CASE REPORT

Mesalazine-induced myopericarditis in a patient with ulcerative colitis

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Summary

A 25-year-old male with a background of ulcerative colitis presented with a two-week history of central chest pain. His ECG on presentation showed global T wave inversion with a peak troponin I of 165 ng/mL. Clinical diagnosis of myopericarditis/myocarditis was made. Echocardiography and cardiac magnetic resonance (MR) confirmed the diagnosis. On detailed assessment of his medication history, mesalazine was suspected as an etiological factor, with discontinuation resulting in an improvement in symptoms, inflammatory markers and cardiac enzymes. This is a unique case of mesalazine-induced myopericarditis on a background of inflammatory bowel disease.

Key Words

▶ magnetic resonance imaging

▶ echocardiography

▶ mesalazine

▶ myopericarditis

▶ myocarditis

Learning points:

- Myopericarditis can be due to infectious and non-infectious causes.
- Myopericarditis may be related to systemic diseases such as inflammatory bowel disease (IBD) or as a consequence of its treatment.
- Cardiac magnetic resonance has proven to be a valuable technique for assessing myocardial injury and inflammation in myocarditis.
- Importance of taking a thorough medical history to distinguish the type of chest pain in order to make a correct diagnosis.

Background

Myocarditis

Pathophysiology

Myocarditis is an inflammatory disorder affecting the myocardium. It can be caused by a variety of infective organisms such as coxsackie and herpes virus, drugs including endotoxins and autoimmune conditions such as systemic lupus erythematosus (SLE) (1). The disease process, regardless of the cause tends to follow a common course. The acute phase is mediated by direct cytotoxic damage induced by the causative agent, which instigates the release of various inflammatory mediators such as TNF-a and IL1 and IL6 (1). This augments the immune response and leads to further myocyte damage. In certain cases, the inflammatory cascade can persist and the disease progresses into a chronic phase. This can either be driven by persistence of the causative agent or a genetic predisposition initiating an autoimmune response (1). Autoimmunity plays a central role in chronic myocarditis and is mediated by T and B cells, various autoantibodies and cytokines (1, 2). Eventually the continued inflammation leads to cardiac remodeling (either diffuse or focal) and progresses to dilated cardiomyopathy and

ventricular dysfunction (1). In most cases of myocarditis, the disease process can involve the pericardium resulting in myopericarditis (2).

Signs and symptoms

Typically, patients present with sharp retrosternal chest pain, which is relieved by sitting forward and aggravated lying back. Clinical examination may reveal a pericardial friction rub.

Complications and prognosis

Complications of myocarditis include tachyarrhythmias, heart block, left ventricular dysfunction, dilated cardiomyopathy and cardiac arrest (3). The vast majority of patients make a full recovery with minimal impairment in left ventricular (LV) function, however, a few (between 5 and 10%) may progress to dilated cardiomyopathy and congestive cardiac failure (3).

Diagnosis

There is no definitive diagnostic test to confirm myocarditis. The diagnosis is based on the clinical picture and often involves an integrated approach with characteristic ECG changes and a rise in serial troponins. The ECG can show features of widespread saddle-shaped ST elevation, T wave inversion and occasional arrhythmias with a corresponding rise in cardiac enzymes (troponin and creatinine kinase) (4).

Table 1 Diagnostic cardiac magnetic resonance (CMR) criteria for myocarditis (4).

In the setting of clinically suspected myocarditis, CMR findings are consistent with myocardial inflammation, if at least two of the following criteria are present:
1. Regional or global myocardial signal intensity increase in T2-weighted images
2. Increased global myocardial early gadolinium enhancement ratio between myocardium and skeletal muscle in gadolinium-enhanced T1-weigthed images
3. There is at least one focal lesion with non-ischemic regional distribution in inversion recovery-prepared gadolinium-enhanced T1-weighted images (late gadolinium enhancement)

A CMR study is consistent with myocyte injury and/or scar caused by myocardial inflammation if criterion 3 is present

A repeat CMR study between 1 and 2 weeks after the initial CMR study is recommended if:
1. None of the criteria are present, but the onset of symptoms has been very recent and there is strong clinical evidence for myocardial inflammation
2. One of the criteria is present

The presence of LV dysfunction or pericardial effusion provides additional, supportive evidence for myocarditis

