CASE REPORT

Acute Pericarditis Associated with 5-Aminosalicylic Acid (5-ASA) Treatment for Severe Active Ulcerative Colitis

Naoto Ishikawa, Takuroh Imamura, Kouji Nakajima, Junichi Yamaga, Hiroaki Yuchi, Masaaki Ootsuka, Haruhiko Inatsu, Toshihiro Aoki and Tanenao Eto

Abstract

A 17-year-old male who had been diagnosed with ulcerative colitis was prescribed 80 mg prednisolone and 1,500 mg 5-aminosalicylic acid (5-ASA) per day. Two weeks after initiating therapy, he was referred to our hospital for evaluation of chest pain and high fever. Electrocardiography (ECG) showed ST elevation in limb and precordial leads. Chest pain with high fever and ECG changes were resolved after 5-ASA was discontinued. Three weeks later, the administration of a low dose of 5-ASA was associated with the immediate recurrence of pericarditis associated with chest pain, suggesting a hypersensitive reaction to 5-ASA in this patient.

Introduction

Acute pericarditis is a syndrome caused by inflammation of the pericardium characterized by chest pain. The most common causes of acute pericarditis include idiopathic or viral pericarditis, uremia, bacterial infection, trauma, acute myocardial infarction, pericardiotomy associated with cardiac surgery, tuberculosis, neoplasm and drugs (1). Acute pericarditis has also been identified in patients with inflammatory bowel diseases (IBD), in whom it may appear as an intestinal manifestation (2–8) or as an adverse reaction to therapeutic compounds (9–14). We describe 5-aminosalicylic acid (5-ASA) induced pericarditis in a 17-year-old male treated for ulcerative colitis, and discuss with the literature relative to this reaction.

Case Report

A 17-year-old male with severely active ulcerative colitis was diagnosed based upon his medical history, including findings of colonoscopy, air-contrast radiography, and histopathology. Therapy of 80 mg of prednisolone and 1,500 mg of 5-ASA per day was administered. The dosage of prednisolone was gradually reduced at a rate of 10 mg per week.

Two weeks after the initiation of the therapy, he complained of acute, severe and substernal chest pain and profound fatigue. A physical examination revealed the following: body temperature of 38.6°C, blood pressure of 120/70 mmHg, and a pulse of 110 beats/minute. The third heart sound was not clear and the friction rub component was not audible upon admission. Electrocardiography (ECG) revealed ST-segment elevation in the limb and precordial leads (II, III, aVF and V5-6) (Fig. 1A). Echocardiography revealed diffuse hypokinesis of the left ventricle (LV), ejection fraction reduced by 40% and a small pericardial effusion (Fig. 2A). A complete blood cell count (CBC) revealed that the number of white blood cells (WBC) had increased to 18,400/μl. Blood chemistry results, namely creatine phosphokinase (CK), creatine phosphokinase-MB (CK-MB), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH), were normal, whereas troponin T was slightly increased to 0.13 ng/ml. The C-reactive protein (CRP) level was 8.7 mg/dl. At this point, 5-ASA was discontinued and prednisolone was maintained at a dose of 60 mg per day. These measures improved his symptoms, normalized the range of WBC and CRP, resolved the ST-segment elevation (Fig. 1B), and improved cardiac function; further pericardial effusion disappeared (Fig. 2B). In addition to prednisolone treatment, granulocytapheresis (GCAP) therapy was implemented in place of 5-ASA once each week using a G-1 column.

