CASE REPORT

Cardiac MRI-confirmed mesalamine-induced myocarditis

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SUMMARY

A 38-year-old Caucasian man with a medical history significant for inflammatory bowel disease (IBD) and mesalamine use presented to the emergency department with stabbing, pleuritic, substernal chest pain over the previous 2 days. Findings of leucocytosis, elevated cardiac enzymes and inflammatory markers, T-wave or ST-segment abnormalities and left ventricular systolic dysfunction suggested mesalamine-induced myocarditis. However, a cardiac MRI confirmed the diagnosis. Signs and symptoms improved within days of withdrawal of mesalamine, and initiation of corticosteroids and follow-up studies within the next year were unremarkable. Importantly, the diagnosis of mesalamine-induced myocarditis confirmed via cardiac MRI is a step rarely performed in published cases.

BACKGROUND

Mesalamine is a 5-aminosalicylate (5-ASA) anti-inflammatory agent used as first-line treatment of inflammatory bowel disease (IBD). Myocarditis has, rarely, been reported as a side effect in patients taking mesalamine; however, most cases did not confirm diagnosis using cardiac MRI.^{1–4} We present a case of probable⁵ mesalamine-induced myocarditis confirmed via cardiac MRI.

CASE PRESENTATION

A 38-year-old Caucasian man presented to the emergency department (ED) with stabbing, pleuritic, substernal chest pain over the previous 2 days. The patient's chest pain was worsened by lying down and was accompanied by nausea, vomiting, dyspnoea and a fever of 104.4°F. His medical history was significant for IBD diagnosed following a flexible sigmoidoscopy ~3 weeks prior (later diagnosed as Crohn's disease); on diagnosis of IBD, he was started on mesalamine delayed-release capsules (Delzicol) 800 mg three times/day (2.4 g/day) and a mesalamine suppository (Canasa) 1000 mg at bedtime. Despite 1 week on this regimen, the patient continued to have bloody diarrhoea two to three times/day and his oral mesalamine was increased to 2.4 g twice/day (4.8 g/day). One-week later, he developed multiple aphthous ulcers in his mouth and throat and was started on prednisone 40 mg daily to be slowly tapered over 1 month (prednisone was 20 mg once daily on admission). Other home medications included escitalopram 20 mg once daily for anxiety. The patient had no prior surgeries, was a non-smoker and was abstinent from alcohol for the previous month. The

Figure 1 12-lead ECG demonstrating sinus tachycardia with non-specific T wave abnormality in lateral leads.

patient had no family history of premature coronary artery disease or sudden cardiac death.

INVESTIGATIONS

Vital signs in the ED were heart rate (HR) 127 bpm, blood pressure 101/64 mm Hg, respiratory rate 18 per minute, oxygen saturation 94% breathing room air and temperature 99.2°F. Physical examination revealed laboured breathing and normally split S1 and S2 heart sounds with no murmurs, rubs or gallops. Significant abnormal laboratory values on presentation were: troponin I=3.37 ng/mL, creatinine kinase-MB isoenzyme (CK-MB)=14.1 ng/mL, white cell count= $12.2 \times 10^3/\text{mm}^3$, C reactive protein=6.08 mg/dL, erythrocyte sedimentation rate=29 mm/hour, lactate=5.5 mmol/L, aspartate aminotransferase=62 U/L, amylase=107 U/L, lipase=121 U/L and phosphorus=1.1 mg/dL. An ECG revealed sinus tachycardia (HR=127 bpm) with T-wave flattening (figure 1). Contrast-enhanced CT of the chest showed no pulmonary embolism, normal appearance of the thoracic aorta and no pleural effusion, pneumothorax

Figure 2 Late gadolinium enhanced cardiac MRI obtained on hospital day 3. Mid-ventricular short-axis cardiac MRI obtained approximately 10 min following administration of gadolinium demonstrating patchy hyper-enhancement with a mid-myocardial distribution in the posterior left ventricular wall and interventricular septum (arrows) (present case).

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Figure 3 MRI. (A) T2-weighted short-tau inversion recovery (STIR) MRI, four-chamber view. The normal myocardium is whitish-grey; the dark grey area in the basal lateral wall of the left ventricle represents myocardial oedema. (B) Delayed gadolinium enhanced MRI, four-chamber view. The normal myocardium appears black with this technique. The light grey area in the basal lateral wall of the left ventricle represents inflammation. (C) Delayed gadolinium enhanced MRI, short-axis view. This image orthogonal to image B better demonstrates the extent of inflammation in the lateral wall.

or consolidation. A transthoracic echocardiogram showed mildly impaired left ventricle systolic function (LVSD) with an ejection fraction (EF) of 40% and inferolateral wall hypokinesia. The patient was given a nitroglycerin 0.4 mg sublingual tablet with minimal improvement in chest pain. The chest pain was relieved following administration of fentanyl 50 µg. While in the ED, the patient empirically received single intravenous doses of ceftriaxone 1 g and azithromycin 500 mg for possible pneumonia.