Echocardiography allows general morphological and functional assessment of the heart and can be used to assess myocardial contraction, ejection fraction and to exclude other valvular lesions; however, it gives very limited insight into myocardial inflammation and tissue characterization in the acute setting (4, 5). Percutaneous angiography and CT pulmonary angiography can be used to exclude coronary artery disease and other
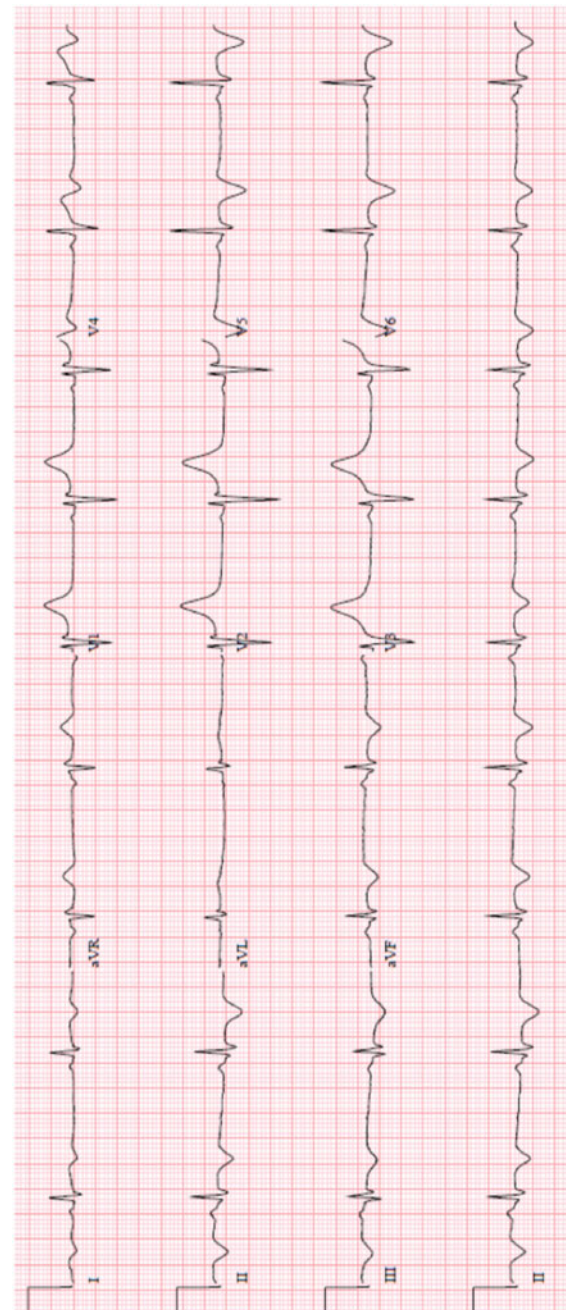

Figure 1
Admission ECG showing T wave inversion in I, II, III, aVF and V4 to V6.

causes of chest pain respectively. A myocardial biopsy is gold standard; however, it carries procedural risks and is therefore not necessary when the clinical picture is highly suggestive of myocarditis (4).

Cardiac MR has proven to be a valuable technique for assessing myocardial injury and inflammation in myocarditis (4). Furthermore, it has an important role in establishing the diagnosis and monitoring disease progression in myocarditis (6). This important role has been highlighted in the latest position paper on myocarditis from the European Society of Cardiology (6). In addition to being a superior imaging modality in assessing cardiac function and morphological features, it can detect hyperaemia, capillary leak and most importantly the degree of fibrosis and myocyte necrosis (4). However, such features may be difficult to distinguish as they can all manifest in myocardial edema, early gadolinium enhancement (EGE) or late gadolinium enhancement (LGE) (4). An International Consensus Group on Cardiac MR Diagnosis of Myocarditis incorporates three MR techniques (Table 1) (4, 6).

Treatment

Treatment of myocarditis is mainly tailored toward the underlying causative factor (1). In disease progression, treatment is aimed at managing complications and the ensuing cardiac failure (7). In the vast majority of cases, the underlying cause is not known, mostly attributed to viruses in particular coxsackie. Symptomatic control of pain in isolated pericarditis can be achieved with non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine; however, in experimental murine models of viral myocarditis, NSAIDs have been found to increase mortality (7). Hence, the lowest dose of NSAIDs should be used for myopericarditis with preserved LV function and pain secondary to pericarditis (7). Otherwise, NSAIDs are not recommended until conclusive data from clinical trials become available (7).

