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Case Report

A teenage boy with acute myocarditis and reversible microvascular angina: A case report

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ABSTRACT

A 17-year-old male was diagnosed with acute myocarditis based on the presence of CD3-positive T-lymphocytes in myocardial biopsy, normal coronary angiography, and focal increase in late gadolinium enhancement, T2 intensity and native T1 value. On day 2, the patient suffered from recurrence of chest pain with new ST segment elevations on electrocardiogram. A transient metabolic alteration (inversed lactate level of the coronary sinus relative to that of the coronary artery) accompanied by chest pain and electrocardiographic changes without epicardial coronary spasm in acetylcholine provocation test led to the diagnosis of microvascular angina, which is characterized by a transient myocardial ischemia secondary to a dysfunction of the resistance coronary vessels (<500 μm) that, because of their small size, are not visualized at coronary angiography. Benidipine, a dihydropyridine calcium channel antagonist, was started for chest pain due to microvascular angina. On 6 months after admission, when the findings of cardiac magnetic resonance were recovered, intracoronary infusion of acetylcholine did not induce chest pain, electrocardiographic changes, epicardial coronary spasm, and adverse changes of lactate levels of the coronary artery and sinus. The patient had no chest symptoms 2 years after discontinuation of benidipine.

Learning objective: The present case of microvascular angina, which was complicated with acute myocarditis on acute phase and recovered in chronic phase, indicates an association of myocardial inflammation with reversible coronary microvascular dysfunction.

Introduction

Microvascular angina (MVA) is characterized by a transient myocardial ischemia secondary to a dysfunction of the resistance coronary vessels (<500 μm) that, because of their small size, are not visualized at coronary angiography [1]. Although it remains elusive, a possible cause of microvascular dysfunction could be found in the increased subclinical inflammatory status, as manifested by higher plasma levels of C-reactive protein [2]. We herein report a teenage male with acute myocarditis, who experienced MVA on acute phase and its recovery in chronic phase.

Case report

A 17-year-old male was admitted to our hospital for acute myocarditis. He had a fever and right cervical lymphadenopathy with tenderness a week before admission and was diagnosed as having viral lymphadenitis. Although the neck pain was improving, the fever continued, and chest pain appeared a day before admission. On admission, the patient did not have chest pain with blood pressure, heart rate, SpO_2 (room air), and body temperature of 125/68 mm Hg, 86 bpm, 97 %, and 37.9 °C. Electrocardiogram (ECG) showed ST elevations on the multiple leads and creatinine kinase, its myocardial band and troponin T levels were elevated with 946 IU, 98 IU and 1.340 ng/mL, respectively. Transthoracic echocardiography showed global left-ventricular hypokinesis with ejection fraction of 31 % while no stenosis was found on coronary angiography (CAG). As myocardial biopsy in the interventricular wall from the right ventricle showed the presence of CD3-

