Images in Cardiovascular Medicine

Cardiac Magnetic Resonance Imaging in Giant Cell Myocarditis
Intriguing Associations With Clinical and Pathological Features

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t cell myocarditis (GCM) is rare and often fatal. Proper diagnosis is crucial, because immunosuppressive therapy has been reported to increase the median transplant-free survival time from 3.0 to 12.3 months.1 Although endomyocardial biopsy plays an essential role in early diagnosis, it may yield false-negative results. Imaging examinations including cardiac magnetic resonance (CMR) may facilitate the diagnosis, but the associations between specific CMR findings and the clinical features and pathological findings remain unclear. We present a patient with characteristic CMR findings, with intriguing associations with the clinical features and pathological findings of the biopsy and autopsy.

Case Presentation
A 73-year-old woman presented with acute chest pain and dyspnea that had continued for 7 hours. Her medical history was unremarkable, with the exception of uveitis and dyslipidemia. Initial examination showed resting blood pressure 132/83 mm Hg, heart rate 103 bpm, and respiratory rate 17 breaths/min. She required 5 L/min of oxygen via facemask to maintain SpO2 > 98%. Coarse crackles were heard over both lung fields. X-ray demonstrated mild cardiomegaly with bilateral pulmonary congestion (Figure 1). Electrocardiography, which had been within normal limits 2 years previously, showed changes resembling acute myocardial infarction (Figure I in the online-only Data Supplement). Echocardiography showed global hypokinesis in the left ventricular (LV) wall, and regional akinesia in the septum and inferoseptal wall. Coronary artery angiography revealed no significant stenosis or intracoronary thrombus. Her serum creatinine kinase level was high at 2558 IU/L. CMR was performed on day 7. Cine-CMR showed global hypokinesis in the LV wall, with regional akinesia in the septum and inferoseptal wall at the basal and middle levels (LV end-systolic/diastolic volume index=92/73.3 mL/m2, LV ejection fraction=20.8%, LV mass=49 g; Movies I and II in the online-only Data Supplement). T2-weighted images showed high-intensity signals in the septum and inferoseptal wall at the base of the LV (Figure 2A). Late-gadolinium enhancement (LGE) was detected in the transmural inferoseptal and inferior LV wall and the subendocardial anterolateral LV wall at the basal and middle levels and in the right ventricular side of the septum at the apex (Figure 2B, short-axis view at the base; Figure IIA in the online-only Data Supplement, 4-chamber view; Figure IIB in the online-only Data Supplement, short-axis view at the apex). Myocardial strain was evaluated by using Diagnosoft strain-encoded MRI (SENC-MRI, version 3.0; Diagnosoft, Palo Alto, CA), which shows areas of myocardium with severely impaired or absent strain in white and areas of myocardium with normal strain in red.2 The LV longitudinal strain was diffusely impaired (Figure 3A), whereas the circumferential strain was preserved in the lateral wall (Figure 3B). Endomyocardial biopsy from the right ventricular septum was performed on day 3. The pathological examination findings were consistent with GCM, showing multinucleated giant cells with necrosis and prominent lymphocytic and eosinophilic infiltration, but no granuloma (Figure IIA and IIB in the online-only Data Supplement). Cardiac sarcoidosis was unlikely because of these pathological findings, lack of elevation of angiotensin-converting enzyme, and negative extracardiac fluorodeoxy-glucose positron emission tomography findings.

The patient developed low-output syndrome and intermittent ventricular arrhythmia. Oral prednisone (30 mg daily) was commenced, followed by cyclosporine A with trough levels titrated below 150 ng/mL. She appeared to stabilize initially, but over the next few weeks, her heart failure gradually progressed despite an increasing steroid dose. She became inotrope-dependent, and died of low-output syndrome 11 months after the onset of symptoms.

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At autopsy, macroscopic examination of the heart showed transmural fibrotic changes in the inferoseptal and inferior LV wall and subendocardial anterolateral LV wall at the base (Figure 2C), which were consistent with the distribution of LGE on CMR. Masson trichrome staining confirmed fibrotic changes (Figure 2F). Microscopically, multinucleated giant cells were observed on the right ventricular side of the septum, at the presumed site of the previous biopsy (Figure 2E). The lateral LV wall had extensive lymphocytic infiltration without giant cells and did not show extensive fibrotic changes (Figure 2D).