Case presentation

A 25-year-old male with a background of ulcerative colitis on mesalazine 2g BD in remission, presented with a two-week history of sharp central chest pain. Prior to his chest pain, he had a self-limiting episode of increased frequency of bowel movements with a prodromal flu-like illness.

Investigation

Admission ECG showed T wave inversion in I, II, III, aVF and V4 to V6 (Fig. 1) with a peak troponin I of 165 ng/mL (other blood tests were normal). Patient was immediately commenced on acute coronary syndrome (ACS) treatment. A CT pulmonary angiogram was performed, which excluded a pulmonary embolism (PE). A clinical diagnosis of myopericarditis was made; therefore, coronary angiography was not performed. Viral serology was negative. A transthoracic echocardiogram was performed, which revealed a small rim of pericardial fluid with hypokinesis of the apical anterolateral and inferior walls with a left ventricular ejection fraction (LVEF) of 45–50% (Fig. 2). A cardiac MR was later performed and
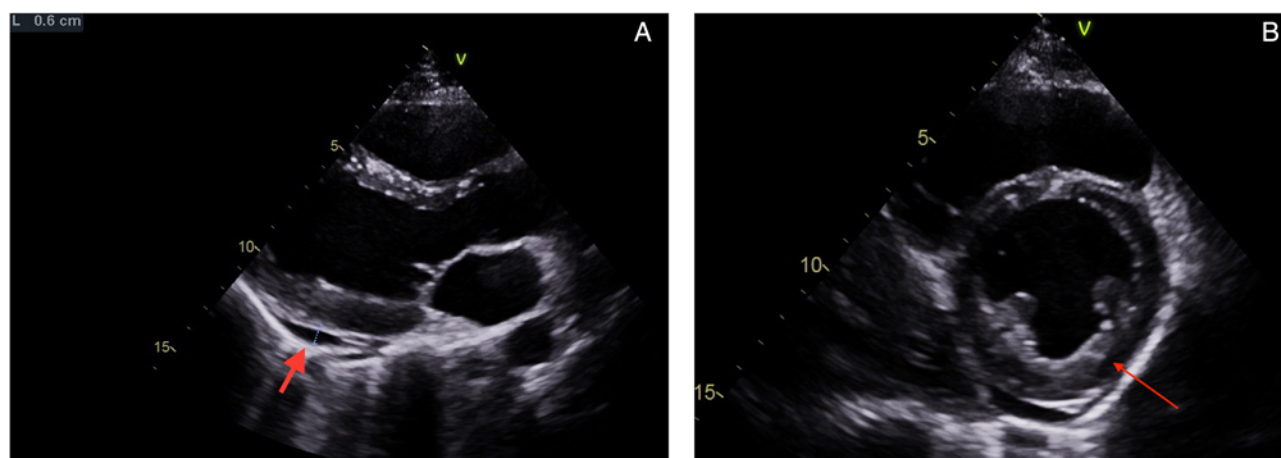

Figure 2
Parasternal long axis (A) and parasternal short axis (B) showing increased echogenicity and thickness of the inferolateral wall that may suggest myocardial regional wall edema, with a rim of pericardial fluid measuring 0.6cm on the long axis.

Figure 3
2-Chamber (left ventricular) T2-STIR view showing myocardial edema of mid (red arrowhead) to apical inferior wall (blue arrowhead).

showed normal RV and LV systolic function, myocardial edema of mid-to-apical inferior wall (Fig. 3) and epicardial/myocardial fibrosis of the inferolateral wall (Fig. 4). Overall, features were consistent with acute myocarditis. At the time of discharge, inflammatory markers and troponin were normal.
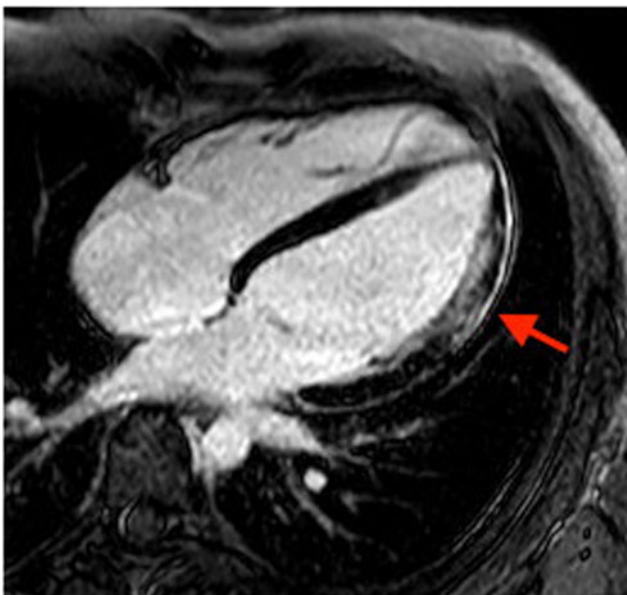