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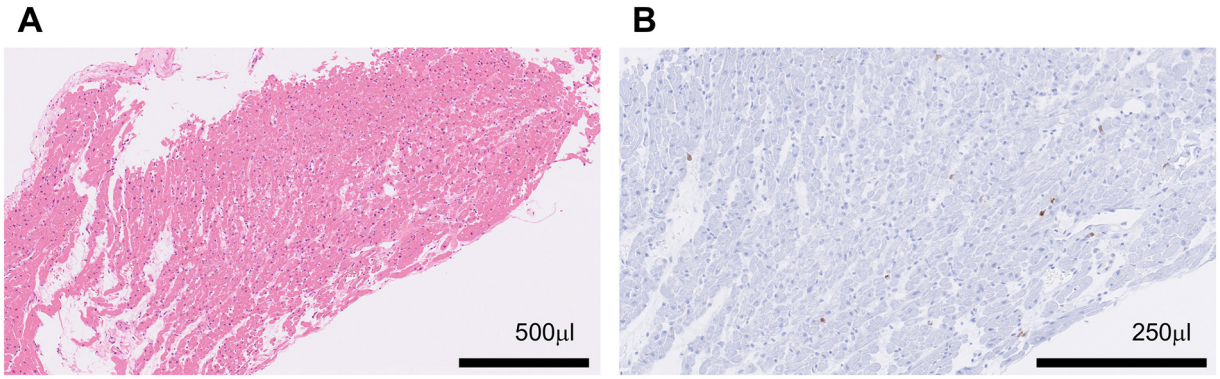
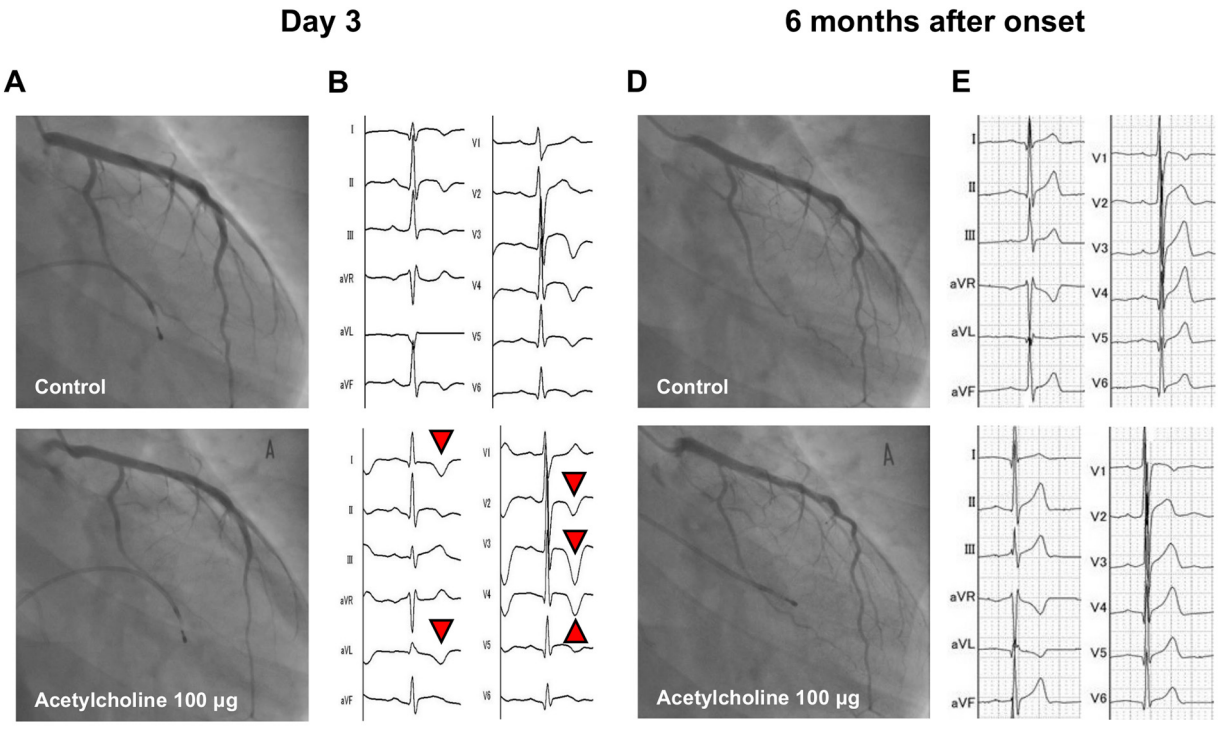


Fig. 1. Histopathological findings of myocardial biopsy with hematoxylin eosin staining (A) and CD3 immunostaining (B). CD3-positive T-lymphocytes were stained as brown-colored cells.

positive T-lymphocytes ≥7 cells/mm^2 (Fig. 1) [3], the patient was diagnosed as having acute myocarditis and was hospitalized without inotropes or mechanical hemodynamic support.

On day 2, the patient had chest pain with cold sweats. ECG showed ST elevations on the leads I, II, III, aVF and V5–6 with reciprocal changes on the leads V1–3 (Online Fig. 1). His symptoms were improved after



C

Control	0.00 (CA:0.4/CS:0.4)
Acetylcholine 20 μg	–0.67 (CA:0.3/CS:0.5)
Acetylcholine 50 μg	–0.67 (CA:0.3/CS:0.5)
Acetylcholine 100 μg	–0.20 (CA:0.5/CS:0.6)
Isosorbide dinitrate	–0.25 (CA:0.4/CS:0.5)
Fasudil	0.25 (CA:0.4/CS:0.3)

