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CASE REPORT

The Vulnerability of the Heart During Diarrhea: A Case Report on Pericarditis Linked to Inflammatory Bowel Disease

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Abstract

Introduction: **Inflammatory bowel disease (IBD), encompassing ulcerative colitis (UC) and Crohn's disease, often involves extraintestinal manifestations, affecting up to 40% of patients. Cardiovascular complications, although rare, can include pericarditis, the most common cardiac manifestation in IBD.**

Case presentation: **We report the case of a 34-year-old male with a long-standing history of UC who presented with pleuritic chest pain, shortness of breath, and worsening colitis symptoms. This case is particularly noteworthy due to the complexity added by the patient's 24-year history of UC, diverse treatment modalities (including mesalamine, 6-mercaptopurine, infliximab, vedolizumab, upadacitinib, and ustekinumab), and the patient not being on any 5-aminosalicylic acid (5- ASA) medications known to cause pericarditis at the time of presentation. The pericarditis episodes were temporally associated with UC flare-ups, complicating the distinction between disease-induced and medication-induced pericarditis. The patient experienced two recurrent episodes within 14 weeks, and comprehensive investigations excluded other common causes, narrowing down the potential etiologies. Clinical evaluation revealed pericarditis with a moderate pericardial effusion, elevated inflammatory markers, and normal cardiac biomarkers. The patient's pericarditis was managed with corticosteroids and colchicine, leading to rapid symptom resolution. This case underscores the challenge of distinguishing between disease-induced and medication-induced pericarditis in IBD patients.**

Conclusion: **Pericarditis, although a rare extraintestinal manifestation of IBD, should be considered in patients with UC presenting with chest pain. This report highlights the need for heightened awareness and careful management of pericarditis in UC patients. Clinicians should maintain a high index of suspicion for cardiovascular complications in IBD, ensuring timely diagnosis and intervention.**

Keywords: Inflammatory bowel disease, Ulcerative colitis, Pericarditis, Extraintestinal manifestations, Cardiovascular complications, Colchicine

1. Introduction

Inflammatory bowel disease (IBD), which includes ulcerative colitis and Crohn's disease, is a chronic condition mainly affecting the gastrointestinal tract. However, it is also associated with various extraintestinal manifestations (EIM) seen in 25−40% of patients. These symptoms can affect the joints (peripheral and axial arthropathies), skin (erythema nodosum, pyoderma gangrenosum, Sweet's syndrome, aphthous stomatitis), hepatobiliary tract (primary sclerosing cholangitis), and eyes (episcleritis, uveitis).[1] Rarely, EIM can affect the cardiovascular system, resulting in conditions such as vascular thrombosis, atherosclerotic cardiovascular disorders (CVD), heart failure, arrhythmia, myocarditis, and pericarditis.[2,3] The correlation between IBD and CVD is well documented, with a notably higher prevalence of cardiovascular disorders within this population subset. Pericarditis, which accounts for

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70% of cardiovascular complications related to IBD, is the most common cardiovascular EIM in IBD patients, with a prevalence of 0.19% in Crohn's disease (CD) patients and 0.23% in ulcerative colitis (UC) patients.[4] Herein, we present a case illustrating the rare association between IBD and pericarditis and a review of the existing literature on this association.

2. Case presentation

A 34-year-old male with a long-standing history of ulcerative colitis (UC) diagnosed at age 10 presented to the emergency department with pleuritic chest pain, shortness of breath, and worsening colitis symptoms. His chest pain, localized in the upper chest and radiating to the neck, improved with an upright position and leaning forward but was exacerbated by inspiration. He reported nearly six bowel movements per day, bright red blood during bowel movements, straining, urgency, and abdominal pain. He denied fevers, contact with sick individuals, night sweats, joint pain, or an ongoing rash.

