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Case Report

Crohn's colitis-induced myocarditis

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ABSTRACT

Myocarditis can be idiopathic or arise in response to numerous systemic insults. Myocarditis occurring in the setting of an exacerbation of inflammatory bowel disease is a rare extra-intestinal manifestation of both ulcerative and Crohn's-related colitis. Here, we present a unique case of a 56-year-old female patient presenting with an acute Crohn's colitis flare that was eventually complicated by myocarditis. Our case is unique in that we clearly delineate the clinical course and development of myocarditis in a patient with focal myocardial inflammation in a pattern that is atypical for myocarditis.

<**Learning objective:** To illustrate the clinical course and resolution, along with cardiac magnetic resonance imaging and echocardiographic findings, of Crohn's-induced myocarditis.>

Introduction

Extra-intestinal manifestations of inflammatory bowel disease (IBD) are common and occur in nearly 25–30% of patients [1]. Extra-intestinal complications of IBD include: musculoskeletal, ocular, dermatologic, hepatobiliary, immunologic, hematologic, renal/urologic, pulmonary, and cardiac disorders. Myocarditis is a rare extra-intestinal cardiac complication of IBD. Registry data reported 6 cases of myocarditis in over 15,000 patients [2]. Interestingly, the incidence of myocarditis was slightly higher among patients with IBD relative to the general population [2]. Ulcerative colitis-induced myocarditis has been documented previously [3]. Also, fulminant myocarditis in association with active Crohn's disease has been described [4,5]. We present a case of focal myocarditis occurring secondary to an acute flare of Crohn's colitis. This case is unique in that we illustrate the clinical manifestation and course of myocarditis in a patient with a Crohn's flare. Also, we display atypical cardiac magnetic resonance imaging (MRI) features of myocarditis and illustrate regional wall motion abnormalities and mild global left ventricular systolic dysfunction on echocardiography. To our knowledge, this is the first such case of its type.

Case report

A 56-year-old female with a history of Crohn's disease (not on active maintenance treatment) presented complaining of diffuse abdominal pain (relieved with bowel movements, worsened with eating), diarrhea (5–6 loose bowel movements daily), and bright red blood per rectum for the previous 2 weeks. On day 0 (day of admission), she underwent computed tomography (CT) of the abdomen/pelvis which revealed mural thickening and pericolonic stranding of the ascending colon and cecum as well as mild mural thickening of the descending colon (Fig. 1). On day 2, she underwent MR abdomen enterography which revealed diffuse wall thickening, mucosal hyperenhancement, and surrounding inflammatory changes suggestive of active bowel disease as well as associated acute on chronic inflammation of the cecum, ascending colon, and proximal and mid transverse colon (Fig. 2). The findings on CT and MR were collectively consistent with active Crohn's colitis. Relevant laboratory results revealed white blood cell (WBC) count 13,700 cells/μl, hemoglobin 12.7 g/dL, and platelets 436,000 cells/μl, C-reactive protein (CRP) 22.7 mg/dL (normal 0–0.5 mg/dL), and erythrocyte sedimentation rate (ESR) 47 mm/hr (normal <20 mm/hr). Accordingly, she was diagnosed with an acute Crohn's flare and was treated with solumedrol IV 20 mg BID.

On hospital day 3, she complained of sudden onset, pleuritic chest pain, which she described as a "net-like pain" around her heart with radiation to her back and shoulders bilaterally. It lasted for roughly 10 minutes before self-resolving. Her d-dimer was

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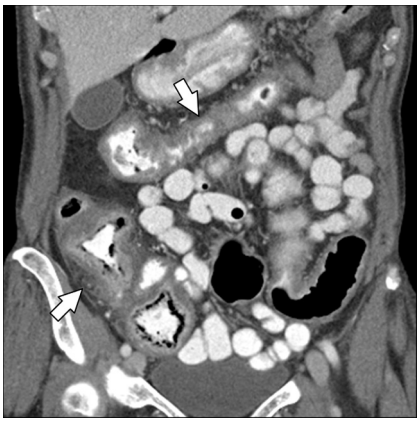

Fig. 1. Coronal reformatted contrast-enhanced computed tomography shows abnormal thickening of the ascending and transverse colon.