F

Control	0.44 (CA:0.9/CS:0.5)
Acetylcholine 20 μg	0.40 (CA:1.0/CS:0.6)
Acetylcholine 50 μg	0.36 (CA:1.1/CS:0.7)
Acetylcholine 100 μg	0.11 (CA:0.9/CS:0.8)
Isosorbide dinitrate	0.10 (CA:1.0/CS:0.9)
Fasudil	0.00 (CA:1.0/CS:1.0)

Fig. 2. Acetylcholine provocation tests on day 3 (A–C) and 6 months after onset (D–F). Findings of coronary angiography (A,D), electrocardiogram (B,E), and myocardial lactate extraction ratio [lactate level (mmol/L) in coronary sinus (CS) relative to coronary artery (CA)] (C,F) were shown either on control or intracoronary infusion of acetylcholine 20, 50, or 100 μg, isosorbide dinitrate or fasudil.

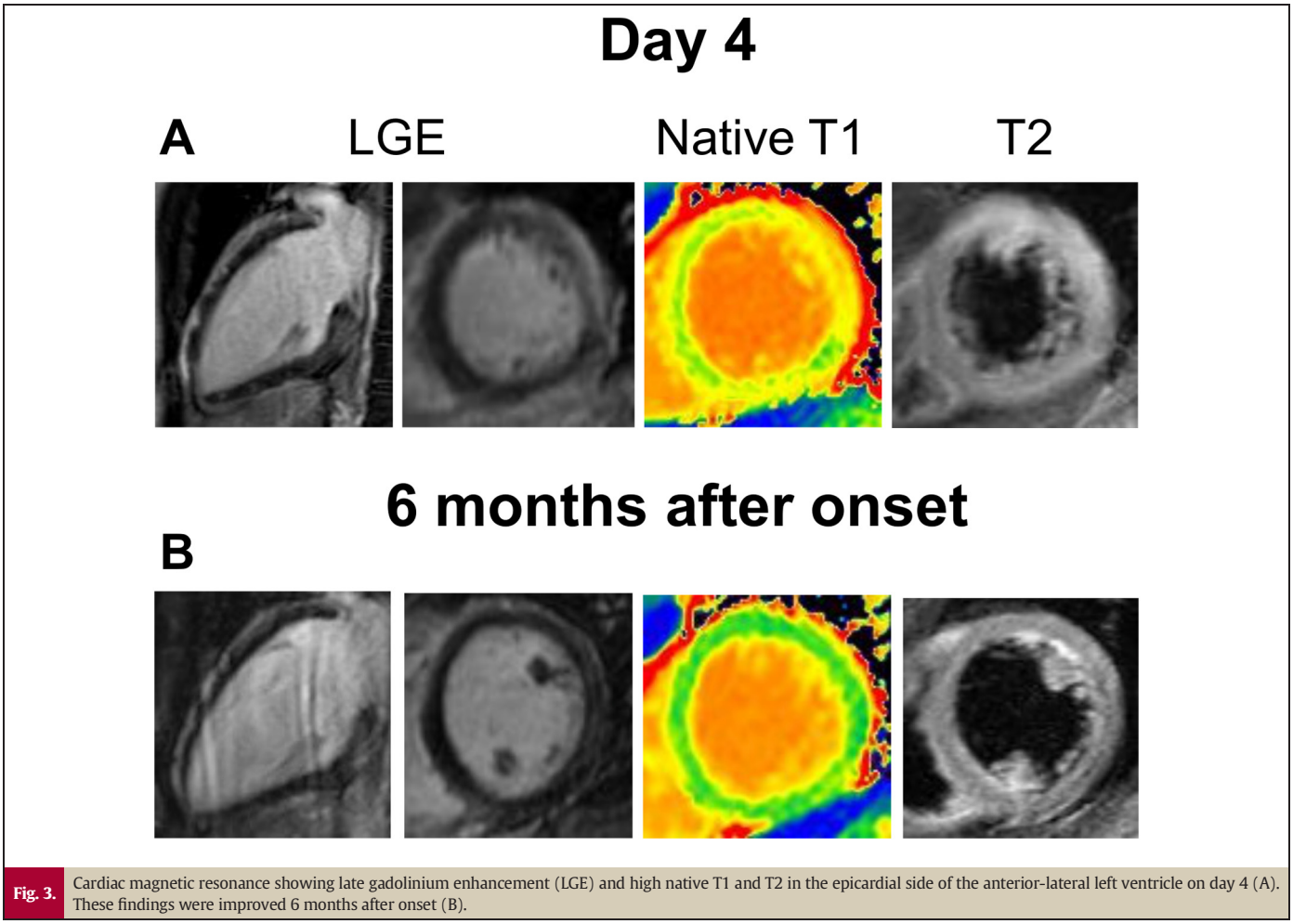


Fig. 3. Cardiac magnetic resonance showing late gadolinium enhancement (LGE) and high native T1 and T2 in the epicardial side of the anterior-lateral left ventricle on day 4 (A). These findings were improved 6 months after onset (B).

