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Clinical characteristics and outcomes of patients with myocarditis mimicking ST-segment elevation myocardial infarction

Analysis of a case series

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Abstract

Acute myocarditis mimicking ST-segment elevation myocardial infarction (STEMI) is highly deceptive for an accurate diagnosis, and a systematic study is lacking with regard to the clinical features and prognosis of this distinct clinical entity.

Patients with suspected STEMI and eventually diagnosed with myocarditis by cardiac magnetic resonance (CMR) from January 2012 to April 2016 at Fuwai Hospital were identified by reviewing medical records and electronic databases. Follow-up was conducted by clinical visits and phone contacts in a median duration of 17 months.

A total of 18 patients were included in the study, with 17 males and 1 female. They were relatively young, and their mean age was 30.8 years. 94.4% of the patients had a high prevalence of infectious prodrome, and inflammatory biomarkers were notably elevated in all patients. Late gadolinium enhancement on CMR was detected in 13 patients. Three patients underwent fulminant course, and left ventricular ejection fraction (LVEF) <45% on admission occurred in 3 patients. The median LVEF improved from 59% on admission to 65% at discharge ($P < .001$), and none developed cardiac insufficiency, heart transplantation, or death during a median follow-up of 17 months.

Myocarditis mimicking STEMI is featured by young age and an existence of flu-like prodrome. CMR benefits the differential diagnosis of this unique clinical entity. Notably, patients with myocarditis mimicking STEMI had a favorable prognosis, and establishing an accurate diagnosis is crucial to avoid unreasonable treatments for them.

Abbreviations: AMI = acute myocardial infarction, AVB = atrioventricular block, CMR = cardiac magnetic resonance, CPAP = continuous positive airway pressure, ECG = electrocardiogram, EMB = endomyocardial biopsy, IABP = intra-aortic balloon pumping, ICD = implantable cardioverter defibrillator, IVIG = intravenous immunoglobulin, IVS = interventricular spetal, LAD = left atrium diameter, LGE = late gadolinium enhancement, LVEDD = left ventricular end-diastolic diameter, LVEF = left ventricular ejection fraction, MI = myocardial infarction, MINOCA = myocardial infarction with nonobstructive coronary artery disease, STEMI = ST-segment elevation myocardial infarction.

Keywords: cardiac magnetic resonance, characteristics, myocarditis, prognosis, ST-segment elevation myocardial infarction

1. Introduction

Previous studies indicated 2.6% to 25% of patients with suspected myocardial infarction (MI) turned out to be MI with nonobstructive coronary artery disease (MINOCA).[1–3] Several causes of suspected MI with culprit-free angiograms were identified,[4] among which acute myocarditis has been recognized as a particularly important entity.[5–8] Myocarditis is defined as an inflammatory infiltrate of the myocardium with necrosis and degeneration of adjacent myocytes as the result of virus infection, autoimmune diseases, or cardiotoxic agents, characterized by a wide spectrum of clinical presentations, from subclinical myocardial dysfunction to severe heart failure.[9] Although myocarditis accounts for 1% to 9% of autopsies in general and 3% to 12% of sudden death in adults, there is an extremely low diagnostic rate in clinical practice.[10,11] And for myocarditis mimicking MI, an estimated clinical diagnostic incidence was 0.17 per 1000 man-years.[12]

Clinically, myocarditis mimicking ST-segment elevation MI (STEMI) is extremely deceptive for physicians to make an accurate diagnosis. Moreover, a correct diagnosis of myocarditis per se is a challenge due to nonspecific patterns of its clinical presentations and the lack of an accurate and reliable diagnostic method.[9,10] Although an endomyocardial biopsy (EMB) was recommended in guidelines,[11] the diagnosis of myocarditis in routine practice is generally based on comprehensive considerations of patients' medical history, clinical manifestations, and accessory examinations, among which cardiac magnetic resonance (CMR) has exerted significant advantage in detecting

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myocardial abnormalities and accurately discriminating patients with myocarditis from those with true MI.[5–8,13–15]

Although patients with myocarditis mimicking STEMI have been described in prior case reports,[16–20] a systematic study focused on the clinical features and prognosis of this distinct clinical entity is lacking, especially in the setting of Chinese patients. Therefore, in the present study, we aimed to document the clinical characteristics and outcomes of patients with suspected STEMI but eventually diagnosed with myocarditis indicated by CMR.