On admission, the patient was hemodynamically stable and afebrile. Physical examination revealed mild tenderness in the lower abdomen, with no signs of jugular venous distension or paradoxical pulse, and clear lungs bilaterally. Laboratory tests showed elevated C-reactive protein (CRP) at 15.8 mg/dL (reference range: 0.0–0.8 mg/dL), erythrocyte sedimentation rate (ESR) at 44 mm/h (reference range: 0–15 mm/h), anemia with Hb 7.2 g/dL (reference range:14–17 g/dL), and leukocytosis with WBC 31k (reference range: 4.0–10.0 $\times$ $10^3/\mu L$). An EKG (Fig. 1) indicated normal sinus rhythm at 100 beats per minute with diffuse ST elevations, suggesting early repolarization pericarditis, while troponin levels were unremarkable. An echocardiogram (Fig. 2) revealed a normal ejection fraction, mild aortic and tricuspid

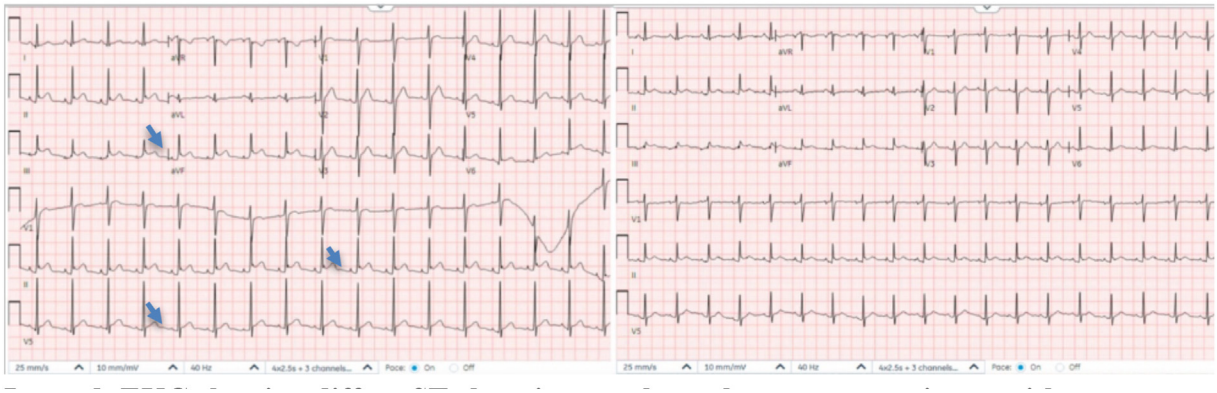

Fig. 1. EKG images. Legend: EKG showing diffuse ST elevations as shown by arrows consistent with pericarditis.

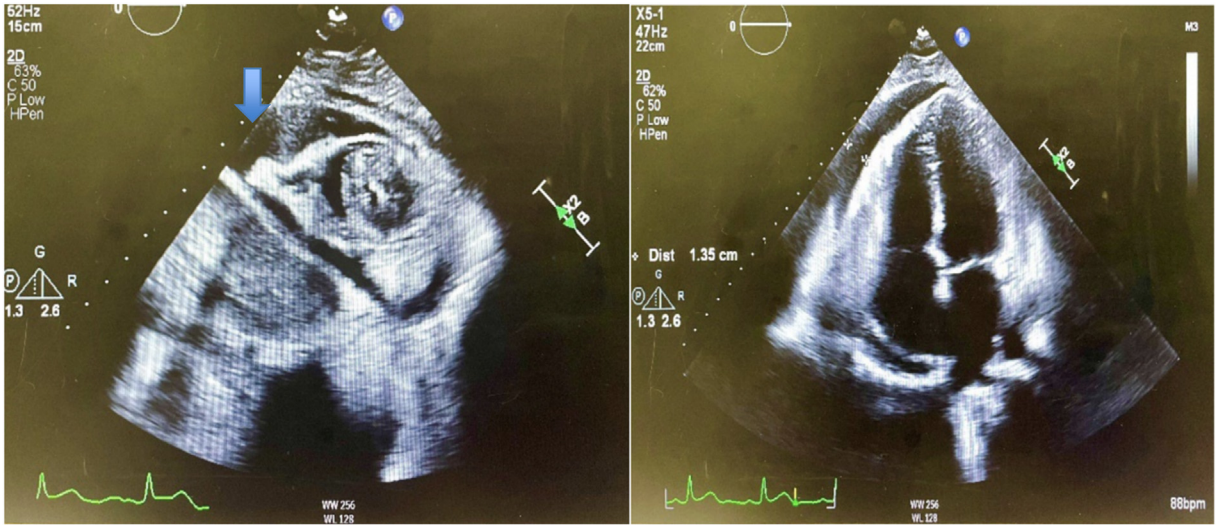

Fig. 2. ECHO images. Legend: Images (Short axis view & four chamber view) showing mildly thickened pericardium. Arrow shows moderate pericardial effusion (1–2 cm).