administering nitroglycerin. As normal CAG on admission, we performed an acetylcholine provocation test for coronary spasm on day 3. Briefly, incremental doses of acetylcholine were injected into the left coronary artery (LCA) at 20, 50, and 100 μg and into the right coronary artery (RCA) at 20 and 50 μg over 20 s with at least a 3-min interval between each injection, followed by CAG 1 min after each injection or whenever chest pain or ischemic ECG changes developed. Although an epicardial coronary spasm was not found (Fig. 2A), intracoronary infusion of acetylcholine (100 μg) to LCA induced chest pain with inverted and/or deeper T-waves on the I, aVL, and V2–4 leads (Fig. 2B). The lactate level of the coronary sinus became higher compared with that of LCA (Fig. 2C), indicating the development of myocardial ischemia due to microvascular spasm [4,5]. His chest pain was temporary and the inversion of the lactate levels was improved after intracoronary infusion of fasudil (Fig. 2C), a Rho-kinase inhibitor [6]. Intracoronary infusion of acetylcholine to RCA did not induce epicardial coronary spasm.

Then, we started benidipine, a second-generation dihydropyridine calcium channel antagonist, for prevention of his chest pain due to MVA. Cardiac magnetic resonance (CMR) on day 4 showed late gadolinium enhancement (LGE) and high native T1 and T2 in the epicardial side of the anterior-lateral left ventricle (Fig. 3A), which supported the diagnosis of acute myocarditis. The patient did not suffer from chest pain after administration of benidipine and his left-ventricular wall motion was normalized with ejection fraction of 61 % on day 9. The patient was discharged from our hospital on day 10 with benidipine 4 mg/day. Paired serum antibody tests on days 2 and 17 did not show a significant elevation of titer against echoviruses, parainfluenza viruses, enteroviruses, or adenoviruses.

At 6 months after admission, the acetylcholine provocation test was repeated after two-day discontinuation of benidipine. Intracoronary infusion of acetylcholine did not induce chest pain, epicardial coronary spasm (Fig. 2D), ECG changes (Fig. 2E), or myocardial lactate production (Fig. 2F). The follow-up CMR showed that the LGE and high native T1 and T2 found in the epicardial side of the anterior-lateral left ventricle on acute phase were improved (Fig. 3B). The patient had no chest symptoms 2 years after discontinuation of benidipine.

Discussion

MVA is the clinical manifestation of myocardial ischemia caused by coronary microvascular dysfunction (CMD), whose diagnosis is based on four criteria: symptoms of myocardial ischemia, absence of obstructive coronary artery disease, objective evidence of myocardial ischemia, and evidence of CMD [7]. The patient had chest pain on day 2 in spite of normal CAG on admission. The acetylcholine provocation test on day 3 showed chest pain and ECG changes without an epicardial coronary spasm. Myocardial lactate production is indicative of myocardial ischemia due to CMD [4,5,7]. The findings of coronary functional testing and CMR were restored in 6 months, along with recovered clinical course of acute myocarditis.

The causes of CMD remain elusive. In the present 17-year-old male, accumulation of cardiovascular risk factors or estrogen action is unlikely to be involved. There is accumulating evidence highlighting a close relationship between inflammation and CMD in various experimental and clinical settings (e.g. chronic inflammatory rheumatoid diseases) [8]. Acute myocarditis can be complicated with coronary adventitial and

perivascular inflammation [9], possibly extending to microvascular level. It should be also mentioned that treatment of angina pectoris associated with CMD is challenging as the underlying mechanisms are often diverse and overlapping [10]. In the present case, inflammation seems to play an important role in CMD and its improvement relieved MVA in the chronic phase even after the discontinuation of benidipine treatment.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jccase.2023.02.007.

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Patient consent statement

Written informed consent was obtained from the patient for publication of the case and accompanying images.

Declaration of competing interest

None declared.

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