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Case Report

T-wave alternans in a case with systemic lupus erythematosus-related myocarditis

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ABSTRACT

A 42-year-old woman presented with fever, dyspnea, lower-leg edema, significant pulmonary congestion, pleural effusion, and severely reduced left ventricular contractions. She was resistant to treatment for heart failure, including catecholamines, furosemide, phosphodiesterase III inhibitors, and human atrial natriuretic peptide, and antibiotics failed to reduce her inflammation. She had renal dysfunction and hypocomplementemia and was positive for anti-nuclear and anti-ds-DNA antibodies. The patient was diagnosed with myocarditis and pleurisy associated with systemic lupus erythematosus (SLE). Prednisolone administration improved her general condition, reducing inflammation and improving left ventricular function. On day 1, an electrocardiography (ECG) revealed a T-wave inversion similar to a T-U complex configuration in leads II, aVF, and V3-6. By day 8, however, ECG showed prolonged corrected QT (QTc) and T-wave alternans (alternating beat-to-beat T-wave patterns) in lead V3-6. Careful ECG monitoring should be used to identify potentially fatal ventricular arrhythmias during the recovery phase of SLE-related myocarditis.

<**Learning objective:** This was a case of significant T-wave alternans (TWA) during recovery from systemic lupus erythematosus (SLE)-related myocarditis. Fatal ventricular arrhythmia appears to be a risk during recovery from myocardial damage caused by SLE. Up to now, there have been no published case reports of TWA during this period. Patients with myocarditis should be carefully monitored for arrhythmia, even after ventricular function and inflammation have improved with prednisolone therapy.>

Introduction

Systemic lupus erythematosus (SLE) causes pleurisy related to myocarditis and inflammation of the serosa; however, symptomatic myocarditis is an uncommon complication in SLE patients. In patients with acute lupus myocarditis, segmental wall motion abnormalities and decreased left ventricular ejection fraction (LVEF) are commonly observed echocardiographic findings. Nonspecific ST/T-wave changes are found on electrocardiography (ECG) in most patients [1]. Immunosuppressive therapy with high-dose corticosteroids and pulse intravenous cyclophosphamide are reported to result in the restoration of LVEF and a good cardiac outcome [1].

We experienced a case of SLE-related myocarditis associated with T-wave alternans (TWA) during the recovery phase following acute hemodynamic deterioration.

Case report

A 42-year-old woman presented in our department with a 1-month history of anorexia and lower-leg edema. Her dyspnea and edema had worsened over the days leading up to the hospital visit. At an outpatient clinic, the patient was found to have significant pulmonary congestion, pleural effusion, severe left

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ventricular (LV) systolic dysfunction, and a fever of 38 °C. She was admitted to another hospital as an emergency case, where she was diagnosed with acute heart failure and treated with catecholamines, furosemide, phosphodiesterase-III inhibitors, human atrial natriuretic peptide, and meropenem because sepsis could not be ruled out. Despite administration of high-dose catecholamines for heart failure, her respiratory and circulatory status continued to worsen. Finally, she was transported to our hospital.

Physical examination revealed that the patient was underweight with a blood pressure of 130/85 mmHg, heart rate of 135 beats/min, respiratory rate of 26 breaths/min, and SpO_2 of 95% (O_2 4L). Chest auscultation was not clear at the lower part of both lungs, though cardiac auscultation revealed normal S_1 and S_2 with no S_3 or murmurs. The patient had pitting edema in her legs with no jugular venous distention or hepatosplenomegaly. She was photosensitive and had a history of bronchial asthma and atopic dermatitis until the age of 12 years. She had no history of coronary risk factors except for smoking. She also had no history of pregnancy, childbirth, or drug or alcohol abuse. In addition, there was no family history of heart or collagen disease.

The patient's laboratory findings are presented in Table 1. Her white blood cell count and C-reactive protein and brain natriuretic protein levels were elevated. Normocytic anemia, hypoalbuminemia, and reduced renal function were observed. She also showed albuminuria and hematuria, and her urine contained numerous granular, waxy, and epithelial cell casts. An ECG showed a T-wave inversion similar to a T-U complex configuration (Fig. 1A). A chest radiographic examination revealed pleural effusion on both sides and enhancement of pulmonary vascular shadows (Fig. 1B). Echocardiography revealed diffuse LV hypokinesis and a LVEF of 35%. Doppler showed moderate mitral regurgitation (Fig. 1C and Supplementary videos 1–4). Coronary angiography and right heart catheterization revealed no coronary artery stenosis. The patient had a cardiac output of 6.8 (L/min) and cardiac index of 4.3 (L/min/m^2) with tachycardia (heart rate of 120 beats/min). Thus, the stroke volume measured by thermodilution was as low as 56.6 (mL/beat). Mean pulmonary capillary wedge pressure was 17 mmHg.