2. Methods

This study was a single-center retrospective analysis and undertaken by reviewing medical records and electronic databases to search for patients with myocarditis mimicking STEMI from January 2012 to April 2016 at Fuwai Hospital, and the study inclusion criteria were as follows: patients with a preliminary diagnosis of STEMI, that is, patients presented with chest pain/distress, ST-segment elevation in electrocardiogram (ECG), and elevated levels of cardiac markers by laboratory tests, however, coronary computed tomography angiography or coronary angiography revealed normal coronary arteries, then myocarditis was raised as the primary diagnosis, and a CMR examination was recommended; patients with a definite diagnosis of myocarditis based on patients' medical history, clinical manifestations, and accessory examinations, especially results of CMR. The study was approved by the ethics committee of Fuwai hospital.

A total of 18 patients hospitalized with suspected STEMI but finally diagnosed with myocarditis indicated by CMR were identified and included in this analysis. The Lake Louise criteria, that is, the presence ≥2 of the 3 following criteria: edema seen on T2-weighted images, hyperemia seen on early contrast-enhanced images, and myocardial injury on late gadolinium enhancement (LGE), was used to indicate the existence of acute myocarditis.[21] Blood viral serologic studies were conducted by extracting baseline and follow-up (between 7 and 28 days after admission) serum samples of patients, and acute viral infection was diagnosed by serological detection of immunoglobulin (Ig)M or IgA in the baseline sample or IgG seroconversion between baseline and follow-up samples in enzyme immuno- or immunofluorescence assays, and a 4-fold increase in titer between baseline and follow-up samples or a significantly high titer (1:256 in the neutralization assay or 1:80 in the complement fixation reaction) defined an acute infection in quantitative assays such as the neutralization assay or the complement fixation reaction. In our present study, Coxsackie virus, cytomegalovirus, Epstein–Barr virus, herpes simple virus, echovirus, and influenza virus were detected using commercial kits, and all assays were applied according to the manufacturer's instructions. Complete investigations were performed to rule out congenial heart malformations and other underlying disorders known to be related to myocarditis.[22] Fulminant course of myocarditis was defined as an existence of severe hemodynamic compromise requiring vasopressors (≥5 μg of dopamine or dobutamine per kilogram of body weight per minute), intra-aortic balloon pumping (IABP), or percutaneous cardiopulmonary support during the hospitalization, besides, at least 2 of the following clinical features had to be present: fever, distinct onset of symptoms of heart failure, and a history consistent with the presence of symptoms of infection within 2 weeks before admission.[23]

The medical records of the 18 patients were carefully reviewed and the following clinical data were collected: age, sex, risk factors of ischemic heart disease, vital signs on admission, prodromal symptoms, cardiac discomfort, New York Heart Association (NYHA) classification, arrhythmias during the hospitalization, and results of accessory examinations, that is, laboratory tests, ECG, echocardiography, CMR, blood viral serologic studies, and EMB. ECGs performed during the hospitalization were separately evaluated by 2 cardiologists to identify any abnormal findings. ST-segment elevation was defined as the elevation of J point in at least 2 contiguous leads of ≥0.2 mV in leads V_2–V_3 and/or of ≥0.1 mV in other contiguous chest leads or limb leads.[4] Arrhythmias, including premature beat, sinus tachycardia or bradycarida, supraventricular tachycardia, atrioventricular block (AVB), and new bundle branch block, were identified by referring to ECG, Holter and ECG monitoring. Left ventricular ejection fraction (LVEF) was assessed by transthoracic echocardiography using modified Simpson's rule. Left ventricular end-diastolic diameter (LVEDD), left atrium diameter (LAD), and interventricular spetal (IVS) were assessed in the parasternal long-axis view. Special treatments, including the usage of corticosteroids, intravenous immunoglobulin (IVIG), IABP, continuous positive airway pressure (CPAP), hemofiltration, and pacemaker, or implantable cardioverter defibrillator (ICD) installation, were identified and tabulated by reviewing patients' medical records and medical orders. Follow-up was conducted by clinical visits, phone contact with patients, and reviewing records of patients' subsequent consultations, and the median follow-up time was 17 months.