Over the next three weeks, the prednisolone dose was reduced to 30 mg per week, which did not exacerbate the symptoms of pericarditis or colitis. A trial low-dose 5-ASA of 62.5 mg was administered according to Katsumata et al (15) because the delayed onset of initial pericarditis indicated that drug allergy remained questionable. Furthermore, pericarditis is a complication of ulcerative colitis (2–8). After written, informed consent was obtained, a low dose 5-ASA was given to the patient under ECG monitoring. However, 6 hours after taking a...
low dose 5-ASA, chest pain acutely recurred and high fever accompanied ST-segment elevation in the limb and precordial leads. Five hours later, his symptoms and ST elevation on ECG had completely improved. In place of 5-ASA, an enema containing 1.25 mg of beclomethasone dipropionate (BDP) was administered daily and prednisolone was tapered. Three weeks later, the ulcerative colitis was controlled by 20 mg prednisolone and a 1.25 mg BDP enema, and remained quiescent.

**Discussion**

Pericarditis represents a rare extra intestinal manifestation of inflammatory bowel disease such as ulcerative colitis and Crohn's disease (2–8), and it may occur independently of disease activity and may even be present during the inactive phase of the disease. The drugs used to treat IBD can also occasionally cause pericarditis (9–14). Iizuka et al suggested that myocarditis and pleuropерicarditis associated with IBD could be divided into drug-induced disease and autoimmune disease in relation to IBD (16). The patient described here developed acute pericarditis two weeks after the initiation of 5-ASA therapy, a condition that was resolved by discontinuation of the drug. The later administration of 5-ASA rapidly reproduced the chest pain and ST-segment elevation on ECG, suggesting a drug hypersensitive allergic response.

The pathogenesis of pericarditis induced by 5-ASA remains unknown. Gujral et al proposed that sulfasalazine-induced lupus-like syndrome typically presents pleuropерicarditis associated with an elevated titer of anti-nuclear and anti-double-stranded DNA antibodies (9). Jenss et al performed serial lymphocyte stimulation tests on the serum of a patient with pericarditis or pericardial effusion induced by 5-ASA. Because the proliferation index of lymphocytes from the patient increased, they speculated that this phenomenon constitutes an immedi-
Pericarditis Caused by 5-ASA Treatment

Figure 2. Echocardiogram shows diffuse hypokinesis of the LV and small pericardial effusion (arrows) (A) as well as improved LV function two days after initial symptoms. (B) PE: pericardial effusion, LV: left ventricle.

We postulate that pericarditis in our patient occurred because an autoimmune disease, namely ulcerative colitis caused 5-ASA induced hypersensitivity, and that the two-week delay in the initial symptoms was caused by the high dose of steroid that inadvertently abrogated the hypersensitivity. Furthermore, GCAP therapy may have removed activated neutrophils as well as lymphocytes, thus preventing an autoimmune reaction associated with ulcerative colitis.

Because 5-ASA is effective against IBD, it was necessary to estimate its use in maintaining remission for this patient. Furthermore, because the first drug lymphocyte stimulation test (DLST) was negative, we confirmed whether or not pericarditis had been induced by 5-ASA. We therefore administered a low dose of 5-ASA to the patient after obtaining his written informed consent.

We could not confirm the presence of the 3rd heart sound and friction rub on admission. Although friction rub is usually audible in patients with pericarditis, frequent examination is necessary to detect it because of its evanescent nature (18). Systolic dysfunction was revealed by echocardiography as well as pericardial effusion, suggesting myocarditis in addition to pericarditis. However, increases in the levels of cardiac enzyme such as CK, AST and LDH were not evident, whereas the troponin T level was slightly increased upon admission. This may account for the myocardial involvement in this patient.

In conclusion, we presented a case of pericarditis that was most likely related to the ingestion of 5-ASA. The timing of the symptoms and the recurrence with low dose 5-ASA therapy indicate drug-hypersensitivity. Any patient treated with 5-ASA who develops chest pain, shortness of breath, or pericardial friction rub, should be considered as having pericarditis induced by drug-hypersensitivity or as having an extra manifestation of an underlying intestinal condition. The present report found that pericarditis induced by 5-ASA is a life-threatening hypersensitive reaction that requires prompt diagnosis and immediate discontinuation of the drug.

References

4) Thompson DG, Lennard-Jones JE, Swarbrick ET, Bown R. Pericarditis