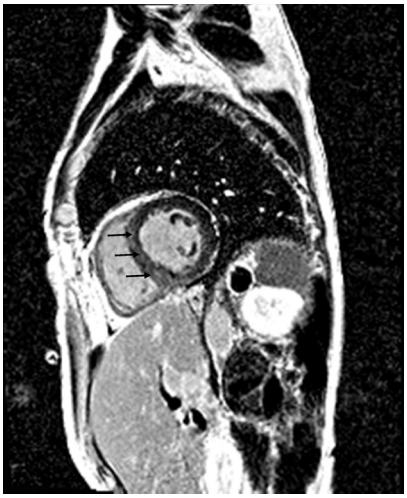

Fig. 3. Cardiac magnetic resonance imaging delayed gadolinium enhancement short-axis view illustrating patchy inflammation within the inferoseptum and anteroseptum (black arrows) in patient with Crohn's colitis flare-induced focal myocarditis.

mildly elevated at 233 ng/mL (range: 0–230 ng/mL). On examination, she was afebrile, normocardic, and normotensive. Physical examination was unremarkable. Electrocardiography revealed normal sinus rhythm, normal intervals, voltage criteria for left ventricular hypertrophy, without ST-T wave changes. Laboratory results revealed troponins of 1.14 ng/mL and 1.63 ng/mL (peak), creatine kinase-MB 2.1 ng/mL, and B-type natriuretic peptide 166 pg/mL (normal 0.2–100 pg/mL). She was transferred to the coronary care unit for presumed non-ST elevation myocardial infarction and treated with ticagrelor, aspirin, and heparin. During continuous telemetry monitoring, she had no atrial or ventricular arrhythmias. Chest X-ray showed clear lung fields and a small left-sided pleural effusion. The initial transthoracic echocardiogram (TTE) revealed a left ventricular ejection fraction (LVEF) of 45–50% and mild systolic LV dysfunction with basal to mid anteroseptal, inferoseptal, and mid inferolateral hypokinesis (Video Clip 1). On day 4, a coronary angiogram displayed angiographically normal coronaries, left heart catheterization revealed normal left ventricular end-diastolic pressure, and left ventriculogram showed normal LV systolic function without regional wall motion abnormalities. On day 5, cardiac MRI showed severe hypokinesis of the basal to mid anteroseptal LV. Delayed gadolinium enhancement (DGE) was notable for elevated extracellular volume in the septum (35–36%, normal 25%), patchy midwall (with sparing of the endocardium), delayed enhancement in the mid anteroseptal and inferoseptal LV in a non-vascular pattern suggestive of myocarditis, and normal pericardial thickness and enhancement (Fig. 3). Cardiac MRI T1 mapping revealed elevated T1 values in the mid septum due to myocardial edema (Fig. 4). Cardiac MRI T2 mapping illustrated high T2 values in the inferoseptum (62) and normal T2 values in the LV apical septum (40) and basal anterolateral LV (42) (Fig. 5A). Dark blood short T1 inversion recovery (STIR) short axis revealed increased signal intensity in mid septum illustrating myocardial edema (Fig. 5B). Collectively, this pattern of DGE, elevated extracellular volume, as well as elevated T1 and T2 values characterize the key cardiac MRI features of myocarditis [6]. Liver function (aspartate transaminase, alanine transaminase, alkaline phosphatase, total bilirubin, unconjugated/conjugated bilirubin) and thyroid function (thyroid stimulating hormone) tests were normal. Her *Clostridium difficile*, stool, and blood cultures were all negative. Stool ova and parasite examination was negative. Cytomegalovirus (CMV) viral load polymerase chain reaction was < 137 IU/mL (negative) as were her hepatitis serologies. Quantiferon gold analysis was indeterminant, but chest X-ray showed no infiltrate.

Given the amalgam of clinical, biochemical, and imaging data and the clinical time course presented above, we believe this is a

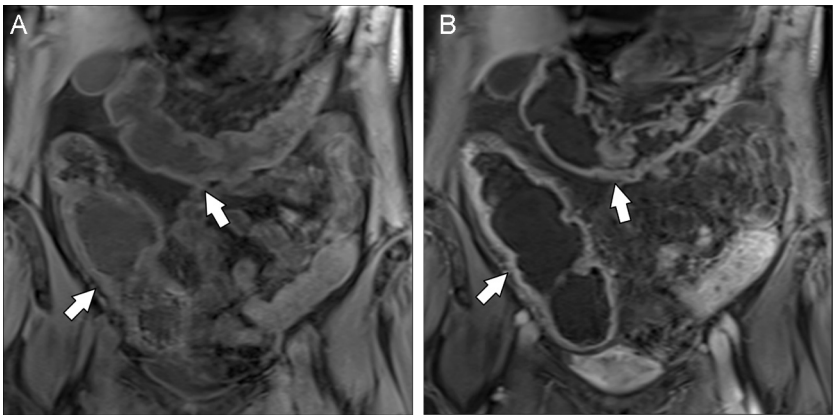

Fig. 2. (A) Coronal fat suppressed magnetic resonance imaging T1-weighted image shows abnormal thickening of the ascending and transverse colon. (B) Following IV contrast, there is enhancement of the wall and vasa recta from active inflammation consistent with colitis.

