

CASE REPORTS

Mesalamine-induced myopericarditis - A case report

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ABSTRACT

Myopericarditis has occasionally been reported as a side effect of mesalamine in patients with inflammatory bowel disease. We present a 20-year-old woman with ulcerative colitis admitted with chest pain. After thorough investigation she was diagnosed with myopericarditis potentially related to mesalamine. There was complete clinical and laboratorial recovery following drug withdrawal. Although uncommon, the possibility of myopericarditis should be considered in patients with inflammatory bowel disease presenting with cardiac complaints. Early recognition can avoid potential life-threatening complications.

Key words: Mesalamine. Ulcerative colitis. Myopericarditis.

INTRODUCTION

Myopericarditis represents an inflammatory process affecting the heart muscle and pericardium. Acute pericarditis is responsible for up to 5% of admissions to the emergency department and may result from drugs, infections and autoimmune or idiopathic disorders (1). Several factors may be responsible for extraintestinal organ involvement in inflammatory bowel disease (IBD) and sometimes it can be difficult to differentiate the true extraintestinal manifestations, i.e., primary systemic affection by the disease itself, from secondary extraintestinal complications of the disease, caused by malnutrition, chronic inflammation or therapy side effects (2). Although uncommon, cardiac involvement has been reported in patients with IBD, especially in ulcerative colitis (UC) (3-5). Mesalamine is the standard treatment for patients with mild to moderate UC. Although uncommon, cardiac adverse events have been reported in patients taking mesalamine, including pericarditis, myocarditis and conduction defects (6). In this paper, we report a case of myopericarditis induced by mesalamine in a patient with UC. We appraise the clinical and laboratorial findings, discuss treatment and prognosis, and review the available literature.

CASE REPORT

We report the case of a 20-year-old woman admitted with asthenia, myalgia, arthralgia and chest pain. Her medical history was relevant for mild ulcerative proctitis diagnosed 4 years before. Her family history was significant for IBD (paternal uncle). Due to a recent flare, the patient had been started on oral (3 g/day) and topical (3 g/week) mesalamine with good response. Two weeks before, she started complaining of asthenia, myalgia and arthralgia involving the wrists and lower back. In the following week, she developed retrosternal discomfort and palpitations. Her physical examination did not show any relevant findings including fever, lymphadenopathies, rash, arthritis or heart murmurs. Her abdominal examination was unremarkable. Blood analysis showed normal white blood cells of 7.82×10^9 ($4.0-11.0 \times 10^9$) with mild eosinophilia (820 eosinophils) and elevated C-reactive protein (CRP) of 1.77 mg/dl (< 0.5 mg/dl). There was also a slight elevation of creatine-kinase (CK) - 510 (< 211 U/L), CK-MB - 587 (< 360 U/L) and lactate dehydrogenase - 418 (< 372 U/L). Troponin I was within normal range - 0.01 (< 0.07 µg/L). Both electrocardiogram and echocardiogram showed no relevant findings. An extensive workup including chest CT, articular X-ray, electromyogram and autoimmune and microbiologic studies failed to show an etiology for her disease (Table I). A presumptive diagnosis of idiopathic myopericarditis was assumed and the patient was discharged with symptomatic therapy. The patient restarted mesalamine. She returned to our emergency department two days later with the same complaints. A recap of her medical history showed that mesalamine was a drug potentially involved. After exclusion of other causes, we assumed the diagnosis of mesalamine-induced myopericarditis. Mesalamine was stopped and the patient started on oral prednisolone and azathioprine, with clinical and laboratorial resolution (Fig. 1). Follow-up cardiac

Received: 27-09-2015

Accepted: 29-09-2015

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Bernardo S, Fernandes SR, Araújo-Correia L. Mesalamine-induced myopericarditis - A case report. *Rev Esp Enferm Dig* 2016;108(11):753-756.

DOI: 10.17235/reed.2016.4016/2015

Table I. Autoimmune and microbiologic investigation

ANAs (titer)	1:60
Anti-sDNA, HLAB27, ANCA, ASMA, anti-SSA, anti-SSB, anti-RNP, anti-scl70, anti-JO1	Negative
Cytomegalovirus	IgG+, IgM-
Parvovirus	IgG+, IgM-
Herpes virus type I	IgG+, IgM-

ANA: Antinuclear antibody; anti-sDNA: Anti-double stranded DNA antibody; HLAB27: Human leukocyte antigen B27; ANCA: Anti-neutrophil cytoplasmic antibody; ASMA: Anti-smooth muscle antibody; anti-SSA and SSB: Sjögren's-syndrome-related antigen A and B antibody; anti-RNP: Small nuclear ribonucleoprotein antibody; anti-scl70: Anti-topoisomerase I antibody; anti-JO1: Aminoacyl-tRNAsynthetases antibody.

