

Rapid Resolution of Severe Myocardial Dysfunction in a Patient with Rheumatoid Arthritis by Intravenous Immunoglobulin and Steroid Treatment

Chin-Yu Lin,^{1,2} Chien-Yi Hsu^{1,2} and Po-Hsun Huang^{1,2,3}

A 64-year-old man with rheumatoid arthritis (RA) presented to our emergency department with severe chest tightness and dyspnea. His electrocardiography (ECG) showed multiple premature atrial complexes (PACs) with wide QRS, and transthoracic echocardiography revealed severe hypokinesis of the left ventricle. The patient later developed sudden cardiovascular collapse with presumed fulminant myocarditis and cardiogenic shock. Further investigation showed that coronary angiogram, viral studies and autoimmune vasculitis markers were all negative. After high-dose intravenous immunoglobulin (IVIG) and systemic steroid were administered, a dramatic improvement of clinical conditions was observed, with an increase of the left ventricular ejection fraction (LVEF) from 10% to 42% within one week, and a resolution of the wide QRS on the ECG. The rapid recovery from left ventricular dysfunction by treatment with IVIG and systemic steroid suggests immunotherapy might be effective in RA patients with acute fulminant myocarditis.

Key Words: Fulminant myocarditis • Intravenous immunoglobulin • Rheumatoid arthritis • Systemic steroid

INTRODUCTION

Rheumatoid arthritis (RA) is one of the most common types of inflammatory arthritis and affects about one percent of the population.¹ Patients with RA are at an increased risk of mortality attributed to increased risk of cardiovascular death, ischemic heart disease, and heart failure, but rarely myocarditis.² Immunosuppressive therapy has been investigated in acute myocarditis, but its efficacy has not yet been proven in a large ran-

domized trial.³ Here, we report a case of presumed acute fulminant myocarditis in a 64-year-old male with RA who had presented with severe myocardial dysfunction but then recovered dramatically after high-dose intravenous immunoglobulin (IVIG) and systemic steroid therapy.

CASE REPORT

A 64-year-old man had been diagnosed with RA at the age of 60 (according to the 2010 RA Classification Criteria⁴) and was under regular clinical follow-up thereafter. He had RA-related secondary osteoarthritis, and had undergone bilateral total knee and right total hip arthroplasty. His regular medications included hydroxychloroquine (200 mg twice daily), methylprednisolone (4 mg twice daily), leflunomide (20 mg once daily) and etoricoxib (60 mg once daily). Progressive migratory ar-

Received: July 4, 2013

Accepted: November 2, 2013

¹Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital; ²Cardiovascular Research Center; ³Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan.

Address correspondence and reprint requests to: Dr. Po-Hsun Huang, Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, No. 201, Sec. 2, Shih-Pai Road, Taipei 112, Taiwan. Tel: 886-2-2875-7434; Fax: 886-2-2876-3336; E-mail: huangbs@vghtpe.gov.tw

thrititis with intermittent onset was noted two months prior to admission, with the patient's Disease Activity Score (DAS-28) for RA based on C-reactive protein (CRP) increasing from 1.79 to 3.85 (from remission status to moderate activity in RA). Unfortunately, the patient suffered from acute onset chest tightness and shortness of breath in the early morning, and presented to our emergency department when symptoms had persisted for 3 hours.

Electrocardiography (ECG) showed multiple premature atrial complexes (PACs) with wide QRS and right bundle branch block (RBBB) morphology (Figure 1). A subsequent chest X-ray showed cardiomegaly and pulmonary congestion. Laboratory data indicated mildly elevated cardiac troponin level (troponin I: 0.08 ng/ml; normal range: < 0.05 ng/ml). However, the patient experienced sudden cardiovascular collapse two hours af-

ter arrival at the emergency department with pulseless electrical activity and refractory to cardiopulmonary resuscitation.

Venoarterial extracorporeal membrane oxygenation (ECMO) was applied immediately to the patient. Emergent chest computed tomography revealed neither aortic dissection nor pulmonary embolism. Thereafter, urgent coronary arteriography was performed, given the tentative diagnosis of acute myocardial infarction complicated with cardiovascular collapse. The patient's coronary angiogram showed normal coronary artery, but left ventricular end diastolic pressure was highly elevated (41 mmHg). Additionally, transthoracic echocardiogram showed severe global hypokinesis with left ventricular ejection fraction (LVEF, 10%) and engorged inferior vena cava (IVC), indicating cardiogenic shock. The following arterial blood gases revealed metabolic acidosis (PH



Figure 1. (A) The initial electrocardiography shows premature atrial complexes with wide QRS and right bundle branch block morphology. (B) The electrocardiography on day 2 after treatment shows sinus tachycardia with narrow QRS.

7.09, PaO₂ 526 mmHg, PaCO₂ 36 mmHg, HCO₃ 10.9 mmHg); blood pressure was 90/60 mmHg under high dose of norepinephrine and dopamine infusion. The following biochemical data revealed extreme elevation of creatine kinase (CK) = 9999 U/L (normal range from 27 to 168 U/L), CK-MB = 627 U/L (normal range < 13 U/L) and troponin I >1000 ng/ml (normal range < 0.05 ng/mL). Studies evaluating vasculitis, including anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies (c-ANCA and p-ANCA), thyroid function, and procalcitonin were within normal values, and myocarditis-related viral studies were negative. Moreover, the viral profiles (hepatitis A, hepatitis B, hepatitis C, human immunodeficiency virus, cytomegalovirus PCR, Epstein-Barr virus profile, herpes simplex virus IgM, mumps IgM, measles IgM, enterovirus IgM, Varicella zoster virus IgM, and influenza antigen test) all showed negative.

