Cardiac Magnetic Resonance Imaging and 2-Dimensional Speckle Tracking Echocardiography in Secondary Cardiac Amyloidosis

Kenya Kusunose, MD, PhD; Hirotugu Yamada, MD, PhD; Takashi Iwase, MD, PhD; Susumu Nishio; Noriko Tomita, MD, PhD; Toshiyuki Niki, MD; Koji Yamaguchi, MD, PhD; Kunihiro Koshiba, MD, PhD; Yoshio Taketani, MD, PhD; Takeshi Soeki, MD, PhD; Tetsuzo Wakatsuki, MD, PhD; Masashi Akaike, MD, PhD; Takao Shoichiro, MD, PhD; Masafumi Harada, MD, PhD; Noriko Kagawa, MD, PhD; Eiji Kudo, MD, PhD; Masataka Sata, MD, PhD

Figure 1. ECG, M-mode, Doppler and 2D-STE findings in September 2005 and May 2008. (A-1) ECG was normal sinus rhythm with poor R progression in V₁₋₂. (A-2) ECG was normal sinus rhythm with low voltage and electrical intraventricular conduction progression. (B-1) M-mode echocardiography showed normal wall motion of left and right ventricle with mildly increased wall thicknesses. (B-2) M-mode echocardiography showed a fractional shortening of lower than 15%. (C-1) Transmittal flow velocity profile showed relaxation failure pattern. (C-2) Transmittal flow velocity profile showed restrictive pattern. (D-1) e' was normal. (D-2) e' was impaired. (E-1) 2D-STE demonstrated impaired myocardial systolic radial strain in the antero-septal to septal walls. (E-2) 2D-STE demonstrated marked impairment of myocardial systolic radial strain particularly in the antero-septal to septal walls. 2D-STE, 2-dimensional speckle tracking echocardiography; LV, left ventricle; E, early diastolic transmitral flow velocity; A, atrial systolic transmitral flow velocity; e', early diastolic mitral annular velocity; asp, antero-septal wall; ant, anterior wall; lat, lateral wall; pst, posterior wall; inf, inferior wall; sp, septal wall.

Deposition of amyloid fibrils causes systemic secondary (AA) amyloidosis, a serious complication of many chronic inflammatory disorders (rheumatoid arthritis,

systemic lupus erythematosus etc). Cardiac AA amyloidosis is a rare clinical disease. Lachmann et al reported that cardiac failure attributable to AA amyloidosis was present in only 1

Received February 17, 2010; revised manuscript received April 9, 2010; accepted April 13, 2010; released online May 22, 2010 Time for primary review: 18 days

Department of Cardiovascular Medicine (K.Kusunose, H.Y., T.I., S.N., N.T., T.N., K.Y., K.Koshiba, Y.T., T.Soeki, T.W., M.A., M.S.), Department of Radiologic Science and Technology (T.Shochiro, M.H.), Institute of Health Biosciences, University of Tokushima Graduate School, Tokushima; and Department of Pathology (N.K., E.K.), University of Tokushima School of Medicine, Tokushima, Japan

Mailing address: Hirotugu Yamada, MD, PhD, Department of Cardiovascular Medicine, Institute of Health Biosciences, University of Tokushima Graduate School, 2-50-1 Kuramoto, Tokushima 770-8503, Japan. E-mail: yamadah@clin.med.tokushima-u.ac.jp

ISSN-1346-9843 doi:10.1253/circj.CJ-10-0141

All rights are reserved to the Japanese Circulation Society. For permissions, please e-mail: cj@j-circ.or.jp

Figure 2. Comparison of CMRI, 2D-STE and histopathological findings. (A-1) 2D-STE demonstrated marked impairment of myocardial systolic transmural radial strain particularly in the antero-septal and septal walls (red arrow). (A-2) Strain was calculated in inner and outer myocardial LV wall separately. The outer strain was preserved in posterior to lateral wall (red arrow). (A-3) The inner strain was impaired in posterior to lateral wall (red arrow). (B) The CMRI showed a characteristic pattern of late enhancement in LV septum wall (red arrow). A dark banding artifact existed along endocardial borders. (C) Post-mortem macroscopic examination showed a part of yellow-white deposition in the septum wall. (D) The histopathological studies of the LV septum wall showed extensive interstitial deposition of homogeneous hyaline material that showed metachromasia with Congo red positively with apple-green birefringence (red arrow). CMRI, cardiac magnetic resonance imaging. Other abbreviations see in Figure 1.

of 224 amyloidosis patients who underwent echocardiography.¹ Recently, cardiac magnetic resonance imaging (CMRI) has been proposed to detect transmural tissue involvement of cardiac amyloidosis, which usually occurred from the subendocardium.² In contrast, tissue Doppler imaging or 2-dimensional speckle tracking echocardiography (2D-STE) has been applied as a useful tool to augment echocardiographic assessment in the diagnosis of a variety of cardiac diseases including cardiac amyloidosis.³⁻⁶ Comparison with these images and pathology, however, was not performed directly in these studies. We herein present a case of cardiac AA amyloidosis in which amyloid deposit lesions were observed on CMRI and 2D-STE.