In addition, we conducted comparative analyses of patients with myocarditis mimicking STEMI to those with other main patterns of disease onset, as well as to patients with authentic MI reported in the previous literature.[24,25] Continuous variables were expressed as means with standard deviations or medians with quartiles; categorical variables were expressed as frequencies and percentages. Comparisons of continuous variables were conducted by variance analysis or the Mann–Whitney U test, and differences in categorical variables were analyzed using the χ^2 test or Fisher exact test. All statistical tests were 2-tailed, and a P value $<.05$ were considered significant. The software package SPSS V.22.0 (IBM Corporation, New York, NY) was used for statistical analysis.

3. Results

Demographic data and clinical presentations of patients with myocarditis mimicking STEMI are summarized in Table 1. Among the 18 patients, 17 were males and 1 was female. The mean age of the patients was 30.8 years. Ten patients (55.6%) had cardiovascular risk factors, among whom 6 had a history of smoking, 1 had hyperlipidemia, and 3 patients had multiple risk factors. On admission, 5 patients presented with hypotension, 8 had an accelerated pulse, 1 had a slow pulse, and 4 had a high temperature. All but 1 of the patients experienced prodromal infection, 11 patients underwent fever, 15 suffered from symptoms of upper respiratory infections, and 1 patient had symptoms of digestive tract infections. The median duration of prodrome was 5 days. For cardiac manifestations, chest pain and distress were most frequent symptoms of those patients. Fourteen patients had NYHA classification I/II, and 4 patients had more severe cardiac dysfunction with NYHA classification III/IV. During the hospitalization, life-threatening arrhythmia was observed in 3 patients (16.7%), among whom 2 developed high-grade AVB and 1 patient underwent ventricular tachycardia.

Data of accessory examinations are shown in Tables 2 and 3. Eight patients (44.4%) had a remarkably elevated white blood

Table 1

Demographic data and clinical presentations of patients with myocarditis mimicking STEMI.

Case	Sex	Age, years	IHD risk factors	BP, mm Hg	*P*, bpm	*T*, celsius	Prodrome	Duration, days	Cardiac manifestation	NYHA class	In-hospital arrhythmia
1	Male	26	Smoking	95/52	97	36.0	Fever, flu	12	Palpitation, chest distress/pain	III	Premature beat/high-grade AVB
2	Male	68	HTN, HLP, FH, smoking	122/62	129	38.2	Fever, flu	8	Chest distress/pain	III	Sinus tachycardia
3	Male	15	None	84/48	120	36.5	Flu	30	Chest pain	I	Premature beat/sinus tachycardia
4	Male	16	None	92/49	49	36.5	Flu	2	Chest pain, dizziness	I	Sinus bradycardia
5	Male	19	Smoking	104/58	96	38.0	Fever, flu	5	Chest pain	I	None
6	Male	26	Smoking	100/85	88	37.0	Fever, flu	2	Chest distress/pain	I	Premature beat
7	Male	26	None	124/67	77	36.0	Flu	7	Chest distress	I	Ventricular tachycardia
8	Male	32	Smoking	115/68	102	36.5	Flu	10	Palpitation, chest distress/pain	I	Sinus tachycardia
9	Male	36	HLP	130/65	83	36.0	Fever, flu	10	Chest pain	I	Sinus bradycardia/low-grade AVB
10	Male	45	HTN, DM, HLP	102/72	105	37.6	Fever	3	Chest distress	I	Sinus tachycardia
11	Male	47	Smoking	108/68	110	39.0	Fever, enteric	3	Chest distress/tightness	III	Premature beat/ventricular tachycardia/LBBB
12	Male	58	None	110/70	106	36.5	None	NA	Epigastric discomfort	II	Atrial flutter/fibrillation/ high-grade AVB
13	Female	45	None	80/70	107	36.8	Flu	7	Palpitation, chest distress	IV	Sinus tachycardia/premature beat
14	Male	14	None	107/56	89	36.5	Flu	2	Chest pain/distress	I	Low-grade AVB
15	Male	19	None	116/80	89	36.6	Fever, flu	5	Chest pain	I	Premature beat
16	Male	22	None	120/70	78	36.5	Fever, flu	5	Chest pain	I	Premature beat/sinus bradycardia
17	Male	33	Smoking	97/65	80	36.0	Fever, flu	8	Chest pain/distress	I	None
18	Male	34	HTN, HLP, smoking	106/80	108	36.9	Fever, flu	4	Palpitation	I	Sinus tachycardia/premature beat/LBBB/RBBB

