Atypical presentation in the elderly with minimal or no symptoms and signs is well recognised.

Caution needs to be exercised with colchicine dosing, especially in an older person with renal impairment.

Colchicine-induced pancreatitis is a rare side effect; which doctors need to be aware.

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