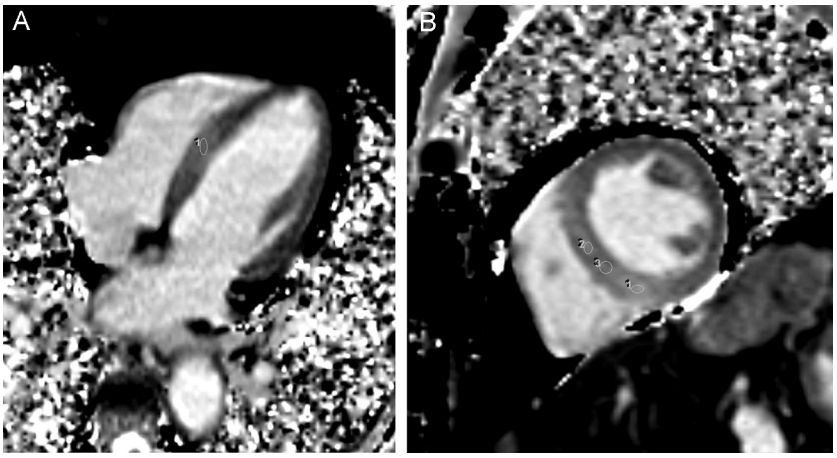

Fig. 4. Cardiac magnetic resonance imaging (MRI) T1 mapping. (A) T1 mapping, 4 chamber view shows high T1 values (1157) in the mid inferoseptum. (B) T1 mapping, short-axis view at mid septum demonstrates high T1 values of 1331, 1274, and 1192 in regions 1, 2, and 3, respectively.

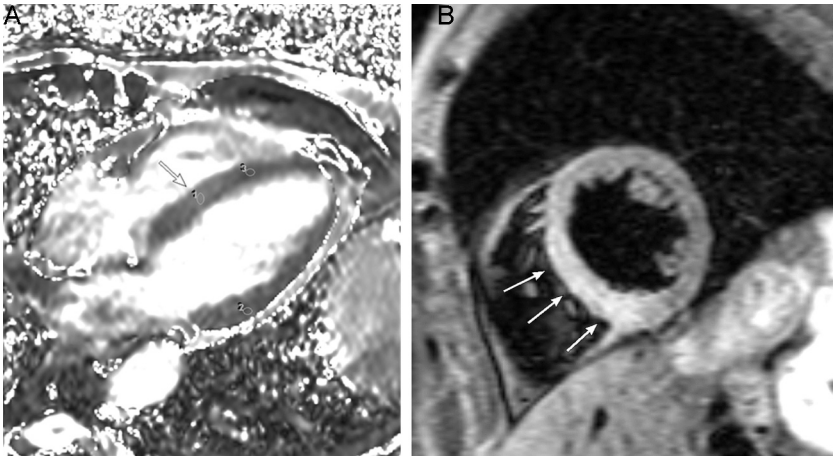

Fig. 5. Cardiac magnetic resonance imaging T2 mapping. (A) T2 mapping, 4-chamber view at mid septum [arrow, region of interest (ROI) 1] shows high T2 value of 62, indicating myocardial edema. T2 value is normal in left ventricular myocardium (ROI 2 at apical septum: 40 and ROI 3 at basal anterolateral: 42). (B) Dark blood short T1 inversion recovery short-axis view reveals increased signal intensity in the mid inferoseptum and anteroseptum due to myocardial edema.

unique case of Crohn's colitis-induced myocarditis. On day 6, she remained with abdominal pain with eating and fecal urgency, while her gastrointestinal bleeding had resolved and for this she received infliximab 5 mg/kg (300 mg IVPB). Over the next 3 days, her abdominal pain gradually improved. She was re-dosed with infliximab on hospital day 9. After this, her stools became more formed and her abdominal pain had completely resolved. On day 11, she underwent a flexible sigmoidoscopy which showed grossly normal appearing rectum and recto-sigmoid colon. The pathology showed normal colonic mucosa without pathologic change. Her CRP normalized to $<$0.5 ng/mL and ESR declined to 39 mm/hr. On day 12, she was discharged on an oral prednisone taper (40 mg on discharge, tapered over 3 months), metoprolol succinate 25 mg PO, and ramipril 2.5 mg PO. The follow-up TTE obtained 3 months later displayed normal LVEF of 60% without significant regional wall motion abnormalities (Video Clip 2).