AVB = atrioventricular block, BP = blood pressure, DM = diabetes mellitus, FH = family history, HLP = hyperlipidemia, HTN = hypertension, IHD = ischemic heart disease, LBBB = left bundle branch block, NA = not applicable, P = pulse, RBBB = right bundle branch block, STEMI = ST-segment elevation myocardial infarction, T = temperature.

count, and all patients had raised high-sensitivity C reactive protein (hsCRP). Creatine kinase (CK) and CK isoenzyme (CK-MB) ranged from a minimum of 64/5 to a maximum of 3560/252 IU/L, and the mean value of lactate dehydrogenase was 364 IU/L. Peak cardiac troponin I (CTnI) was elevated in all patients with a median value of 6.53 ng/mL, and the median value of peak N-terminal B-type natriuretic peptide was 807 fmol/mL. The median values of IVS, LVEDD, and LAD evaluated by echocardiography on admission were 10, 47, and 35 mm, and LVEF <45% was observed in 3 patients (cases 2, 4, and 12). Five patients presented with moderate/mild pericardial effusion, and 10 patients had ventricular wall motion abnormalities. No significant change existed in values of IVS, LAD, and LVEDD, while median LVEF was notably elevated, from 59% on admission to 65% at discharge ($P < .001$), and ventricular wall motion recovered in most patients. The median timing of CMR was 7 days after admission, and LGE with a subepicardial or an intramural distribution was observed in 13 patients (Fig. 1). Eight patients

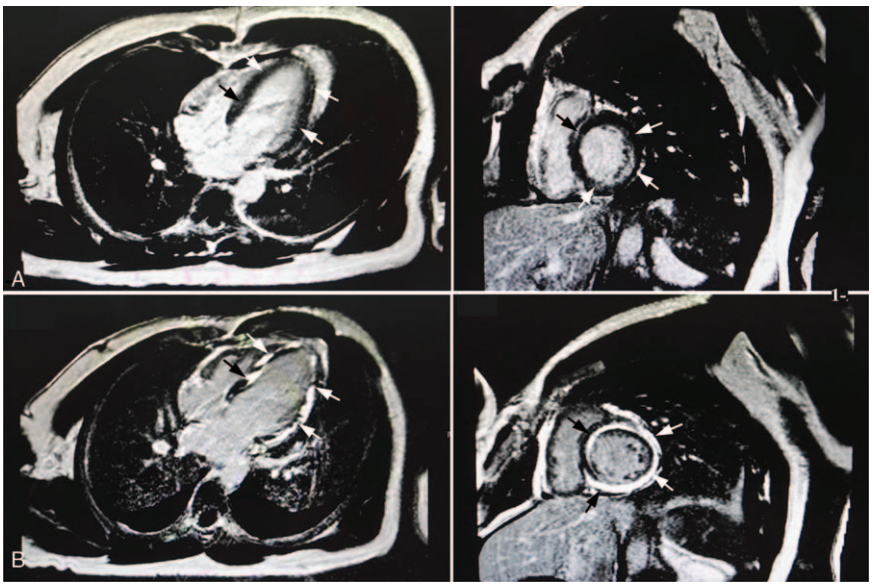

Figure 1. Cardiac magnetic resonance of case 9 (1) and case 11 (2). Long-axis (A) and short-axis (B) late gadolinium enhancement sequences indicated patchy myocardial enhancement (arrows, including both white arrows and black arrows) in a subepicardial or intramural distribution suggestive of a myocarditic process.

Table 2

Laboratory data and ECG results of patients with myocarditis mimicking STEMI.

