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CASE REPORT

BEGINNER

CLINICAL CASE

Acute Myocarditis Revealing Adult-Onset Still's Disease

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ABSTRACT

A 34-year-old man presented with fever, palpitations, maculopapular rash, pharyngitis, left cheilitis, and bilateral gonalgia. High-sensitivity troponin I concentration was 4,900 ng/l. Transthoracic echocardiogram revealed reduced global longitudinal strain. Cardiac magnetic resonance imaging showed acute myocarditis. Adult-onset Still's disease was diagnosed, and treatment with intravenous corticosteroids and tocilizumab was initiated. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2021;3:1002–6) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 34-year-old man was admitted to the emergency department with a 6-day history of fever (40°C) associated with palpitations, maculopapular rash (Supplemental Figure 1), pharyngitis, and bilateral gonalgia without synovitis. The patient reported no chest pain. At admission, his blood pressure was 117/74 mm Hg, heart rate was 94 beats/min, and temperature was 38.3°C. Clinical examination revealed a fixed, pseudourticarial, nonpruritic erythematous rash of the extremities.

LEARNING OBJECTIVES

- To consider systemic disease as a possible cause during a myocarditis workup.
- To consider using a biologic immunomodulator as the first-line treatment in myocarditis with an inflammatory disease.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis included acute coronary syndromes, Takotsubo syndrome, parvovirus B19 infection, COVID-19 infection, and Kawasaki disease.

MEDICAL HISTORY

The patient had no documented allergies, cardiovascular risk factors, or signs of recent acute infection. He reported recurrent sinusitis in recent years. He had not traveled abroad.

INVESTIGATIONS

The pharyngeal streptococcal test result was negative. Cardiac auscultation revealed systolic murmur

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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compatible with mitral regurgitation. Electrocardiogram showed sinus rhythm, heart rate of 75 beats/min; nonspecific subendocardial ischemia with negative T waves in V_4, V_5, and V_6; and normal QT interval corrected for heart rate (430 ms) (Figure 1). High-sensitivity troponin I concentration was raised (4,900 ng/l). The patient was transferred to intensive care.

Notable laboratory findings were creatinine level of 0.73 mg/dl, creatinine kinase level of 162 IU/l, B-type natriuretic peptide level of 95 pg/ml, and C-reactive protein level of 345 mg/l. Minor liver cytolysis was detected (alanine transaminase level of 212 IU/l and aspartate transaminase level of 58 IU/l) without cholestasis. Transthoracic echocardiogram (TTE) revealed normal left ventricular ejection fraction (LVEF) (65%) but showed patchy abnormal wall motion in the basal inferior, inferolateral, and mid anterior myocardial segments (3 of 17) with altered global longitudinal strain (GLS) (−16%) (Figure 2). There were no signs of right ventricular dysfunction. Mitral regurgitation was mild. Posterior pericardial effusion (4 mm) was present. Cardiac magnetic resonance imaging was compatible with acute myocarditis, with hyper-T_2 of the anterior, lateral, and inferior walls of the left ventricle; late gadolinium enhancement of the lateral and inferior left ventricular walls; and moderate pericardial effusion (Figure 3).

Serology test results for parvovirus B19 immunoglobulin M, HIV, hepatitis B or C virus, Epstein-Barr virus, and cytomegalovirus were negative. Polymerase chain reaction results were negative for severe acute respiratory syndrome coronavirus 2 and weakly positive (500 copies/ml) for human herpesvirus 6. Serology results were negative for severe acute respiratory syndrome coronavirus 2. Ferritin level peaked at 14,423 pg/l with 8% glycosylated ferritin. The lipid profile was normal; the fibrinogen concentration was 4.53 g/l. Acute myocarditis due to adult-onset Still's disease (AOSD) was considered.

