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RECURRENT PLEUROPERICARDITIS ASSOCIATED WITH MESALAZINE THERAPY MASKED BY STEROID USE

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ABSTRACT

Introduction: Mesalazine is a cornerstone therapy for ulcerative colitis (UC). Although generally safe, it can cause rare but life-threatening cardiopulmonary complications such as pleuropericarditis.

Case description: We report on a patient with a UC flare who presented with dyspnoea, where concurrent pericardial and pleural effusions were detected. The inflammatory response was likely suppressed by concomitant corticosteroid therapy, which masked the clinical manifestations of mesalazine-induced serositis and delayed diagnosis. Two years later, the patient re-presented with recurrent massive pericardial effusion causing tamponade physiology and pleural effusion. Pericardial fluid analysis revealed a haemorrhagic, neutrophil-dominant profile (95% polymorphonuclear leukocyte, mimicking bacterial infection rather than the typically described eosinophilic pattern. Extensive cultures were negative. Following the discontinuation of mesalazine, rapid clinical and radiologic improvement was observed, confirming drug-induced pleuropericarditis.

Discussion: This case highlights that mesalazine-associated pleuropericarditis can be obscured by corticosteroids, leading to diagnostic delays. Furthermore, sterile inflammatory reactions to mesalazine can present with atypical neutrophilic features resembling bacterial infection, necessitating a high index of suspicion in inflammatory bowel disease patients presenting with serositis.

KEYWORDS

Mesalamine, ulcerative colitis, pericardial effusion, pleural effusion, drug toxicity

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LEARNING POINTS

- A high index of suspicion for drug-induced serositis: in patients with inflammatory bowel disease, pleuropericarditis should be evaluated as a potential side effect of mesalazine rather than assuming it is an extraintestinal manifestation, especially when symptoms recur upon drug re-exposure.
- Corticosteroids may mask drug toxicity: concomitant corticosteroid therapy can temporarily suppress the clinical symptoms and effusion of mesalazine-induced pleuropericarditis, leading to a 'wrong footing error' and delayed diagnosis once steroids are tapered.
- Atypical laboratory features: mesalazine-induced sterile inflammatory reactions can present with a neutrophil-dominant effusion profile (rather than the typical eosinophilic pattern), which may mislead the clinician towards an infectious aetiology.

INTRODUCTION

Inflammatory bowel disease is characterised by chronic gastrointestinal inflammation and may involve extraintestinal organs. Although cardiovascular manifestations are uncommon, pericarditis and myocarditis occur more frequently in inflammatory bowel disease patients than in the general population[1]. Cardiopulmonary symptoms in ulcerative colitis (UC) should not automatically be attributed to extraintestinal manifestations (EIM) without considering potential drug toxicity[1].

Mesalamine, a cornerstone therapy for mild-to-moderate UC, is generally well tolerated. However, rare idiosyncratic cardiac reactions (<0.3%) may be life-threatening[2]. Mesalamine cardiotoxicity most often presents as myopericarditis, though isolated pericardial effusion has been reported[3]. Concurrent pleural and pericardial involvement is exceptionally rare and may mimic EIM or infection. Diagnosis is particularly challenging in patients receiving corticosteroids, as these agents may suppress hypersensitivity-mediated inflammatory responses, which can mask drug-induced toxicity and delay its recognition[4]. We report a case of haemorrhagic mesalamine-associated pleuropericarditis masked for two years by corticosteroid therapy and ultimately presenting with impending cardiac tamponade.

CASE DESCRIPTION

A 22-year-old man with newly diagnosed UC presented three weeks after starting oral and rectal mesalamine, with bloody diarrhoea and dyspnoea. Laboratory evaluation showed elevated inflammatory markers (C-reactive protein 176 mg/l, white blood cell count 12,700/µl) and faecal calprotectin >1,000 µg/g. Thoracic computed tomography (CT) revealed 15 mm pericardial and left pleural effusions *(Fig. 1)*. Echocardiography demonstrated preserved left ventricular function (ejection fraction 60%) and a 1.5 cm circumferential pericardial effusion without haemodynamic compromise. Colonoscopy confirmed severe active colitis. The presentation was initially interpreted as UC-related EIM. Autoimmune testing was negative. The patient was treated with systemic corticosteroids (prednisolone 40 mg/day) and colchicine, resulting in clinical and radiologic improvement. This apparent improvement was likely related to suppression of the underlying inflammatory response rather than resolution of the causative factor. Mesalamine was continued as maintenance therapy.

Two years later, while in UC remission, the patient presented with acute severe dyspnoea. Imaging revealed a 20–22 mm circumferential pericardial effusion compressing the right heart chambers with impending tamponade physiology, along with a 2 cm left pleural effusion *(Fig. 2)*. Emergency pericardiocentesis was performed. Fluid analysis showed haemorrhagic exudate (protein 5.6 g/dl)



Figure 1. *Initial thoracic CT reveals concurrent pericardial and left basal pleural effusions, each measuring approximately 15 mm.*



Figure 2. Follow-up thoracic CT and echocardiography obtained two years after the initial presentation reveal concurrent circumferential pericardial and left pleural effusions, measuring 20–22 mm and 2 cm respectively, with associated compression of the right cardiac chambers and impending tamponade physiology.

with neutrophil predominance (95% polymorphonuclear leukocyte; cultures were sterile.

Infectious, autoimmune and metabolic causes were excluded. Given the temporal relationship between mesalamine exposure and recurrence of pleuropericardial effusions, mesalamine was discontinued. The Naranjo adverse drug reaction probability scale score was 8, indicating a probable drug reaction[5]; detailed scoring components are presented in *Table 1*. Effusions resolved completely after withdrawal. Three months later, follow-up thoracic CT and echocardiography confirmed complete resolution, supporting a temporal association with mesalamine *(Fig. 3)*.