The patient's urine levels were low and, by day 2, her condition had worsened and required intubation. Treatment with broad-spectrum antibiotics had no effect on the inflammation. Interestingly, the patient had anemia, renal dysfunction with the excretion of large numbers of hyaline cylinders, and exudative pleural effusion. It was difficult to think that all these findings were solely caused by heart failure. On day 4, screening tests for the causes of secondary cardiomyopathy were positive for anti-nuclear antibody (2560-times the normal level), anti-ds-DNA antibody 45.0 (IU/mL), and hypocomplementemia. The patient thus met the diagnostic criteria for SLE and was further diagnosed with myocarditis and pleurisy associated with SLE. Administration of prednisolone at 60 mg/day was started immediately. Gradually her urine volume increased and pleural effusion decreased. By day 7, the patient's LV wall motion had improved such that her LVEF was 43% and functional mitral regurgitation was reduced, as were her blood levels of inflammatory markers.

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Table 1 Laboratory findings.

WBC	13,980/μL
RBC	290×10^4/μL
Hb	8.4 g/dL
Plt	28.7×10^4/μL
MCV	90.4 fL
MCH	28.5 pg
MCH	31.6%
TP	5.7 g/dL
Alb	1.4 g/dL
UN	31.8 mg/dL
Cr	1.52 mg/dL
eGFR	31 mL/min/1.73 m^2
UA	11.0 mg/dL
Na	139 mEq/L
K	3.5 mEq/L
Cl	106 mEq/L
CRP	14.9 mg/dL
BNP	417 pg/mL
	+

WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Plt, platelet; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; TP, total protein; Alb, albumin; UN, urea nitrogen; Cr, creatinine; eGFR, estimated glomerular filtration rate; UA, uric acid; CK, creatinine kinase; Na, sodium; K, potassium; Cl, chlorine; CRP, C-reactive protein; BNP, brain natriuretic peptide.

Despite the improved hemodynamics after administration of prednisolone, the patient's ECG revealed prolonged corrected QT (QTc) and TWA on day 8 (Fig. 2A). She had no chest symptoms and the improvement in her LV function was sustained. There were also no abnormalities in her serum Na^+, K^+, Mg^{2+}, or Ca^{2+} levels, which were potential risk factors for ventricular arrhythmia. Although an increase in the number of premature ventricular contractions was noted on the ECG, there was no unsustained/sustained ventricular tachycardia (VT) or ventricular fibrillation, and her TWA and QTc prolongation improved spontaneously. Moreover, the improvements in cardiac function and respiration, with reduced pleural effusion and inflammation, were sufficient to allow extubation. The patient was subsequently taken off catecholamines on day 16 and moved to the Department of Collagen Diseases for immunosuppressant therapy. Six months later, her LVEF had improved to 55% and her inverted T-wave had become much shallower (Fig. 2B).

Discussion

Here we report a case of SLE-related myocarditis with TWA, despite apparent improvement in cardiac function following the administration of prednisolone. TWA is a cardiac electrokinetic index that reflects repolarization abnormalities and changes in the shape of the T-wave on a beat-by-beat basis [2]. During the cardiac action potential (AP), the cytoplasmic Ca^{2+} concentration within cardiomyocytes first increases as a result of Ca^{2+} release from the sarcoplasmic reticulum (SR) and influx of extracellular Ca^{2+}. This Ca^{2+} is then resequestered into the SR or transported across the plasma membrane into the extracellular space [2–4]. The time course of this process is a key role in determining the duration of the plateau phase of the cardiac AP and can vary on a beat-by-beat basis. This presents as TWA on ECGs [2]. When there is discordance in the alternans at different sites within the myocardium related to repolarization and electrical heterogeneity, the myocardium is prone to fatal ventricular arrhythmias [2]. Indeed, evidence suggests that microvolt TWA is predictive of sudden cardiac arrest in patients with coronary heart disease or heart failure [5]. Ambulatory ECG-based TWA is also reportedly useful for predicting sudden cardiac death in post-myocardial infarction [2].

In the present case, TWA was observed during the resolution of SLE-related myocarditis. In an earlier report, young myocarditis patients recovering with or without steroid therapy experienced ventricular arrhythmias, including unsustained and sustained VT, despite apparent histological improvement of myocardial inflammation in biopsy specimens [6]. In rats, longer AP duration, slower conduction velocity (CV) and greater CV heterogeneity and myocardial fibrosis were seen in animals with experimental autoimmune myocarditis as compared to healthy controls [7]. In addition, levels of inflammatory cytokines and oxidative stress were higher in rats with myocarditis, and there was dysregulation of myocardial Ca^{2+}-handling proteins. Upon steroid administration, the fibrosis, prolonged AP duration, CV delay, and elevated inflammatory cytokines were all relieved, although levels of some

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