Discussion

The associations between CMR and histological findings in GCM remain unclear. LGE can be observed not only in fibrosis or necrosis, but also in other pathological processes such as inflammation and edema. In our patient, the area with LGE on CMR, which may reflect the most severely damaged area, showed not only fibrotic changes, but also findings specific for GCM on autopsy examination. An area with LGE may therefore be a suitable site for biopsy. Although not specific, this pattern of LGE distribution (ie, multiple myocardial areas in different myocardial layers) is atypical for acute (viral) lymphocytic or eosinophilic myocarditis, and may narrow the possible diagnoses down to GCM besides cardiac sarcoidosis.

The LV lateral wall did not show LGE on CMR, even though it had extensive cellular infiltration on autopsy examination. We assume that the diffuse LV hypokinesis, which was well delineated on cine-CMR, may have resulted from pathological changes associated with this diffuse cellular infiltration. Interestingly, the patient’s longitudinal myocardial strain showed diffuse severe impairment, whereas her circumferential myocardial strain was preserved in the LV lateral wall. The longitudinal myocardial strain, which is the most vulnerable component of LV mechanics, may have been associated with the extensive cellular infiltration. In contrast, the circumferential strain, which has less susceptible mechanics reflecting myocardial intramural shortening, can be preserved unless intramural or transmural myocardial insult occurs. In our case, the circumferential strain was preserved in the LV lateral wall, possibly because the middle myocardial layer was not extensively replaced by fibrosis in this area.

In conclusion, our patient with GCM had characteristic CMR findings of LGE, cine-MRI, and myocardial strain, which are related to the clinical features and pathological findings. LGE reflected areas of fibrosis, inflammation, and edema, and possibly specific findings for GCM. On the other hand, diffuse LV hypokinesis and impaired longitudinal strain, which were the primary cause of low-output syndrome, reflected the area with extensive nonspecific cellular infiltration.

Disclosures

None.

References

Figure 1. Electrocardiography showed changes resembling acute myocardial infarction, with intraventricular conduction disturbance with a QRS duration of 129 ms and ST-segment elevation in leads II, III, and aVF with reciprocal changes (arrows).

Figure 2. Cardiac MRI and autopsy examination findings. A, T2-weighted images showed high-intensity signals in the septum and inferoseptal wall at the base (arrows). B, Late-gadolinium enhancement (LGE) was detected in the transmural inferoseptal and inferolateral left ventricular (LV) wall and the subepicardial anterolateral LV wall at the base (arrowheads). C, At autopsy, macroscopic examination of the base of the left ventricle showed transmural fibrotic changes in the inferoseptal and inferior LV wall and in the subendocardial anterolateral LV wall. D and E, Microscopic examination showed multinucleated giant cells on the right ventricular side of the septum at the presumed site of the biopsy, and extensive lymphocytic infiltration without giant cells in the lateral LV wall (hematoxylin and eosin staining; original magnification: D, ×20; E, ×40. F, Masson trichrome staining showed fibrotic foci.

Figure 3. Myocardial strain was evaluated by using Diagnosoft strain-encoded MRI (SENC-MRI). A, Left ventricular longitudinal strain was diffusely impaired. B, Left ventricular circumferential strain was preserved in the lateral wall. SENC-MRI uses tag planes parallel and not orthogonal to the image planes. Therefore, the short-axis view shows longitudinal myocardial strain, and the 4-chamber view shows circumferential strain. Areas of myocardium with severely impaired or absent strain are shown in white, and areas of myocardium with normal strain are shown in red.
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SUPPLEMENTAL MATERIAL
Supplemental Figure 2
Supplemental Figure 3
Supplemental Figure 1

On admission, chest X-ray showed mild cardiomegaly with bilateral pulmonary congestion.

Supplemental Figure 2

A: Four-chamber view, B: short axis view at the apex. Late-gadolinium enhancement (LGE) was detected in the right-ventricular side of the septum at the apex (arrowheads).

Supplemental Figure 3
Endomyocardial biopsy, hematoxyline and eosin staining

Endomyocardial biopsy taken from the right-ventricle was consistent with giant cell myocarditis, revealing multinucleated giant cells (arrow) accompanied with necrosis and prominent lymphocytic and eosinophilic infiltration. No granuloma was found (original magnification; A: × 60, B: × 20)