Case	WBC, 10^9/L	hsCRP, mg/L	ESR, mm/h	CK, IU/L	CK-MB, IU/L	LDH, IU/L	Peak CTnI, ng/mL	Peak NT-proBNP, fmol/mL	ECG on admission	ECG on discharge
1	13.91	9.61	6	495	35	305	3.46	2453	ST↑: V_2–V_6	ST-segment resolution, T wave inversion: V_3–V_6, I, aVL
2	9.55	14.76	30	504	52	549	16.00	8278	ST↑: I, aVL, V_3–V_6, abnormal Q wave: V_2–V_4	ST-segment resolution, flat T wave: V_3–V_6
3	8.16	1.18	3	1387	76	588	100.00	694	ST↑: II, III, aVF	ST-segment resolution, T wave inversion: II, III, aVF
4	12.92	12.61	21	485	22	502	36.96	1093	ST↑: II, III, aVF, V_3–V_6	Normal
5	6.99	14.93	27	136	12	261	8.67	6808	ST↑: V_2–V_5	ST-segment resolution, T wave inversion: V_2–V_6
6	19.05	11.68	25	88	24	198	1.01	105	ST↑: I, aVL, II, aVF, V_3–V_6	Normal
7	9.53	3.21	13	64	5	86	2.24	342	ST↑: V_1–V_3	Normal
8	12.58	9.82	2	178	18	177	3.39	558	ST↑: II, III, aVF	ST-segment resolution, abnormal Q wave: II, III, aVF
9	14.20	10.87	4	3560	252	585	102.00	3182	ST↑: I, aVL, II, III, aVF, V_2–V_6, V_7–V_9	ST-segment resolution, abnormal Q wave: II, III, aVF
10	18.45	15.84	60	312	43	278	2.19	747	ST↑: I, aVL, V_2–V_6	Normal
11	9.79	9.47	16	200	32	530	14.50	2433	LBBB, ST↓: V_2–V_6, abnormal Q wave: II, III, aVF	Abnormal Q wave: V_1–V_2, flat or inverted T wave
12	6.26	10.22	6	71	9	182	13.30	3549	ST↑: V_1–V_3, ST↓: I, aVL	Abnormal Q wave: II, III, aVF, diphasic T wave: V_4–V_6
13	12.52	9.19	5	548	46	378	1.27	2887	ST↑: V_2–V_4	Normal
14	11.47	11.59	10	164	38	231	1.99	413	ST↑: I, aVL, V_3–V_6	ST-segment resolution, diphasic T wave: V_3–V_6
15	7.44	11.42	55	770	61	346	8.13	507	ST↑: II, III, aVF	Normal
16	5.15	4.31	13	745	50	265	4.70	29	ST↑: II, III, aVF, V_1–V_6, V_7–V_9	Normal
17	7.78	6.88	22	1751	139	694	4.93	418	ST↑: I, aVL, II, III, aVF, V_3–V_6	T wave inversion: V_4–V_6, abnormal Q wave: I, aVL
18	7.08	6.43	11	102	19	218	0.16	867	ST↑: V_1–V_6, LBBB/RBBB	ST-segment resolution

CK = creatine kinase, CTnI = cardiac troponin I, ECG = electrocardiography, ESR = erythrocyte sedimentation rate, hsCRP = high-sensitivity C reactive protein, LBBB = left bundle branch block, LDH = lactate dehydrogenase, NT-proBNP = N-terminal B-type natriuretic peptide, RBBB = right bundle branch block, STEMI = ST-segment elevation myocardial infarction, ST↑ = ST-segment elevation, ST↓ = ST-segment depression, WBC = white blood count.

Table 3

Results of echocardiography, CMR, and blood viral serologic studies of patients with myocarditis mimicking STEMI.

	Echocardiography on admission					Echocardiography at discharge									
Case	IVS, mm	LVEDD, mm	LAD, mm	LVEF, %	Pericardium	LV alterations	IVS, mm	LVEDD, mm	LAD, mm	LVEF, %	Pericardium	LV alterations	CMR timing, days	LGE	Blood viral serologic studies
1	11	48	35	47	Mild effusion	Segmental	10	47	32	72.6	Mild effusion	None	15	LV	Negative
2	12	55	37	31	Mild effusion	Diffuse	12	55	33	37	Mild effusion	Diffuse	16	LV	CMV, HSV
3	10	44	26	62	Normal	Segmental	8	49	30	67	Normal	None	6	Septal	Not performed
4	12	26	50	42	Normal	Diffuse	10	45	27	62	Normal	None	4	Septal, LV	EBV, echovirus
5	14	50	33	55	Mild effusion	Diffuse	13	46	32	71.9	Normal	None	5	LV	Negative
6	9.6	48	34	61.9	Normal	None	10	45	32	65	Normal	None	2	Septal, LV	Not performed
7	9	56	37	60	Normal	Segmental	10	54	36	65	Normal	None	7	None	Not performed
8	8	46	32	55	Mild effusion	Diffuse	8	50	35	71.6	Mild effusion	None	6	None	Not performed
9	9.8	46	35	63	Normal	None	9.2	53	35	62.2	Normal	None	3	Septal, LV	Negative
10	10	48	35	60	Normal	Segmental	9	46	32	70	Mild effusion	None	9	None	Not performed
11	10	60	38	53	Normal	Segmental	8.4	57	31	66.7	Normal	None	6	LV, RV, septal	Not performed
12	9	56	39	33	Normal	Diffuse	9	55	39	50	Normal	Diffuse	6	LV, RV	CMV, influenza virus
13	11	40	34	58	Moderate effusion	None	10	45	37	62	Mild effusion	None	2	RV, septal	Negative
14	10	48	33	62	Normal	None	10	48	28	66	Normal	None	4	None	Not performed
15	12	46	31	60	Normal	None	11	45	33	69.5	Normal	None	6	LV, septal	Not performed
16	9	44	27	62	Normal	None	8	45	33	65	Normal	None	8	None	Coxsackie virus
17	8	44	26	54	Normal	None	8	45	32	65	Normal	None	6	Septal, LV	Not performed
18	8	43	39	60	Normal	None	8.2	51	38	61.3	Normal	None	5	Spetal	Not performed