Acute fulminant myocarditis was strongly suspected. We administered methylprednisolone (125 mg/day) and IVIG at a total dose of 1.3 g/kg. The patient's clinical improvement was dramatic, such that he discontinued the inotropic agent on day 2, removed the ECMO on day 6, and stopped continuous veno-venous hemofiltration on day 7. The patient's LVEF improved to 45 % (Figure 2) on day 7 with merely mild apical hypokinesis, and his EKG returned to a normal sinus rhythm. The ECG changes are presented in Figure 1.

DISCUSSION

Acute myocarditis, an inflammatory process involving the heart muscle, shares similar clinical manifestations with acute myocardial infarction, including chest tightness, hemodynamic instability, regional wall motion abnormalities, and elevated cardiac enzymes.⁵ The presence of myocarditis has been reported in rheumatologic diseases including necrotizing vasculitis, systemic lupus erythematosus, and RA.⁶ However, in the prior literature, RA has seldom been found to cause myocarditis.⁷ Additionally, the regular medications of this patient have not been associated with cardiac toxicity in previous reports. RA-related myocarditis responded favorably to high dose methylprednisolone as initial therapy in previous case reports.⁷ On the other hand, viral myocarditis did not respond well to IVIG therapy in a

previous review article.⁸ In 35% of RA patients, disease infiltration to the atrioventricular node causes RBBB morphology on ECG.⁹

In our patient, the initial ECG showed wide QRS with RBBB morphology and multiple PACs. Interestingly, the QRS complex on ECG became narrower after successful treatment. The acute onset of wide QRS and angina pectoris in RA patients might be an indication of accompanying myocarditis. Currently, there are no reports regarding the effect of IVIG for patients with RA accompanying myocarditis that involve larger patient populations. However, in Kawasaki disease, IVIG at a total dose of 2 g/kg has been suggested as initial treatment. There is some evidence to support the benefit of immunosuppressive therapy in patients with sarcoidosis, giant cell myocarditis and systemic autoimmune diseases, in particular lupus erythematosus, scleroderma, and polymyositis.³ In our patient, systemic steroid and IVIG were administered as an initial dual therapy due to his critical condition and severe left ventricular dysfunction.¹⁰ Of note, the LVEF improved dramatically after immunosuppressive treatment, suggesting that RA-related fulminant myocarditis might be responsive to therapy with IVIG and systemic steroid. We cannot provide direct evidence to demonstrate that the improvement of cardiac function in this patient was related to IVIG and steroid treatment, and the relationship between acute myocarditis and RA. However, further basic research and prospective clinical studies are needed to investigate the mechanism of autoimmune myocarditis and the efficacy of immunosuppressive therapy in dif-

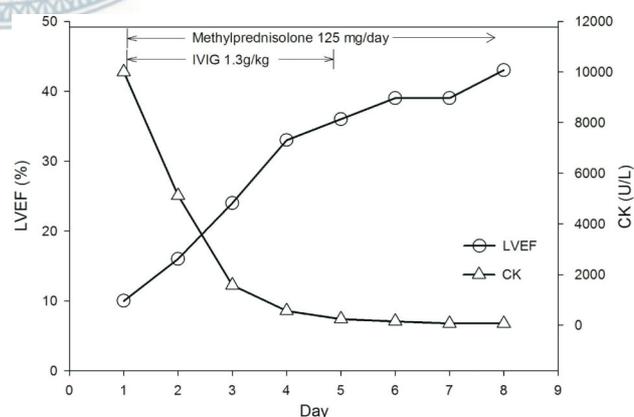


Figure 2. The figure illustrates dynamic change of left ventricular ejection fraction (LVEF) and creatine-kinase (CK) level after systemic steroid and intravenous immunoglobulin (IVIG) treatment.

ferent combination regimens. In conclusion, angina pectoris and conduction disturbance with QRS widening on ECG might be the initial presentation of myocarditis in RA patients. Early intervention with high dose IVIG and systemic steroid can be effective for the treatment of acute fulminant myocarditis in RA patients.

REFERENCES

1. Rothschild BM, Turner KR, DeLuca MA. Symmetrical erosive peripheral polyarthritis in the Late Archaic Period of Alabama. *Science* 1988;241:1498-501.
2. Gabriel SE. Cardiovascular morbidity and mortality in rheumatoid arthritis. *Am J Med* 2008;121:S9-14.
3. Magnani JW, Dec GW. Myocarditis: current trends in diagnosis and treatment. *Circulation* 2006;113:876-90.
4. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2010;69:1580-8.
5. Shauer A, Gotsman I, Keren A, et al. Acute viral myocarditis: current concepts in diagnosis and treatment. *Isr Med Assoc J* 2013; 15:180-5.
6. Pagnoux C, Guillevin L. Cardiac involvement in small and medium-sized vessel vasculitides. *Lupus* 2005;14:718-22.
7. Sigal LH, Friedman HD. Rheumatoid pancarditis in a patient with well controlled rheumatoid arthritis. *J Rheumatol* 1989;16:368-73.
8. Robinson J, Hartling L, Vandermeer B, et al. Intravenous immunoglobulin for presumed viral myocarditis in children and adults. *Cochrane Database Syst Rev* 2005:CD004370.
9. Seferovic PM, Ristic AD, Maksimovic R, et al. Cardiac arrhythmias and conduction disturbances in autoimmune rheumatic diseases. *Rheumatology (Oxford)* 2006;45 Suppl 4:iv39-42.
10. Wang CC, Chen JH, Yu WC, et al. 2012 Guidelines of the Taiwan Society of Cardiology (TSOC) for the diagnosis and treatment of heart failure. *Acta Cardiol Sin* 2012;28:161-95.