Discussion

Myocarditis can be caused by infectious and non-infectious diseases. Infectious causes are the most common and include viral (e.g. hepatitis viruses, CMV, human immunodeficiency virus, influenza A and B), bacterial (staphylococcus, streptococcus, TB), parasitic, and fungal pathogens. Noninfectious causes include hypersensitivity reactions (antibiotics, insect bites, diuretics), systemic diseases (inflammatory bowel diseases, thyroid disorders, sarcoidosis, hypereosinophilia, rheumatoid arthritis, collagen-vascular diseases), cardiotoxins (alcohol, cocaine, medications), and radiation exposure. In terms of our patient, her blood cultures, CMV and hepatitis serologies were all negative. Her thyroid stimulating hormone and WBC with differential were normal and she had no illicit exposures or excess alcohol consumption. She also had no preceding viral prodrome suggestive of viral myocarditis. While, she was started on new medications, these medications were initiated after her clinical symptoms of Crohn's were present. Yet, our patient had clinical (abdominal pain, diarrhea, hematochezia), biochemical (elevated CRP and ESR), and imaging (CT and MR enterography) evidence illustrating Crohn's colitis. Additionally, her *C. difficile* and stool cultures were negative ruling out other common causes of pancolitis. Subsequent to these findings, she displayed clinical (chest pain), biomarker (elevated troponins), echocardiographic (regional wall motion abnormality), and cardiac MR (regional DGE, elevated ECV) evidence illustrating myocarditis. Given the comprehensive clinical, laboratory, and imaging data detailed above we believe our patient represents a unique case of Crohn's colitis-induced focal myocarditis.

Cardiac manifestations of IBD flares are rare, and include pericarditis, pericardial effusion, myocarditis, endocarditis, arrhythmias, and conduction disturbances [1]. There have been previous cases of IBD-associated myocarditis, but our case is different in several ways. Gruenhagen and colleagues reported a case of ulcerative colitis-associated myocarditis where there was subepicardial apical inferior, mid-apical, and inferolateral delayed enhancement on cardiac MR [3]. In contrast, we illustrate an atypical pattern of myocarditis involving the mid septum as well as an elevated ECV indicative of fibrosis on cardiac MR T1 mapping. Weiss et al. described a case of fulminant myocarditis (clinical heart failure, severe LV systolic dysfunction with an LVEF 30%, and inferior and septal hypokinesis) in a patient who one month later developed painful diarrhea in a patient with Crohn's disease [6]. Also, Nishtar and coworkers reported a patient with acute small bowel obstruction from active Crohn's disease who underwent hemicolectomy only to develop fulminant myocarditis (flash pulmonary edema and severe LV systolic dysfunction with LVEF 16%) after treatment of the Crohn's flare [5]. Lastly, Oh and colleagues describe a case in which a patient presented with fulminant myocarditis and mild Crohn's [4]. The patient had severe LV systolic dysfunction with akinesis of the basal to apical inferoseptum, anteroseptum, anterior, and inferior LV with an LVEF of 38%. In their case, the patient was diagnosed with myocarditis four weeks after the clinical manifestation of Crohn's colitis. In contrast to the above-mentioned studies, we present a case in which our patient displayed clinical, biochemical, and imaging evidence confirming a Crohn's colitis flare only to develop myocarditis, as supported by chest pain, elevated troponin levels, regional wall motion abnormalities, as well as DGE and elevated ECV, after having an established Crohn's flare. Classically, in acute myocarditis, there is focal delayed enhancement in a non-coronary distribution with the lesions more often involving the lateral free wall and generally originating more from the subepicardial aspect of the ventricular myocardium [5,7–9]. Contrast enhancement from the subendocardium is generally never seen with myocarditis. Our patient displayed patchy midwall DGE in the mid anteroseptum and inferoseptum, which is an atypical pattern for myocarditis.

In closing, we present a unique case of Crohn's colitis-induced focal myocarditis in which the pattern of myocardial inflammation is atypical and the severity of myocardial systolic dysfunction is mild despite a significant elevation in myocardial fibrosis as measured by the elevated ECV. To our knowledge, this is the first such case of its type.

Conflicts of interest

None declared.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jccase.2016.03.007.

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