Miraculous Recovery of a Dilated Heart after Usage of Supramaximal Titrated Valsartan for 8 Months

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To the Editor: Dilated cardiomyopathy (DCM) is characterized by ventricular chamber enlargement and systolic dysfunction. DCM is identified when complicated by severe clinical symptoms and disability and ultimately leads to progressive heart failure (HF) and a decline in left ventricular (LV) contractile function, ventricular and supraventricular arrhythmias, conduction system abnormalities, thromboembolism, and sudden heart failure-related death. Overactivation of renin-angiotensin-aldosterone systems (RAAS) is one of the key detrimental mechanisms of DCM progression and is associated with poor prognosis. Despite considerable advances in neurohumoral modulation therapy including angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), mortality and morbidity among DCM patients remains high.

A 32-year-old Chinese-American male with a 1-year history of type 2 diabetes was admitted with chest distress and shortness of breath for 1 month. He had no history of alcohol or drug addiction, nor viral infection. The patient visited Mayo Clinic and Cleveland Clinic; echocardiogram showed significant LV enlargement with severe global systolic dysfunction with estimated LV ejection fraction (LVEF) 15–25%. He was diagnosed with DCM on the 1st day of admission; echocardiogram showed LV end-diastolic diameter (LVDd) of 70 mm × 68 mm × 81 mm (anteroposterior × lateral × length diameters), estimated LVEF 25%, end-diastolic volume (EDV) 213 ml, end-systolic volume (ESV) 160 ml, motion pulse of all portions of LV except for the posterolateral wall being generally weak by 2–5 mm [Figure 1a]. Chest X-ray showed mild pulmonary congestion, enlarged left atrial and LV; cardiothoracic ratio was 0.55 [Figure 1c]. The patient received our prescription as follows: valsartan 640 mg daily in total (including 480 mg nightly), hydrochlorothiazide 12.5 mg and carvedilol 6.25 mg twice daily.

At 3 months follow-up, the patient was well and reported no significant discomforts. Echocardiogram showed LV measuring 59 mm × 57 mm × 86 mm as LVDd, estimated LVEF 44%, EDV 150 ml, ESV 80 ml [Figure 1b]. Chest X-ray showed no noteworthy abnormalities, and cardiothoracic ratio was 0.49 [Figure 1d]. Accordingly, the dose of valsartan was reduced to 560 mg once daily in total (including 320 mg nightly). At 8 months follow-up, the patient reported significant improvement in exercise capacity. By echocardiography, the heart size was nearly within a normal size; LV diameters were 55 mm × 52 mm × 83 mm as LVDd, estimated

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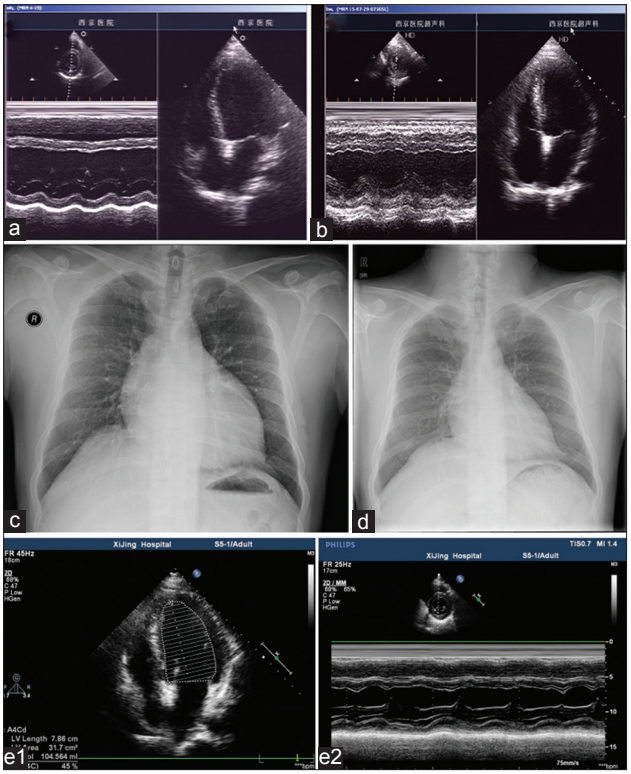

Figure 1: Echocardiogram (a) at admission, (b) after receiving supramaximal doses valsartan for 3 months, (e1 and e2) after receiving supramaximal doses valsartan for 8 months; chest X-ray (c) at admission, (d) after receiving supramaximal doses valsartan for 3 months.

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Table 1: Echocardiography changes during the 8 months

Date	LA (mm)	LV (mm)	RA (mm)	RV (mm)	LVEF (%)	EDV (mm)	ESV (mm)
April 19, 2015	42	70/68/81	39	26	25	213	160
July 29, 2015	39	59/57/86	34	24	44	150	80
December 7, 2015	40	55/52/83	33	29	45	105	58

LV: Left ventricular; RV: Right ventricular; LA: Left atrium; RA: Right atrium; LVEF: Left ventricular ejection fraction; EDV: End-diastolic volume; ESV: End-systolic volume.

LVEF 45%, EDV 105 ml, ESV 58 ml [Figure 1 e1–e2 and Table 1]. No hepatic or renal dysfunction was found. Accordingly, the dosage of valsartan was reduced to 320 mg once daily in total (including 240 mg nightly), and carvedilol maintained 6.25 mg twice daily.

HF is a worldwide public health problem affecting more than 23 million patients.[1] Patients with HF are associated with high rates of hospitalization, readmission, and mortality. Despite remarkable progress in diagnosis and treatment, the prognosis remains unsatisfactory, with mortality rates approaching 20%/year.[2] Numerous clinical trials with ACEI/ARB, including valsartan, have been demonstrated to improve clinical symptoms and cardiac systolic function and decrease rehospitalization and mortality rate. The blockade of RAAS has been established as a basic and crucial guideline-recommended therapy. However, a large amount of patients with DCM still deteriorated to end-stage HF despite the use of standard ACEI/ARB therapy. It is suggested that one possible reason may be the current guideline-recommended dose of ACEI/ARB for the treatment of HF is failed to block tissue-based RAAS, which is activated in HF and participates in myocardial fibrosis, cytokine activation, and ultimately remodeling. The major concern against the use of higher doses of ACEI/ARB in DCM patients with HF is its potential association with hypotension and hyperkalemia. This reported case indicated that valsartan 480–640 mg daily can be well tolerated. Titration of valsartan, up to 640 mg/d, was well tolerated in patients with type 2 diabetes and persistent proteinuria, and no dose-related increases in adverse events, including hypotension and hyperkalemia, was reported in the previous study.[3] Furthermore, bedtime administration was recommended to prevent hypotension-related symptoms. In addition, the prescribed dosage of valsartan, according to the size of LV, was gradually reduced to a standard dosage to prevent possible renal dysfunction resulting from long-term supramaximal dosage.

Maybe, the strategy of supramaximal titrated inhibition of RAAS according to the size of left ventricular will provide a new vision to further reduce mortality and improve survival in DCM patients with HF. At present, we have been committing ourselves to carry out several large-scale prospective clinical studies to verify its good feasibility and safety and afford more strengthful evidence to clinical practice.[4]

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Conflicts of interest

There are no conflicts of interest.

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