CMR = cardiac magnetic resonance, CMV = cytomegalovirus, EBV = Epstein–Barr virus, HSV = herpes simplex virus, IVS = interventricular septal, LAD = left atrium diameter, LGE = late gadolinium, LV = left ventricle, LVEDD = left ventricular end-diastolic diameter, LVEF = left ventricular ejection fraction, RV = right ventricle, STEMI = ST-segment elevation myocardial infarction.

Table 4

Treatments and in-hospital outcomes of patients with myocarditis mimicking STEMI.

	Special treatments during hospitalization						Hospitalization		Long-term outcome	
Case	Corticosteroids	IVIG	IABP	CPAP	Hemofiltration	Pacemaker/ICD	Days	Fulminant course	Cardiac function	Follow-up, months
1	Yes	Yes	No	Yes	No	Yes	21	Yes	Normal	19
2	Yes	Yes	Yes	Yes	No	No	17	Yes	Normal	47
3	No	No	No	No	No	No	8	No	Normal	34
4	No	No	No	No	No	No	12	No	Normal	2
5	No	No	No	No	No	No	19	No	Normal	12
6	No	No	No	No	No	No	6	No	Normal	17
7	No	No	No	No	No	No	9	No	Normal	19
8	No	No	No	No	No	No	12	No	Normal	18
9	No	No	No	No	No	No	13	No	Normal	14
10	No	No	No	No	No	No	9	No	Normal	30
11	No	No	No	No	No	No	10	No	Normal	17
12	No	No	No	No	No	Yes	17	Yes	Normal	14
13	No	No	No	No	No	No	10	No	Normal	2
14	No	No	No	No	No	No	11	No	Normal	16
15	No	No	No	No	No	No	9	No	Normal	16
16	No	No	No	No	No	No	12	No	Normal	19
17	No	No	No	No	No	No	14	No	Normal	77
18	No	No	No	No	No	No	7	No	Normal	17

CPAP = continuous positive airway pressure, IABP = intra-aortic balloon pump, ICD = implantable cardioverter defibrillator; IVIG = intravenous immunoglobulin, STEMI = ST-segment elevation myocardial infarction.

had viral serologic tests, among whom 1 was detected with cytomegalovirus and herpes simplex virus infection, 1 had Epstein–Barr virus and echovirus infection, 1 had cytomegalovirus and influenza virus infection, 1 had Coxsackie virus infection, and none of the rest patients were detected with increase in virus antibody titers. Besides, only 1 patient (case 12) underwent right ventricular EMB within 1 week after admission, and the results were negative.

Treatments and outcomes of patients are shown in Table 4. Special treatments were utilized in 3 patients who underwent a fulminant course (cases 1, 2, and 12). Two patients (cases 1 and 2) received corticosteroids, IVIG, and CPAP, 1 patient (case 2) underwent IABP, 2 patients (cases 1 and 12) installed pacemaker or ICD, and none of them underwent hemofiltration. The median length of hospitalization was 12 days, and all patients were discharged with a significantly improved LVEF on echocardiography (Fig. 2). During a median 17-month follow-up, all patients had normal cardiac function and none developed cardiac insufficiency, heart transplantation, or death, even including the patient (case 2) who was still in worse cardiac state at discharge.