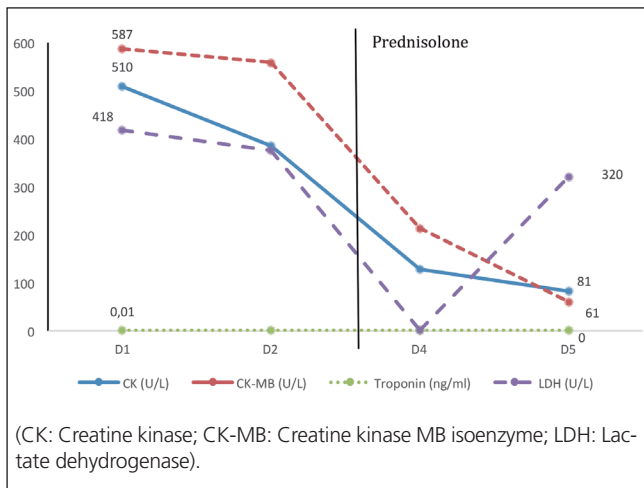


Fig 1. Laboratorial evolution showing rapid improvement of laboratory tests.

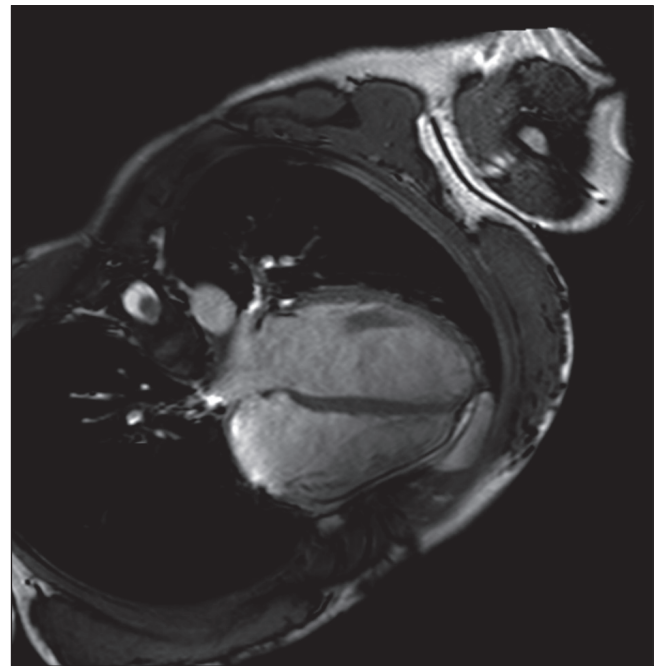


Fig. 2.

magnetic resonance revealed no abnormalities (Fig. 2). The patient remains asymptomatic and in clinical remission of her UC.

DISCUSSION

It is estimated that 25% to 36% of patients with IBD will present at least one extraintestinal manifestation (3). Among cardiologic complications, acute pericarditis appears to be the most common one, accounting for up to 70% of the reported cases (6). Cardiac complications are independent of the bowel disease and the natural history may be highly variable with recurrent episodes having been reported (4). The incidence of myopericarditis appears to be similar between genders (5). As mentioned above, drugs can be involved in the pathogenesis of IBD related cardiac manifestations. It must be noted that most reports of myopericarditis complicating IBD involve concomitant aminosalicylate therapy, making it difficult to exclude a drug-related effect (7-10). Several mechanisms have been proposed for mesalamine-induced myopericarditis: a) IgE-mediated allergic reaction; b) direct cardiac toxicity; c) cell-mediated hypersensitivity;

and d) humoral antibody response. The theory involving cross-reactivity between antibodies produced against mesalamine and the myocardium tissues is considered as the most credible one (7-9). In our case, eosinophilia may have been related to a hypersensitivity reaction. Clinical manifestations typically occur within 2-4 weeks of drug initiation (7,8), but they may occur as early as 48 hours or after years of treatment (11,12). Curiously, steroids may delay the onset of manifestations (7). Withdrawal of mesalamine usually results in resolution of clinical manifestations over 7 to 14 days. Reintroduction of mesalamine can lead to repeated episodes. This holds true regardless of the dose and route of administration (4,13). In one report, pericarditis developed when changing the route of administration of mesalamine from oral to rectal treatment (14). In our case myopericarditis was confirmed by clinical presentation and elevation of cardiac enzymes. After excluding other possible causes, including another autoimmune disorders and viral and bacterial infections, myopericarditis-induced by mesalamine is the most likely cause.

lamine was assumed. In the cases previously described as being the result of medication, there is in fact, as in our case, a clinical and laboratorial resolution with the discontinuation of the therapy, suggesting a cause-effect relationship. The recommended treatment of myopericarditis includes non-steroid anti-inflammatory drugs or steroids (11). Our patient was also started on steroids for control of the UC disease. The intolerance to mesalamine forced us to start azathioprine in order to maintain the patient in remission. Nevertheless, this puts our patient with mild proctitis at risk for azathioprine related side-effects and complications, namely infections and cancer. In conclusion, we report a case of mesalamine-induced myopericarditis successfully managed by drug discontinuation and steroids. Myopericarditis should always be considered in the differential diagnosis of chest pain. In addition, this important side-effect should be considered when administering 5-aminosalicylate compounds.

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