ABBREVIATIONS AND ACRONYMS

AOSD = adult-onset Still's disease

GLS = global longitudinal strain

LVEF = left ventricular ejection fraction

TTE = transthoracic echocardiogram

MANAGEMENT

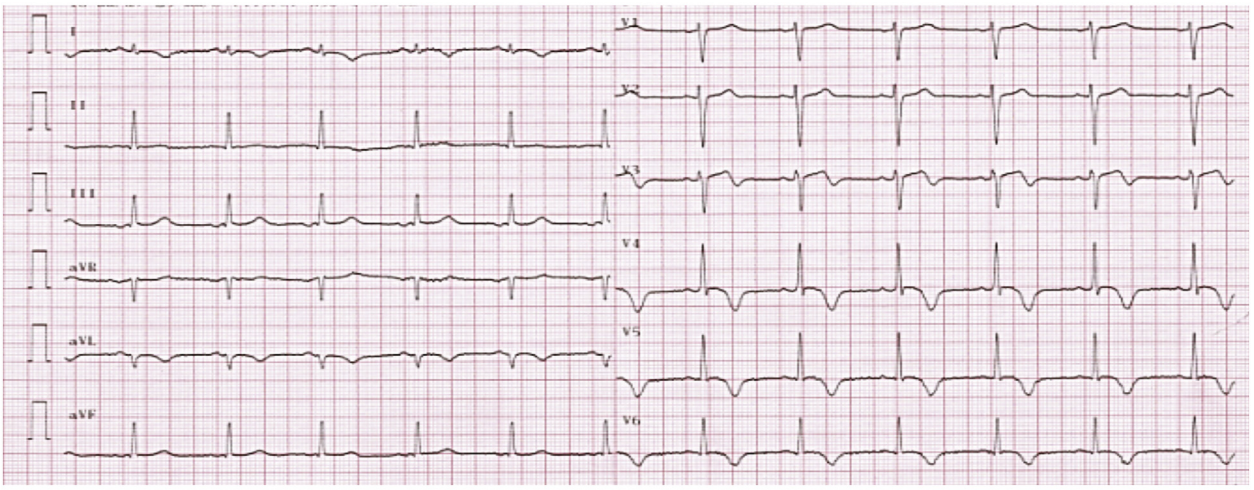
The patient developed nonsustained ventricular tachycardia in the hospital, and beta-blocker therapy was started. Angiotensin-converting enzyme inhibitor therapy was introduced because of the abnormal GLS and despite preserved LVEF. Intravenous corticosteroids (1 mg/kg/day) were given for 1 month; the dosage was progressively decreased thereafter.

Two-dimensional TTE showed an improvement in GLS (−23%). Owing to severe systemic involvement with acute myocarditis, tocilizumab (8 mg/kg/month) was initiated for 6 months.

DISCUSSION

The patient was diagnosed with AOSD because of the coexistence of myocarditis, fever, atypical cutaneous involvement, gonalgia, pharyngitis, biological inflammatory syndrome, and elevated ferritin level with a decreased glycosylated fraction.

FIGURE 1 Electrocardiogram



Negative T waves in lateral leads suggestive of myocarditis. (Non–ST-segment elevation myocardial infarction cannot be ruled out.)