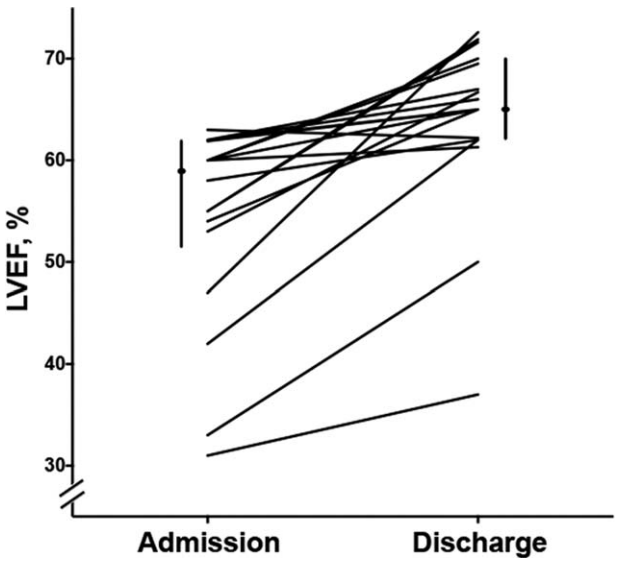

Figure 2. LVEF by echocardiography on admission and at discharge in study patients. The median LVEF was 59% when on admission and 65% at discharge ($P < .001$). LVEF = left ventricular ejection fraction.

Compared to myocarditis patients with other main patterns of disease onset, patients with myocarditis mimicking STEMI had remarkably higher peak CTnI and hsCRP levels, and significantly more favorable prognosis (Supplementary material, Tables S1 and S2, http://links.lww.com/MD/B684). And compared to patients with authentic MI reported in previous literature, patients with myocarditis mimicking STEMI were featured by younger age, lower prevalence of risk factors for ischemic heart disease, and remarkably higher survival rate (Supplementary material, Tables S3 and S4, http://links.lww.com/MD/B684).

4. Discussion

Our present study shed some light on the clinical features and prognosis of Chinese patients with myocarditis mimicking STEMI and revealed that this population was featured by young age and infectious prodrome combined with laboratory evidence of inflammation response. Moreover, a favorable prognosis was observed in this unique clinical entity, as cardiac structure and function were rapidly recovered in most of the patients at discharge, and none experienced cardiac insufficiency, heart transplantation, or death during a median follow-up of 17 months.

Clinically, it is not rare to find that patients with suspected MI are eventually confirmed to have normal coronary arteries, and previous studies showed that the prevalence of MINOCA ranged between 2.6% and 25% of all MIs.[1,2] Actually, the presentations of MINOCA are a set of heterogeneous diseases and various

causes, including coronary artery spasm, angiographically undetectable coronary heart disease, coronary embolism, takotsubo cardiomyopathy, etc, that account for the existence of MINOCA.[4] Besides, previous studies revealed that a substantial proportion of these patients may actually have myocarditis.[5–8] Assomull et al[5] evaluated the diagnostic value of CMR in 60 patients with MINOCA and revealed that the most common underlying cause was myocarditis and the ratio was 50%. Laraudogoitia Zaldumbide et al[7] further estimated the role of CMR in 80 patients with suspected acute coronary syndrome and normal coronary arteries and arrived at 63% of these patients with a final diagnosis of myocarditis and 15% with a diagnosis of MI. Besides, in the study concerning this similar matter conducted by Baccouche et al[6] and Monney et al,[8] the ratio of myocarditis was reported as 58% and 81%, respectively.

In our study, most of the patients presented with ST-segment elevation in partial leads, simulated to ECG alterations caused by blocked coronary arteries in MI. Besides, segmental ventricular wall motion abnormalities highly suggestive of acute MI were also detected in partial patients by echocardiography. Notably, both features were extremely misleading and challenged an accurate diagnosis to be obtained as indicated in previous studies.[26,27] In this case, the existence of other imaging findings, that is, pericardial effusion and ventricular septal thickening, will be beneficial for the diagnosis. Particularly, CMR will provide more information of myocardial alterations, and make it possible for a definite diagnosis to be made noninvasively.[5–8,13–15,21] In the Lake Louise criteria, LGE has the most diagnostic value in differentiating myocarditis from MI. Compared to a transmural or a subendocardial distribution of LGE in authentic MI, myocarditis is characterized by the multifocal existence of LGE predominantly in intramural or subepicardial regions. In our present study, LGE was detected in 13 patients, and the distribution of LGE was in accordance with aforementioned features of myocarditis.[3,7,14,18–20] Besides, an existence of edema on T2-weighted images and hyperemia on early contrast-enhanced images in line with a transmural or a subendocardial distribution were also in favor of the diagnosis of myocarditis, which confirmed a diagnosis of myocarditis in the remaining 5 patients, along with their medical history, existence of pericardial infusion, and positive viral serologic studies.

