

# Left ventricular systolic dysfunction in two patients with ankylosing spondylitis: What is the role of corticosteroids?

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## Abstract

Ankylosing spondylitis (AS) is a chronic inflammatory condition that most commonly affects the axial skeleton. The most common cardiac manifestation in patients with AS is the aortic root and valve disease, followed by conduction and rhythm abnormalities, decreased coronary flow reserve, myocardial infarction, and diastolic dysfunction. However, the presence of systolic dysfunction has been less described in patients with AS. Herein we present two cases of idiopathic dilated cardiomyopathy in patients with AS. These patients were noted to have an improvement of their ejection fraction following treatment of AS. Clinical and echocardiographic improvement on anti-inflammatory treatment might be a clue to the inflammatory nature of this myocardial problem, and further investigations to study the issue is required.

**Keywords:** Ankylosing spondylitis, systolic dysfunction, corticosteroids

## Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory condition that most commonly affects the axial skeleton, including the spine and sacroiliac joints. The most common cardiac manifestation in patients with AS is the aortic root and valve disease, which has been reported in up to 82% of patients (1). Other less common cardiac abnormalities that are observed in patients with AS include conduction and rhythm abnormalities, decreased coronary flow reserve, myocardial infarction, and diastolic dysfunction. However, the presence of systolic dysfunction has been less described in patients with AS. Herein we present two cases of idiopathic dilated cardiomyopathy in patients with AS. These patients were noted to have an improvement of their ejection fractions following treatment of AS, suggesting that cardiomyopathy in AS may be reversible with an effective treatment of the underlying inflammatory process. Written informed consent was obtained from patients who participated in this study.

## Case Presentations

### Case 1

A 25-year-old man, with a known case of AS since 18 months, was referred to our Heart Failure Clinic with the New York Heart Association (NYHA) function class II of dyspnea on exertion. Heart failure was diagnosed prior to his rheumatologic problem, and he was partially treated using an angiotensin-converting enzyme inhibitor [captopril (Captopril, Rouz Darou; Tehran, Iran) 25 mg/BID (i.e., two times a day)] only. Complete rheumatologic panels were ordered, which established the presence of a seronegative spondyloarthropathy. He was receiving indomethacin (Indomethacin, Loghman; Tehran, Iran), sulfasalazine (Sulfasalazine, Mehr Darou; Tehran, Iran), and prednisolone (Prednisolone, Iran Hormone; Tehran, Iran) for AS. Sulfasalazine and prednisolone were initiated after an AS diagnosis, and the doses were maintained at 2000 and 2.5 mg daily, respectively.

On arrival to our clinic, his cardiovascular examination revealed a regular heart rate, normal S1 and S2, and left-sided S3. No jugular venous distension was noted. The baseline echocardiography revealed mild left ventricular (LV) enlargement with severe systolic dysfunction [left ventricular ejection fraction (LVEF)=30%] and grade 2 diastolic dysfunction, normal right ventricular (RV) size and function, estimated systolic pulmonary artery pressure of 30 mmHg, no aortic stenosis or regurgitation, mild mitral regurgitation, and mild tricuspid regurgitation. Tissue Doppler study confirmed a reduced systolic myocardial velocity and a significant diastolic dysfunction. A complete laboratory examination, including electrocardiogram, calcium and magnesium levels, complete blood test, liver function tests, renal function tests (blood urea nitrogen and creatinine levels), serum electrolyte levels, thyroid-stimulating hormone levels, hemoglobin A1C, lipid profile, human immunodeficiency virus serological screening, and antinuclear antibody titer,



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was performed to rule out reversible causes of systolic dysfunction. Coronary artery disease was ruled out according to a normal multislice spiral computed tomography coronary angiography. After initial evaluation, standard heart failure medications, including captopril (Captopril, Rouz Darou; Tehran, Iran), 12.5 mg/TID (i.e., three times a day); carvedilol (Carvedilol, Abidi), 3.125 mg/BID; spironolactone (Spironolactone, Iran Hormone; Tehran, Iran), 12.5 mg/daily; furosemide (Furosemide, Alborz Darou), 40 mg/BID; and vitamin supplementation and recommendations for diet and rehabilitation were prescribed and neurohormonal blockers were up-titrated during the next visits, attempting to get close to the target doses, according to the latest guidelines. The patient became better with respect to the functional class and remained stable; follow-up echocardiography revealed similar findings after 4 months. Five months after the initial visit, he experienced worsening of AS symptoms, and his rheumatologist decided to try higher doses of corticosteroid (1 mg/kg oral prednisone for 3 weeks tapered over a month to 15 mg daily). Thereafter, the clinical symptoms of heart failure dramatically improved. A repeat echocardiography at 2 months after a high dose corticosteroid therapy revealed a significant improvement in LVEF (LVEF=50%), mild LV enlargement, normal RV size and function, and mild diastolic dysfunction (Grade I). After therapy, the patient remained asymptomatic at 6 months follow-up, and a limited echocardiography revealed acceptable LV and RV function.