An 78-year-old man presented with bilateral leg edema and worsening fatigue in September 2005. He had a 3-year history of hypertension and rheumatoid arthritis and was being treated with calcium channel blocker, low-dose prednisone and azathioprine. He developed congestive heart failure. Transthoracic echocardiography demonstrated normal wall motion of the left ventricle (LV) and right ventricle with mildly increased LV wall thicknesses on visual estimation (LV septum and posterior wall thickness of 12 mm; Figure 1 B-1). LV ejection fraction was 55% with LV diastolic failure (relaxation failure transmitral flow velocity pattern; grade 1 of 4; Figures 1 C-1, D-1). Systolic radial strain (S) and strain rate

(SR) of regional myocardium were calculated from transthoracic short-axis images of mid LV using newly developed 2D-STE software (Toshiba Medical Systems, Tochigi, Japan). 2D-STE demonstrated impaired myocardial systolic radial strain in the antero-septal to septal walls with a mean S of 13.5% and SR of 0.55 (1/s) (Figure 1 E-1). Coronary angiography was normal. Although serum and urine samples did not show elevated lambda light-chain proteins and a rectum biopsy did not show amyloid deposit, we diagnosed the patient as having cardiac amyloidosis and treated him with diuretic therapy as well as low-dose β -adrenergic blocker.

In May 2008 the patient presented with symptoms of heart failure (New York Heart Association class IV) and loss of appetite. ECG showed normal sinus rhythm with low voltage and electrical intraventricular conduction progression (Figures 1 A-1, A-2). Transthoracic echocardiography showed concentric hypertrophy of LV, a speckled appearance and fractional shortening of <15% (Figure 1 B-2), and diastolic dysfunction with restrictive LV filling (grade 4 of 4; Figures 1 C-2, D-2). 2D-STE demonstrated marked impairment of myocardial systolic radial strain particularly in the antero-septal and septal walls with a mean S of 4.0% and SR of 0.30 (1/s) (Figures 1 E-2, 2 A-1, red arrow). CMRI demonstrated concentric hypertrophy of LV and reduced LV systolic function. Delayed contrast enhancement imaging (bolus of 0.2 mmol/kg

gadolinium-diethylenetriamine penta-acetic acid) demonstrated suboptimal nulling of the myocardium preceding that of the blood pool and mild transmural heterogeneous (sub-end-mid cardium dominant hyper-enhancement in LV septum wall; **Figure 2B**, red arrow). Strain was calculated in the inner and outer myocardial LV wall separately (**Figures 2 A-2,3**). 2D-STE showed abnormal subendocardial radial strain in the posterior wall. The patient suddenly died of ventricular fibrillation 4 weeks after admission. Post-mortem macroscopic examination showed yellow-white deposition in the septum wall (**Figure 2C**, red arrow). Histopathology of the LV septum wall, liver and kidney indicated extensive interstitial deposition of homogeneous hyaline material with metachromasia, staining positive with Congo red with apple-green birefringence (**Figure 2D**, red arrow). The amyloid was stained negatively with Congo red after potassium permanganate treatment, confirming the diagnosis of AA amyloidosis.

This is an interesting case that addresses the importance of CMRI and 2D-STE in diagnosing cardiac involvement in this disease. Cardiac involvement is one of the major causes of death in patients with AA amyloidosis and is associated with overt congestive heart failure. It was reported that the sensitivity of right ventricular endomyocardial biopsy is high in systemic amyloidosis, but it is unknown whether this fact can be applied in secondary amyloidosis. Abnormal findings on CMRI and 2D-STE were confirmed as amyloid deposit in secondary cardiac amyloidosis on post-mortem macroscopic and histopathologic examination (**Figure 2**). CMRI presented a characteristic pattern of late enhancement in the LV septum wall that is related to the histological distribution of amyloid protein. Follow-up echocardiography for 3 years

showed impaired LV systolic function and demonstrated amyloid deposit. The peak S and SR in segments with cardiac involvement were significantly smaller than these in segments without involvement. CMRI and 2D-STE were useful tools to detect the segments with amyloid deposit and facilitate a diagnosis of secondary cardiac amyloidosis. A combination of these imaging techniques may be useful for non-invasive diagnosis in secondary cardiac amyloidosis.

References

1. Lachmann HJ, Goodman HJ, Gilbertson JA, Gallimore JR, Sabin CA, Gillmore JD, et al. Natural history and outcome in systemic AA amyloidosis. *N Engl J Med* 2007; **356**: 2361–2371.
2. Vogelsberg H, Mahrholdt H, Deluigi CC, Yilmaz A, Kispert EM, Greulich S, et al. Cardiovascular magnetic resonance in clinically suspected cardiac amyloidosis: Noninvasive imaging compared to endomyocardial biopsy. *J Am Coll Cardiol* 2008; **51**: 1022–1030.
3. Sun JP, Stewart WJ, Yang XS, Donnell RO, Leon AR, Felner JM, et al. Differentiation of hypertrophic cardiomyopathy and cardiac amyloidosis from other causes of ventricular wall thickening by two-dimensional strain imaging echocardiography. *Am J Cardiol* 2009; **103**: 411–415.
4. Smedema JP, James R. Tissue Doppler imaging and contrast-enhanced cardiac magnetic resonance in primary cardiac amyloidosis. *Eur J Echocardiogr* 2009; **10**: 984–986.
5. Onishi T, Uematsu M, Nanto S, Morozumi T, Watanabe T, Awata M, et al. Detection of diastolic abnormality by dyssynchrony imaging: Correlation with coronary artery disease in patients presenting with visibly normal wall motion. *Circ J* 2009; **73**: 125–131.
6. Minoshima M, Noda A, Nishizawa T, Hara Y, Sugiura M, Iino S, et al. Endomyocardial radial strain imaging and left ventricular relaxation abnormalities in patients with hypertrophic cardiomyopathy or hypertensive left ventricular hypertrophy. *Circ J* 2009; **73**: 2294–2299.