The diagnosis of MINOCA is complicated in practice, thus, a comparative analysis of myocarditis mimicking STEMI and authentic MI might shed light on this dilemma. In a meta-analysis to study the prevalence and risk markers of myocarditis and "true" MI determined by CMR in patients with suspected MI without obstructive coronary disease performed by Tornvall et al,[25] both young age and high CRP values were identified to be predictors of an existence of myocarditis, whereas male sex, treated hyperlipidemia, high troponin values, and low CRP values were all related to "true" MI. Consistent with above conclusions, our comparative analyses also indicated that patients with myocarditis were featured by younger age, lower prevalence of risk factors for ischemic heart disease, and significantly higher survival rate, compared to patients with authentic MI reported in previous studies (Supplementary File 1, http://links.lww.com/MD/B684).

Furthermore, none of the patients with myocarditis mimicking STEMI in the present study underwent cardiac insufficiency, heart transplantation, or death during a median follow-up of 17 months, indicating this unique clinical entity had a relatively favorable prognosis. Costantini et al[27] conducted an analysis of 11 young men with myocarditis presenting as STEMI, and found that all patients had normal echocardiographic findings at late follow-up examination (>3 months). Besides, markedly improved LVEF and ventricular wall motion were also detected in 12 patients with suspected acute MI and an ultimate diagnosis of myocarditis based on EMB.[26] Moreover, compared to patients with main patterns of disease onset, we found that patients with myocarditis mimicking STEMI had remarkably higher survival rate. In Anzini et al's[28] study recruiting 82 patients with biopsy-proven myocarditis, 9 patients presenting with chest pain on admission had the highest survival rate, in comparison to those with primary presentations of heart failure and arrhythmias. However, in contrast to the above results, 1 death due to cardiac insufficiency and 2 cases of heart failure with NYHA class II/III were detected during a median follow-up of 21 months in the study conducted by Dec et al[29], which included 11 patients with suspected acute MI and biopsy-proven myocarditis. Moreover, Miklozek et al[30] performed an analysis of 10 patients with myocarditis presenting as AMI, and 3 of them developed cardiac dysfunction in a mean duration of 5.8 months. Several mechanisms and explanations, including different populations recruited, chance caused by small sample size, and latent diverse pathological types of myocarditis, might account for the discrepant results obtained. On all accounts, plentiful of studies indicated that damaged cardiac function might be the key predictor of poor prognosis in patients with myocarditis, and patients with myocarditis mimicking STEMI had relative favorable long-term outcomes.[28,31]

Several limitations of this study should be noted. First, this is a retrospective study performed at a single center; therefore, our results cannot be extrapolated to a wider range of population. Second, EMB was performed in only 1 patient, thus diagnostic errors might exist in this study. Nevertheless, on all of the patients CMR was performed with imaging evidence of acute myocarditis. Third, a sample size of 18 cases in our study was quite few, especially only 1 female enrolled was also a strong limitation of our study, however, as a matter of fact, adult myocarditis itself is a quite rare disease, and there is an extremely low diagnostic rate in clinical practice.[12] Despite the strikingly small sample size of this study, our results showed that myocarditis mimicking STEMI was featured by young age, an existence of flu-like prodrome, and a relatively favorable long-term prognosis, thus, establishing an accurate diagnosis is crucial to avoid unreasonable treatments for them, which has certain guiding significance to clinical practice. Last, prospective studies with large sample size and long follow-up duration are highly needed.

5. Conclusions

The present study revealed that patients with myocarditis mimicking STEMI were featured by young age, an existence of infectious prodrome, and elevated inflammation biomarkers. An examination of CMR will provide more data of myocardial alterations for the differential diagnosis of patients with MINOCA, and make it possible for a definite diagnosis of myocarditis to be established noninvasively. Significantly, patients with this clinical entity had a relatively favorable prognosis, and it is vital to establish an accurate diagnosis to avoid unreasonable treatments for these patients.

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