DISCUSSION

Mesalamine-associated serositis typically presents as isolated pericarditis or pleural effusion; combined pleuropericardial involvement is rare and may mimic UC-related EIM[1]. Because no specific biomarker exists, diagnosis requires exclusion of infectious and autoimmune aetiologies[6]. Recent studies have emphasised the importance of recognising inflammatory pericardial involvement and drug-related cardiac complications in clinical practice, as these conditions may present with non-specific findings and mimic other aetiologies.

Most cases occur within 2–4 weeks of therapy initiation, although delayed presentations have been described[7]. In our case, concomitant corticosteroid therapy likely suppressed the inflammatory response associated with mesalazine-induced serositis, thereby masking its clinical presentation. This immunosuppressive effect may lead to transient clinical improvement and misinterpretation of symptoms as extraintestinal manifestations of UC. Consequently, continued exposure to the offending agent may occur, increasing the risk of recurrence and more severe presentations, as observed in this patient[8]. Continued exposure to mesalamine may have predisposed to recurrence after steroid tapering.

The haemorrhagic, neutrophil-predominant pericardial fluid posed an additional diagnostic challenge, mimicking bacterial pericarditis. However, sterile cultures and rapid resolution following drug withdrawal without antibiotics supported a non-infectious inflammatory mechanism. Similar infection-mimicking presentations have been reported[9].

Prompt recognition is essential, as discontinuation of the offending agent typically results in rapid improvement[3].

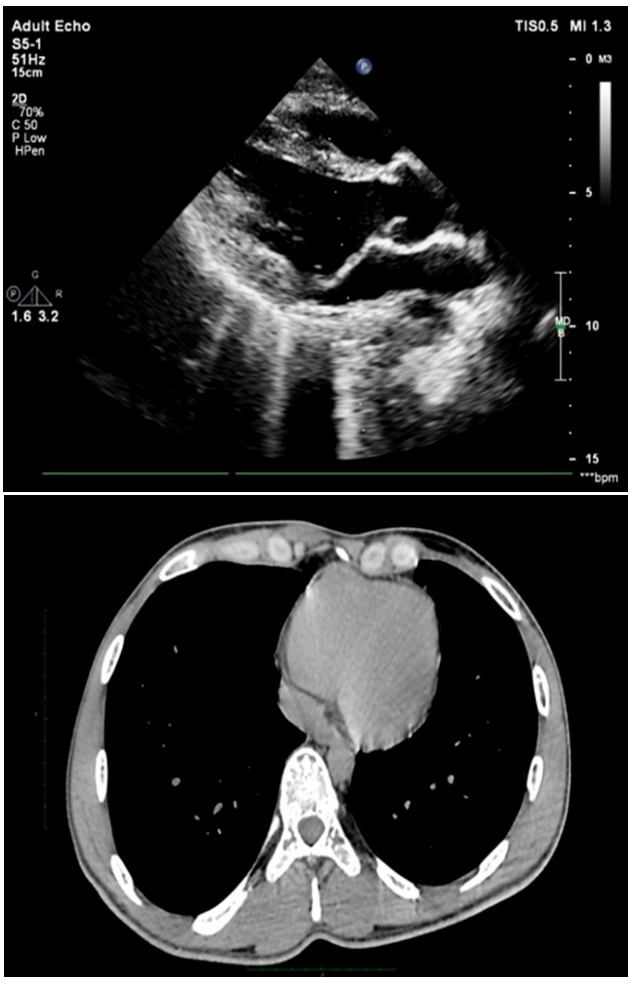


Figure 3. Follow-up thoracic CT and echocardiography performed six weeks after discontinuation of mesalamine demonstrate complete resolution of both the pericardial and pleural effusions.

No	Naranjo question	Possible score	Findings in the present case	Assigned score
1	Are there previous conclusive reports on this reaction?	+1	Mesalamine-induced pericarditis has been previously reported in the literature.	+1
2	Did the adverse event appear after the suspected drug was administered?	+2	Clinical symptoms developed three weeks after initiation of mesalamine therapy.	+2
3	Did the adverse reaction improve when the drug was discontinued?	+1	Complete clinical and radiological resolution was observed within four weeks after drug withdrawal.	+1
4	Did the adverse reaction reappear when the drug was re-administered?	+2	Not performed due to ethical concerns regarding re-challenge.	0
5	Are there alternative causes (other than the drug) that could on their own have caused the reaction?	+2	Autoimmune markers were negative and microbiological cultures were sterile.	+2
6	Did the reaction reappear when a placebo was given?	−1	Not performed.	0
7	Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	Not assessed.	0
8	Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	Dose–response relationship could not be evaluated.	0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	A similar self-limited episode had occurred two years earlier.	+1
10	Was the adverse event confirmed by any objective evidence?	+1	Pericardial effusion was confirmed by transthoracic echocardiography, thoracic CT and fluid analysis.	+1

Table 1. *Naranjo adverse drug reaction probability scale assessment.*

Causality assessment of mesalamine-associated pericarditis was performed using the Naranjo Adverse Drug Reaction Probability Scale. Total Naranjo Score: 8. This score indicates a 'probable' adverse drug reaction.

The complete resolution observed in this case reinforces a drug-induced aetiology.

CONCLUSION

Unexplained pleuropericardial effusion in patients with UC should prompt consideration of mesalamine toxicity. Haemorrhagic, neutrophil-predominant effusions may mimic infection, while corticosteroids can mask drug-induced serositis by suppressing the inflammatory response, potentially delaying diagnosis and increasing the risk of recurrence. Awareness of this rare but potentially life-threatening complication is critical to avoid diagnostic delay and unnecessary treatment.

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