Figure 4
4-Chamber view showing late gadolinium enhancement in keeping with epicardial/myocardial fibrosis of the inferolateral wall.
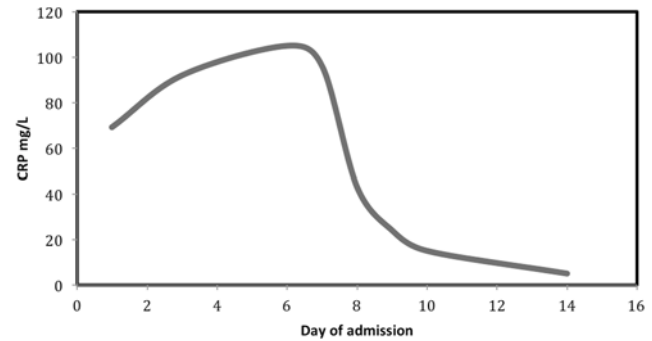
Figure 5
Trend in CRP showing drop in levels after stopping mesalazine on day 6.

Treatment and outcome

Due to persisting chest pain during admission, the possibility of mesalazine-induced myopericarditis was raised. On day 6, mesalazine was discontinued after discussion with the gastroenterologist. This coincided with immediate resolution of the patient's symptomatology and improvement in inflammatory markers and normalization within 7 days (Fig. 5). The discontinuation of mesalazine was not associated with a flare in the patient's GI symptoms. As the patient's GI symptoms remained stable, his mesalazine was completely discontinued with a plan for further review in the outpatient gastroenterology clinic.

Discussion

Cardiac involvement in inflammatory bowel disease (IBD) is a very rare complication and few cases have been reported in the literature. This can either manifest as endocarditis (secondary to infective agents in the context of deranged immunity), myocarditis/myopericarditis or arrhythmias (8). Most of the reported cases of myopericarditis or myocarditis can be attributed to the autoimmune nature of IBD or secondary to the immunomodulating therapies, such as mesalazine and steroids (8). Myocarditis has been reported more in ulcerative colitis (UC) than Crohn's disease (CD) with the etiology undetermined (8).

Mesalazine (5-aminosalicylic acid) is an anti-inflammatory medication used in the treatment of UC and CD. The exact mechanism of action is unknown; however, it is postulated to be mediated by nuclear receptors (9). In the context of IBD, the peroxisome proliferator-activated receptor gamma is the main target by which mesalazine induces its anti-inflammatory effect on macrophages and epithelial cells (9). It is also believed that it retains some inhibitory properties on cyclooxygenase, lipoxygenase,

TNF-a, IL1 and IL6 production (9). Main side effects are related to gastrointestinal disturbances, more rarer ones include myelosuppression, SLE-like reactions, renal injury, erythema multiform and myopericarditis/myocarditis (8, 9). In mesalazine-induced myocarditis, the response tends to be paradoxical and is coupled with upregulation of inflammation within the myocardium, likely secondary to an autoimmune hypersensitivity response to the drug itself rather than an intrinsic toxic property of it (8).

This case report is a good example of non-coronary cardiac disease in UC and highlights the importance of good clinical history taking. Furthermore, it highlights the imaging modalities at our disposal for confirming or refuting a diagnosis of myocarditis. Myopericarditis has been reported in patients with UC and CD independent of mesalazine use (2). The causality of this patient's presentation is difficult to determine, as to whether it was secondary to mesalazine or simply a complication of UC; however, the rapid improvement in symptomology and inflammatory markers after discontinuation strongly favors mesalazine as a culprit. In conclusion, the risk of cardiac involvement in inflammatory bowel disease may be higher than reported in the literature and could occur insidiously in asymptomatic patient culminating in cardiac failure.

Author contribution statement
J A was involved with the patient's care and wrote the report. S S B critically appraised the report and reviewed the images. N A was the consultant in charge of the patient and reviewed the final draft.

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