regurgitation, moderate mitral regurgitation with anterior mitral leaflet prolapse, and a moderate 1−2 cm loculated anterior pericardial effusion.

The patient was diagnosed with pericarditis associated with an exacerbation of UC and was treated with an initial dose of intravenous methylprednisolone 125 mg, followed by 60 mg every 8 h, and oral colchicine 0.6 mg daily, alongside supportive care. Blood, urine, sputum, and throat cultures, as well as serological tests for CMV, Epstein-Barr virus, influenza A/B, coxsackievirus, and *Borrelia burgdorferi*, were all negative. Autoimmune tests (autoantibodies, ANA, ANCA) and thyroid-stimulating hormone levels were also normal. The patient's chest discomfort subsided within 24 h of starting methylprednisolone, and treatment continued with colchicine and a prednisone taper, resulting in gradual symptom improvement. During this period, his colitis remained relatively stable on prednisone. Interestingly, the patient presented with another episode of pericarditis within a short timeframe of 14 weeks.

Of note, the patient had undergone various treatments for his complex history of ulcerative colitis. Initial treatment with mesalamine and 6-mercaptopurine kept the patient stable until age 30, when a significant flare-up led to a diagnosis of pancolitis. Infliximab was added but discontinued due to a severe infusion reaction. Vedolizumab was then introduced, with the dosing interval later shortened due to inadequate response. The patient experienced severe lower right abdominal pain and was diagnosed with ileitis and right-sided colitis at the age of 32. Initial treatment for these new symptoms included steroids, vedolizumab, and balsalazide. A year later, upadacitinib showed a rapid response at the induction dose but was ineffective at maintenance doses. However, at the age of 34, Ustekinumab induction had to be initiated with increased dosing frequency and concurrent prednisone due to ongoing severe colitis. At the time of admission for pericarditis, the patient was only on prednisone, and the last dose of Ustekinumab was administered four weeks before presentation. While biologics are known to potentially induce autoimmune diseases, the FDA label for Ustekinumab does not include any reported cases of pericarditis. Additionally, there is no significant family history of inflammatory bowel disease, colorectal cancer, or autoimmune diseases.

3. Discussion

Pericarditis is a rare but well-recognized extra-intestinal manifestation of IBD, particularly UC.[4] This case report presents a unique and challenging scenario of recurrent pericarditis associated with UC flare-ups in a patient with a long-standing history of UC. The exact etiology of pericarditis in IBD remains unclear. Most proposed theories for drug-induced pericarditis include potential mechanisms such as immune-mediated pericarditis, hypersensitivity reactions to medications, and drug-induced cardiotoxicity. In drug-induced pericarditis, it is hypothesized that antibodies against drugs, especially aminosalicylates, may develop cross-reactivity to the pericardium, thus inducing a cell-mediated hypersensitivity reaction. The mechanism for pericarditis from IBD itself is not fully understood, but mouse models have shown immune-mediated tissue damage through improper T-cell activation.[5,6] The association between inactive IBD and pericarditis has been documented in the literature. For example, Mukhopadhyay et al. reported a case where pericarditis appeared two years before the onset of colitis. In another case, as reported by Rheingold, pericarditis developed after a subtotal colectomy but resolved after the inflamed rectum was removed. While the occurrence of pericarditis in IBD is mainly associated with colonic involvement, pericarditis can rarely occur in Crohn's disease, limited to the small bowel.[6,7] The clinical presentation of pericarditis is similar to that of acute coronary syndrome (ACS) with chest pain and sometimes with heart failure exacerbation, arrhythmias, or sudden death. If pericarditis develops within 28 days of immune modulator therapy, especially 5-ASA derivative drug toxicity should be suspected. The diagnostic tests include Electrocardiograms (ECGs), which may appear normal or show ST-segment elevation or depression, elevated levels of cardiac injury biomarkers (troponin, creatine kinase), B-type natriuretic peptide, and increased acute-phase reactants (erythrocyte sedimentation rate, C-reactive protein, and fibrinogen). Transthoracic echocardiography is recommended for all patients with acute pericarditis. If ACS symptoms are suspected, coronary angiography is recommended. Nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine are the first mainstay of treatment, while corticosteroids can be used in treatment-resistant pericarditis. Colchicine, however, can cause diarrhea, potentially complicating the course of IBD.[6,8]