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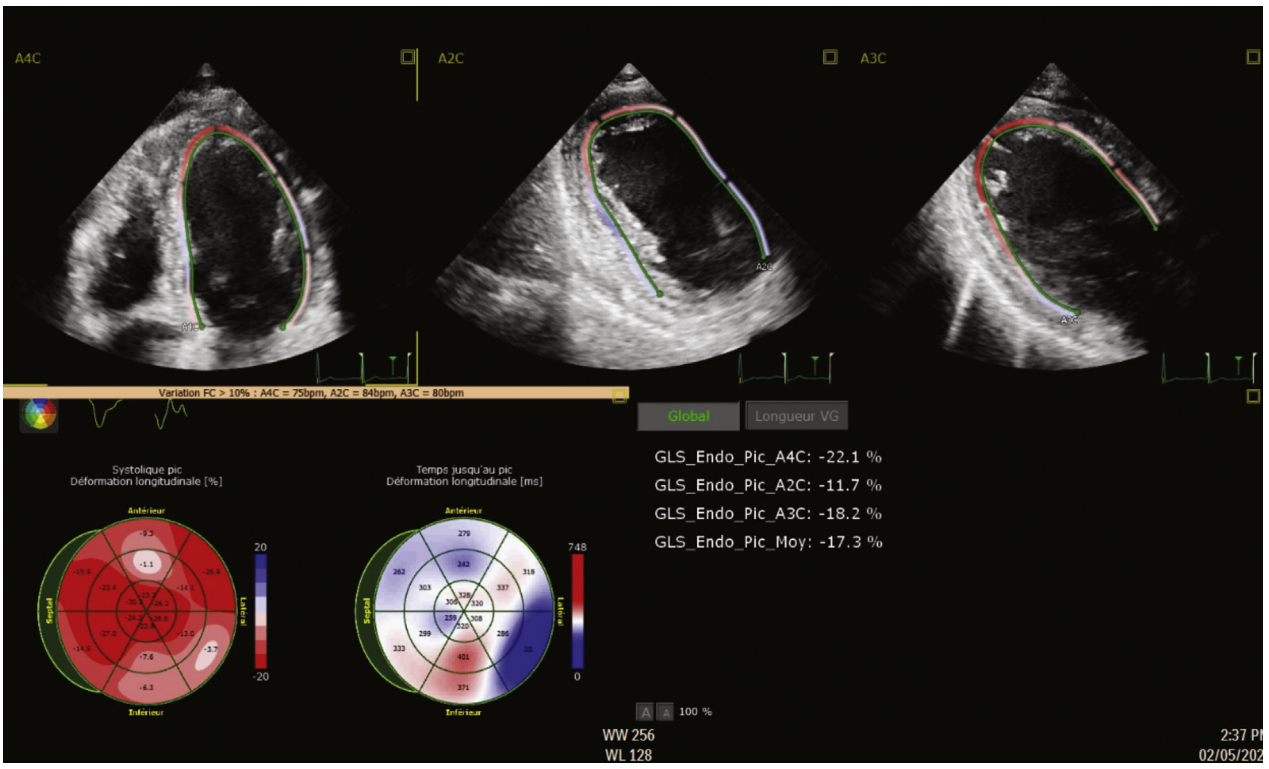
FIGURE 2 **Echocardiogram**



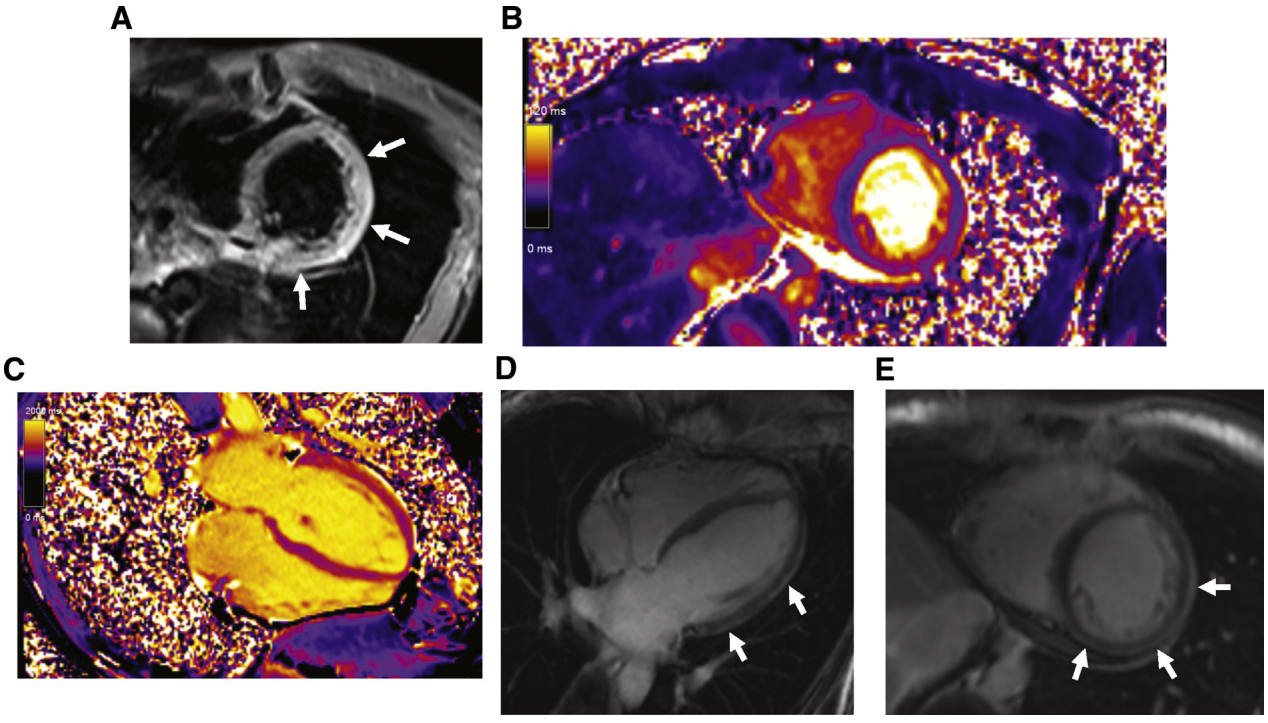
Echocardiogram showing alterations in global longitudinal strain predominantly in the basal inferior, inferolateral, and mid anterior segments.