The patient was admitted to the hospital with a preliminary diagnosis of myocarditis. Intravenous hydromorphone 1 mg was given every 4 h as needed for pain and treatment started with prednisone 20 mg once daily. All other medications were stopped. Approximately 5 h after admission, serum troponin I peaked at 8.70 ng/mL and then began to trend downward. A second ECG showed sinus tachycardia (HR=103 bpm) with a lessening of T-wave flattening. Extended-release metoprolol succinate 25 mg once daily was started for myocardial protection.

A normal coronary angiogram ruled out myocardial infarction on hospital day 2. However, ventriculography confirmed LVSD with estimated EF 40%. On day 3, cardiac MRI with

gadolinium contrast was performed and showed mild global hypokinesia of the left ventricle, and patchy mid-myocardial late gadolinium enhancement in the posterior wall of the left ventricle and, to a lesser degree, in the inferior interventricular septum (figure 2). (Additional four-chamber MRI views are seen in figure 3.) LVEF calculated from the cardiac MRI was 51%. Potential autoimmune causes of myocarditis including vasculitis, systemic lupus erythematosus and Sjögren's syndrome were ruled out.

By day 4, the ECG had normalised, troponin I decreased to 0.92 ng/mL and the CK-MB level was within normal limits (5 ng/mL). The patient's chest pain had resolved and he no longer required analgesia. On day 7, he was discharged on metoprolol succinate 25 mg once daily, alprazolam 0.25 mg every 6 h as needed, prednisone 20 mg once daily and escitalopram 20 mg once daily. One-month and 6-month follow-up ECGs were unremarkable. Repeat echocardiograms at 6 and 12 months revealed EFs of 55% and 60%, respectively. One year after admission, the patient's Crohn's disease was in remission and being managed with infliximab and 6-mercaptopurine.

Figure 4 Simplified summary of late gadolinium enhancement on cardiac MRI in this and prior case reports of mesalamine-induced myocarditis. A, apical; I, inferior; L, lateral; P, posterior; S, septal. Hash shading represents affected area. (A) Patchy, mid-myocardial enhancement in posterior wall and inferior interventricular septum (present case); (B) Subepicardial enhancement in anterior wall and transmural extension in interventricular septum; also in the interatrial septum (not shown);³ (C) Subepicardial enhancement in apical inferior wall and transmural enhancement in interventricular septum;⁴ (D) Subepicardial enhancement in inferior and lateral walls.²

Since prior case reports have shown return of cardiac symptoms on resumption of mesalamine or other 5-ASAs, no rechallenge was performed in our case.⁶

DISCUSSION

The exact mechanism for mesalamine-induced myocarditis is not well established;⁴ however, patients typically present with symptoms within 2–4 weeks after initiation (sometimes delayed when corticosteroids are used concurrently).² Common signs and symptoms of mesalamine-induced myocarditis include substernal chest pain, dyspnoea, fever, leucocytosis, elevated cardiac enzymes and inflammatory markers, T-wave or ST-segment abnormalities (T-wave flattening is particularly common) and LVSD.¹ In the current case, the patient developed the cardiac syndrome ~3 weeks after starting delayed-release and rectal

suppository therapy (the first such case reported for these mesalamine formulations). Resolution of symptoms in this case was faster than observed in many prior cases (4 days vs 1–2 weeks), but symptom resolution may have been expedited because of continued corticosteroid administration in our patient. Most importantly, the diagnosis of mesalamine-induced myocarditis in this case was confirmed via cardiac MRI, a step rarely performed in prior published cases.^{1–4} Interestingly, when comparing the cardiac MRI in this and previous cases, no consistent pattern in late gadolinium enhancement is apparent (figure 4); however, none of the patterns were inconsistent with myocarditis.⁷

Contributors WJS and KE performed data collection and wrote the manuscript. WLB and WJS edited the manuscript, and MWP provided the figures and interpreted the findings.

Competing interests None declared.

Patient consent Obtained.

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Learning points

- ▶ Mesalamine is a common treatment for Crohn's disease and, though rare, there is concern for a severe hypersensitivity reaction presenting as cardiac toxicity.
- ▶ A patient taking mesalamine, who presents with substernal chest pain, dyspnoea, fever, leucocytosis, elevated cardiac enzymes and inflammatory markers, T-wave or ST-segment abnormalities (T-wave flattening is particularly common) and left ventricular systolic dysfunction, should be considered for mesalamine-induced myocarditis.
- ▶ MRI is a useful tool to confirm diagnosis of mesalamine-induced myocarditis.

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