Localized Doxorubicin-Induced Cardiomyopathy Complicated With Shower Emboli Originating From Apical Intramural Thrombi

Hironori Ishiguchi, MD; Shigeki Kobayashi, MD, PhD; Shinichi Okuda, MD, PhD; Takayuki Okamura, MD, PhD; Munemasa Okada, MD, PhD; Genzou Takemura, MD, PhD; Masaya Takahashi, MD, PhD; Akihito Mikamo, MD, PhD; Kimikazu Hamano, MD, PhD; Masafumi Yano, MD, PhD

Figure. (A, B) Enhanced computed tomography showing (A) multiple emboli in the left kidney and spleen, and (B) intramural thrombi in the left ventricle apex. (C) Extracted intramural thrombi. (D, E) Histology on (D) hematoxylin-eosin (scale bar, 100 μm) and (E) Azan stains (scale bar, 5 mm; inset, 100 μm). (F) Cardiac magnetic resonance (axial view).
A 24-year-old man presented to hospital with complaints of lower back pain and pyrexia that had developed over the preceding 2 weeks. After undergoing chemotherapy that included doxorubicin (DOX; total cumulative dose 260 mg/m²) for acute myeloid leukemia 14 years earlier, he had remained in complete remission and was healthy. Upon admission, computed tomography (CT) showed multiple infarctions in the spleen and left kidney (Figure A), while cardiac CT showed a relatively low-density myocardium, suggesting intramural thrombus (Figure B). Electrocardiogram showed normal sinus rhythm with heart rate 72 beats/min, but poor r wave progression and terminal T inversion in V4. Echocardiography indicated decreased wall motion only at the left ventricular (LV) apex and floating intramural thrombi, instead of normal LV ejection fraction (EF; Movie S1). To prevent secondary systemic embolism, emergency surgical thrombectomy was performed (Figure C). Surgical biopsy samples taken from the LV apex showed extensive scattered cardiomyocytes with vacuolar degeneration (adria cells) on hematoxylin-eosin staining (Figure D), and extensive fibrosis on Azan staining (Figure E). Cardiac magnetic resonance imaging (MRI) showed decreased wall motion only at the LV apex (Movie S2), while late gadolinium enhancement (LGE) was limited to the LV apex (Figure F). Therefore, a diagnosis of DOX-induced cardiomyopathy limited to the apex was established.

This is the first report of localized DOX-induced cardiomyopathy with shower emboli originating from the LV apex. DOX causes diffuse LV contractile dysfunction in a dose-dependent manner when the total cumulative dose is >240 mg/m². Histological characteristics of DOX-induced cardiomyopathy are presence of adria cells, fibrosis, and lysis of myofibrils. The oxidative stress, abnormal intracellular calcium handling, apoptosis, and suppression of gene expression are involved in the pathophysiology of DOX-induced cardiomyopathy. Infiltration of inflammatory cells and apoptosis were not observed on biopsy (Figure D,E) or TUNEL assay (data not shown), respectively, possibly because the DOX treatment had been carried out 15 years earlier and therefore, the inflammatory and apoptotic responses to DOX were no longer in effect.

In this case, DOX-induced cardiomyopathy localized at the apex presented as LGE on cardiac MRI, and the corresponding surgical biopsy samples showed extensive fibrosis. Thus, cardiac MRI is central to diagnosis, even though patients who have undergone treatment with DOX have maintained LVEF within the normal range.

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Disclosures

The authors declare no conflicts of interest.

References


Supplementary Files

Supplementary File 1

Movie S1. Echocardiography showed a floating intramural thrombus and normal left ventricular (LV) ejection fraction (60%) and normal LV size (LV end-diastolic dimension, 52 mm).

Supplementary File 2

Movie S2. Cine magnetic resonance imaging showing decreased wall motion only at the left ventricular (LV) apex and intramural thrombi with normal global LV ejection fraction (62%).

Please find supplementary file(s): http://dx.doi.org/10.1253/circj.CJ-17-1231