AOSD is a rare, systemic, autoinflammatory disease characterized by prolonged daily fever, evanescent skin rash polyarthralgia associated with neutrophilic polynucleosis and hyperferritinemia, and a decreased glycosylated fraction of ferritin (1). It can be triggered by environmental exposures, especially viruses. Exogenous (pathogen-associated molecular patterns) or endogenous (damage-associated molecular patterns) danger signals can trigger an uncontrolled inflammatory reaction, with innate immune cells (polynuclear cells, macrophages) releasing proinflammatory cytokines, resulting in systemic inflammation or even macrophage activation syndrome (**Figure 4**). Other nonspecific symptoms have been reported (e.g., pharyngitis with odynophagia, organomegaly, pleural effusion, abdominal pain) (1).

The evolution of Still's disease is marked by relapses with a concomitant inflammatory syndrome, which can be severe. The systemic forms of the disease can cause serious complications, with the onset of an inflammatory cytokine storm (elevation of interleukin-1, -6, and -18), causing macrophage activation syndrome, disseminated intravascular coagulation, and thrombotic microangiopathy (2). Mortality is low (<3%) but rises following macrophage activation (3).

Cardiac involvement secondary to Still's disease is diverse and can affect the 3 layers of the heart. The pericardium is the most frequently involved (3% to 37% of patients) (4). Pericarditis is associated with pleural effusion in 60% to 80% of patients (5). Corticosteroid therapy appears effective, with nonsteroidal anti-inflammatory drugs as the first-line therapy. Nevertheless, anakinra (an interleukin 1R antagonist) or tocilizumab can be initiated early for cortisone saving or if there is no improvement on corticosteroid therapy. Biotherapies can be immediately considered in the presence of severe systemic manifestations (6). In a recent study in 96 patients with AOSD, 28 (29%) presented cardiac involvement, 89% of these at diagnosis, represented mostly by pericarditis and rarely by cardiac tamponade, myocarditis, and 1 case of a noninfectious endocarditis. Patients with cardiac involvement were prone to having an intense inflammatory syndrome, having a refractory pattern to usual treatments, being more frequently admitted to the intensive care unit, and being more often treated with biotherapies (6).

FIGURE 3 Cardiac Magnetic Resonance



(A) Myocardial edema identified on short T_1 inversion recovery images **(arrows)** with myocardial high signal intensity compared with that in peripheral muscle (ratio: >1.9) in the lateral and inferior walls of the left ventricle. **(B)** In these segments, mean myocardial T_2 was increased (50 ± 5 ms). **(C)** Myocardial native T_1 was increased in the corresponding segments (mean values: up to 1,396 ± 81 ms in the lateral wall of the left ventricle). **(D, E)** Late gadolinium enhancement was present in the subepicardial regions of the **(D)** lateral and **(E)** inferior wall of left ventricle **(arrows)** and spared the subendocardial regions, ruling out myocardial infarction. Overall, the cardiovascular magnetic resonance features were consistent with myopericarditis.