### Case 2

A 45-year-old man, with a known case of AS since 8 years, was referred to our Heart Failure Clinic because of the development of dyspnea on exertion with NYHA function class II since 6 months. On arrival to our clinic, his vital signs included a blood pressure of 120/80 mmHg, heart rate of 85/min, respiration of 10/min, and temperature of 36.5°C. On cardiovascular examination, he had elevated jugular venous pulsation, a soft left-sided S3, and Grade 2/6 systolic murmur. Mild ankle edema was noticed as well. He had negative rheumatology screening panels that were performed earlier. His past medications included five courses of infliximab (Remicade, Janssen Biotech; PA, USA) for the treatment of AS. Echocardiography revealed moderate LV enlargement and moderate to severe systolic dysfunction (LVEF=25%), Grade 2 diastolic dysfunction, mild mitral regurgitation, mild RV enlargement, and moderate systolic dysfunction. Reversible causes of systolic dysfunction were ruled out according to a thorough investigation similar to patient 1. Standard anti-failure therapy, in-

cluding lisinopril (Modapril, Modava; Tehran, Iran), 5 mg daily; carvedilol (Carvedilol, Abidi), 3.125/BID; spironolactone (Spironolactone, Iran Hormone), 25 mg daily; and furosemide (Furosemide, Alborz Darou), 40 mg/BID, was initiated, and he was recommended regarding his diet and exercise. Over the next year, after a short period of stabilization, his symptoms worsened and he required higher doses of diuretics and was listed for heart transplantation. Echocardiography findings confirmed progressive decline in both the ventricular function (LVEF=15% and moderate to severe RV dysfunction). Two months later, he experienced a flare up of AS with polyarthritis, and his rheumatologist initiated oral corticosteroid [dexamethasone (Dexamethasone, Iran Hormone; Tehran, Iran), 1.5 mg/day] and maintained it for 6 months. Parallel with relief in arthritis symptoms, his heart failure symptoms improved, which required fewer diuretics; blood pressure increased; and his neurohormonal blocker regimen optimized. A repeat echocardiography study after 3 months following corticosteroid therapy demonstrated a moderate LV enlargement with dramatic improvement in systolic function (LVEF=40%–45%), mild RV enlargement, and systolic dysfunction, mild mitral regurgitation, and Grade 1 diastolic dysfunction. The patient remained stable with NYHA function class I in 1 year follow-up and was removed from transplantation list.

### Discussion

We demonstrated two cases of idiopathic dilated cardiomyopathy in patients with AS whose responses to standard medical treatment of heart failure were suboptimal. After initiating high-dose corticosteroids for their inflammation flare-up, we encountered a dramatic improvement in their clinical symptoms and echocardiographic measurements.

Unique cardiac complications of AS are the aortic root and valve diseases. Systolic dysfunction may arise as a consequence of the aortic valve disease, but coexistence of dilated cardiomyopathy with AS has not been described. Although previous studies have demonstrated the presence of diastolic dysfunction in AS, Yildirim et al. (2) found a significant diastolic dysfunction with an abnormal relaxation pattern in patients with AS. Gould et al. (3) also revealed significant decreases in peak filling and time to peak filling during strenuous activity in patients with AS.

However, as an inflammatory rheumatologic disease, it does not appear to be so weird to observe dilated cardiomyopathy in patients with AS because several rheumatologic disease have been described to be associated

with dilated cardiomyopathy. Cardiomyopathy was described in 3%–30% of patients with rheumatoid arthritis (RA) in postmortem studies (4). Similarly, other population-based (5) and clinic-based RA cohorts (6) demonstrated the association between RA and congestive heart failure. The EUSTAR registry enrolled 7073 consecutive patients with systemic sclerosis and demonstrated an overall prevalence of 5.4% of reduced LVEF in these patients (7).

Herein we described two cases of idiopathic dilated cardiomyopathy in patients with AS. These cases are being reported because to best of our knowledge no similar case has been reported to date. One of the patients had begun to exhibit symptoms of heart failure from the beginning of the symptoms of AS, whereas the other one developed symptoms of heart failure after 2 years following the onset of AS.

Moreover, we demonstrated that the clinical course and echocardiographic measures of both patients dramatically responded to high-dose corticosteroid therapy, which was administered for the underlying AS. The role of corticosteroids in the prevention and/or treatment of cardiomyopathy has been demonstrated in several inflammatory and non-inflammatory conditions. Barber et al. (8) demonstrated that oral corticosteroid treatment in patients with Duchenne muscular dystrophy is associated with delayed onset of cardiomyopathy in these patients. They revealed that the duration of corticosteroid therapy positively correlates with delayed cardiomyopathy onset. Kühl et al. (9) also demonstrated that immunosuppressive treatment in a subgroup of patients with dilated cardiomyopathy having continuing active inflammatory process results in a clinical, hemodynamic, and immunohistological improvement in 60%–70% of patients. Moreover, Wojnicz et al. (10) showed a long-term benefit of immunosuppression with prednisone and azathioprine in patients with dilated cardiomyopathy because of immunohistologically proven myocarditis. However, we had no proven data regarding the status of inflammatory process in the myocardium of our patients with AS. It might be possible that an active ongoing inflammation was present in their myocardium, which improved after initiating high-dose corticosteroid for simultaneous AS flare-up.

In conclusion, AS might be associated with a state of myocardial disease presenting as a progressive systolic dysfunction. Clinical and echocardiographic improvement on anti-inflammatory treatment might be a clue to the inflammatory nature of this myocardial problem, and further investigations to study the issue are required.

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