This patient's case presents several distinctive challenges:

1. **Long-standing IBD history**: A 24-year history of UC complicates the diagnosis of pericarditis. This extensive disease history is uncommon in many reported cases.

2. **Multiple treatment modalities**: Diverse treatments including mesalamine, 6-mercaptopurine, infliximab, vedolizumab, upadacitinib, and ustekinumab adds a layer of complexity in determining if pericarditis is medication-induced or a manifestation of UC.
3. **Absence of 5-ASA therapy**: The absence of recent 5-aminosalicylic acid (5-ASA) exposure, commonly associated with drug-induced pericarditis, suggests other possible etiologies.
4. **Temporal association with UC flare**: The close link between pericarditis episodes and UC flare-ups complicates distinguishing between disease-induced and medication-induced pericarditis.
5. **Recurrent nature**: Two episodes of pericarditis within 14 weeks are relatively uncommon in IBD-associated pericarditis.
6. **Exclusion of other common causes**: Comprehensive investigations excluded other common causes, narrowing down potential etiologies.

These factors create a multifaceted diagnostic scenario, emphasizing the need for thorough evaluation and consideration of the patient's entire clinical picture. In this case, the patient's classic symptoms of pericarditis, including pleuritic chest pain and shortness of breath, along with ECG changes and a moderate pericardial effusion on echocardiography, strongly suggest an extraintestinal manifestation of UC rather than a side effect of 5-ASA therapy. Typically, drug-induced pericarditis symptoms develop within weeks of starting therapy and resolve after discontinuation, often requiring steroid treatment.[6,7] In IBD patients who develop pericarditis, it is challenging to determine whether the manifestation is a consequence of the disease itself or a side effect of the medications. A thorough review of the patient's history and timeline of medications can help pinpoint the cause after excluding common etiologies. Since the association of pericarditis with IBD itself is very rare, physicians should have a high suspicion for its occurrence.

4. Conclusion

This case report highlights the complexity and diagnostic challenges associated with pericarditis as an extraintestinal manifestation of long-standing ulcerative colitis (UC). The patient's 24-year history of UC, along with a diverse and extensive treatment regimen, underscores the multifaceted nature of this case. The absence of recent 5-ASA exposure, close temporal association with UC flare-ups, and the recurrent nature of pericarditis within a short timeframe further complicate the diagnostic process. Additionally, the comprehensive exclusion of other common causes of pericarditis emphasizes the thorough investigative approach required in such cases. This unique presentation underscores the need for heightened awareness among clinicians regarding the potential cardiac complications in patients with complex, long-standing IBD. By sharing this case, we aim to contribute to a deeper understanding of the diverse manifestations and intricate interplay between IBD and its extraintestinal complications, ultimately enhancing patient care and outcomes in similar scenarios.

Disclaimers

We certify that this manuscript is original and has not been submitted for publication elsewhere, nor has it been presented at any professional conference or meeting.

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Conflict of interest

The authors declare no conflicts of interest in relation to this case report. There are no financial, personal, or professional affiliations or relationships that could be perceived as influencing the research or findings presented in this article. No funding was received for the preparation of this manuscript, and no organization or entity had any role in the collection, analysis, or interpretation of the data. The authors have no relevant financial or non-financial interests to disclose.

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