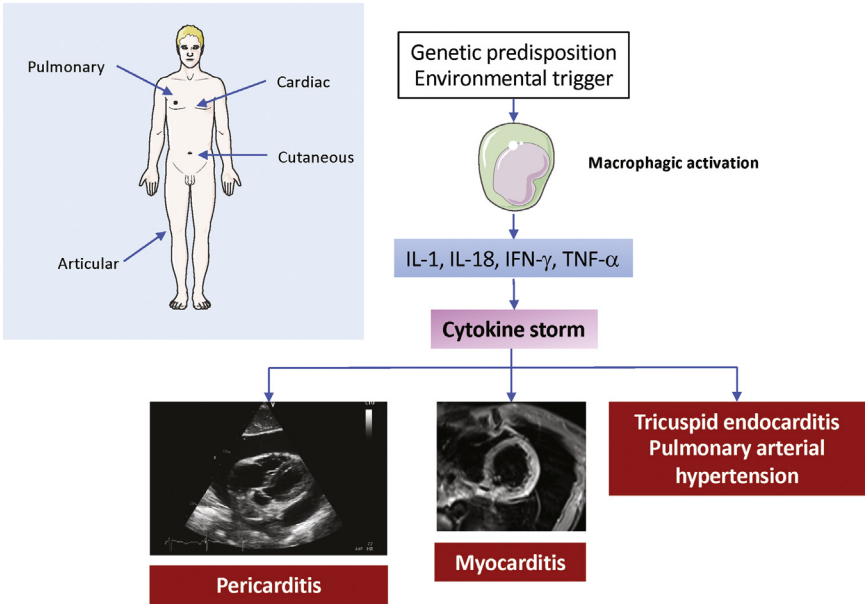
Myocarditis is a less common complication (affecting 7% of patients) and can be associated with pericarditis (31% in a recent overview) (5). Cardiac involvement is more frequent in young men (38%) (mean age: 32 years) and is often present at diagnosis (65%). The most common symptoms are dyspnea (54%) and chest pain (58%) (7). Electrocardiogram findings are unspecific: repolarization disorders, sinus tachycardia, and QT interval prolongation. C-reactive protein and ferritin levels appear to be higher in the presence of myocarditis, probably due to cytokine storm. Abnormalities detected on 2-dimensional echocardiography include left and/or right ventricular systolic dysfunction, alteration of GLS, and increased left ventricular thickness due to edematous infiltration. Cardiac magnetic resonance imaging, with edema in T_2 and late enhancement in T_1, exhibits a sensitivity of 67% and a specificity of 91% (8). Corticosteroids remain the first-line therapy, with an efficacy of 50% to 60% (7). Second-line therapies include methotrexate and biotherapies (interleukin-1 and -6 antagonists). Acute endocarditis with valvular vegetations due to fibrinoid or fibrinocruoric components has been reported, particularly involving the tricuspid valve (8,9).

A rare complication in AOSD is group 1 pulmonary arterial hypertension (9), which is more common in women, expressing as dry cough and with progressive dyspnea. Treatment consists of vasodilators (endothelin antagonists, prostacyclin agonists, nitric oxide agonists) used in pulmonary arterial hypertension in association with biotherapies.

FOLLOW-UP

At the 3-month follow-up, the patient was asymptomatic, with normal findings on clinical examination. The electrocardiogram, TTE, and maximal exercise test results were normal. Cardiac magnetic resonance imaging showed regression of myocardial inflammation, normal LVEF, but persistent left ventricular mild dilatation.

FIGURE 4 Cardiac Manifestations of Adult-Onset Still's Disease



IFN = interferon; IL = interleukin; TNF = tumor necrosis factor.

CONCLUSIONS

Cardiac involvement in AOSD is rare but potentially fatal (due to acute myocarditis) or associated with significant morbidity. Treatment comprises high doses of corticosteroids and rapid use of biotherapies.

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APPENDIX For a supplemental figure, please see the online version of this paper.