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Reverse remodeling in a heart failure patient with cardiomegaly treated with sacubitril/valsartan: a case report

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Sacubitril/valsartan (S/V) has shown promise as a tool for decreasing cardiovascular hospitalization and associated mortality among certain patients with heart failure and has been found to exhibit potential renoprotective and antiarrhythmic activity. This report is describing the case of a patient that suffered acute myocardial infarction within one month after undergoing percutaneous coronary intervention (PCI) stent implantation and who underwent standard guideline-directed medical treatment. Upon readmission, echocardiographic evaluation revealed enlargement of the left heart and reduced ejection fraction. While hospitalized, treatment with S/V was begun. Following sustained treatment with this drug for five months, the patient exhibited vascular remodeling, a 30% injection fraction improvement, a 15 mm reduction in left ventricular diastolic diameter, and a significant change in functional class from class III to I. Overall, this case report emphasizes the association between S/V treatment and reverse ventricular remodeling in a patient that experienced cardiomegaly following AMI.

1. Introduction

Heart failure (HF) is a shocking clinical and public health problem. It is a complex clinical condition that ultimately develops as a result of a range of different cardiovascular diseases, resulting in the worsening of left ventricular function and high rates of consequent morbidity and mortality. In addition, the medical expenses for patients with heart failure are high, especially for the elderly. These costs represent the consequence of heart failure as a chronic and progressive disease, with worsening events requiring hospitalization and readmission from time to time, usually with increasing frequency over time (Orso et al. 2017). Heart failure patients can be divided into heart failure with preserved ejection fraction (HFpEF), usually left ventricular ejection fraction ≥50% or heart failure with reduced ejection fraction (HFrEF), usually LVEF <40% (Ponikowski et al. 2016). The publication of the European Society of Cardiology Guidelines in Paradum-HF 2016 emphasized the advantages of S/V treatment for heart failure patients with reduced ejection fraction (HFREF) relative to enalapril, with the former being associated with lower rates of HF-related hospitalization and mortality (McMurray et al. 2014; Solomon et al. 2016). This breakthrough has promoted the application of S/V in patients with HFrEF. S/V is a novel first-in-class drug combining angiotensin receptor and neprilysin inhibitors. By inhibiting neprilysin, sacubitril can elevate circulating natriuretic peptide (NP) levels. This, together with simultaneous renin-angiotensin-aldosterone system (RAAS) inhibition results in decreased renin secretion, increased glomerular filtration, natriuresis, vasodilation, and reductions in tissue fibrosis and hypertrophy (Khan et al. 2018; Gu et al. 2010). S/V treatment has been successfully used to treat HF and hypertension patients, and its beneficial properties are associated with significant improvements in left ventricular function and with reverse cardiac remodeling (Sackner-Bernstein and Mancini 1995).

Cardiac Reverse Remodeling (CRR) usually refers to the improvement of the volume, size and shape of the damaged ventricle/atrium. It is a form of myocardial fibrosis. It is a series of cell and histological changes in myocardial tissue that cause changes in the size and function of the heart result. There is some prior evidence that such remodeling can be reversed in HFREF patients when cardiac damage is eliminated or treatment with appropriate medication is initiated (Iborra-Egea et al. 2017). S/V therapy has been successfully used to treat patients with heart failure and hypertension, and its beneficial properties are related to the significant improvement of left ventricular function and reversal of cardiac remodeling (Mentz et al. 2013). Although the physiological mechanism of valsartan/valsartan is well known, its effect on left ventricular remodeling and left ventricular ejection fraction (LVEF) has not been well studied. Herein, we describe the case of a male patient who suffered from relapsed myocardial infarction with heart failure following percutaneous transluminal coronary intervention (PCI). For this patient, we found that S/V treatment was associated with significant left ventricular reverse remodeling.

2. Case report

A 49-year-old male patient was admitted to the hospital complaining of chest tightness, dyspnea, and an aggravated dry cough. On December 31, 2019, he was hospitalized for persistent chest tightness. Upon admission, he was diagnosed with coronary atherosclerotic heart disease accompanied by acute myocardial infarction (AMI), and was discharged following PCI. One week after discharge, the patient experienced recurrent chest tightness that improved with medication adjustment. On January 20, 2020, the patient presented himself to the Second Affiliated Hospital of Nanchang University, at which time an echocardiographic assessment of his left ventricular anterior wall and partition mobility revealed an ejection fraction (EF) of 37%. In addition, left atrial left ventricular enlargement was noted, with a left atrial diameter (LAVI) of 51 mm, a left ventricular end-diastolic diameter (LVEDD) of 59 mm, and a left ventricular end systolic diameter (LVESD) of 49 mm. The patient was admitted to the Second Affiliated Hospital of Nanchang University January 24, 2020. Following admission, echocardiographic ultrasound analysis revealed an EF of 33%, a LAVI of 40 mm, an LVEDD of 58 mm, and an LVESD of 48 mm. Standard pharmacological treatment for heart failure was initiated. On January 27, 2020, treatment with S/V (49/51 mg Bid) was initiated. After clinical improvement, the patient was

discharged and S/V treatment was sustained without any change in dosage. On April 16, 2020, the patient appeared at Nanchang First People's Hospital for reexamination, at which time cardiac ultrasound revealed an EF of 47%, a LAVI of 40 mm, an LVEDD of 56 mm, and an LVESD of 43 mm. On June 22, 2020, he again presented himself to Nanchang First People's Hospital for reexamination at which time an EF of 67%, a LAVI of 30 mm, an LVEDD of 44 mm, and an LVESD of 28
mm were observed (Table).

Table: Echocardiographic parameters

	Start of treatment	3 months after starting	5 months after starting
EF (%)	37	47	67
LAVI (mm)	51	40	30
LVEDD (mm)	59	56	44
LVESD (mm)	49	43	28
E/A ratio	119/43	85/97	80/96
e/a ratio	8/5	e<a	e<a

3. Discussion

LVEF has been shown to predict heart failure-related hospitalization, cardiovascular death, and all-cause death among HFREF patients. The patient in the present report suffered from cardiac failure as a result of AMI, and exhibited clinical deterioration despite standard treatment. We therefore elected to treat this patient with S/V, and observed significant improvements in both symptoms and functional capacity after a 5-month treatment period. Echocardiographic evaluation revealed an increase in LVEF from 37% to 67%, while LVEDD fell from 59 mm to 44 mm, and LVESD declined from 49 mm to 28 mm after treatment. The patient also experienced no symptoms of chest tightness following discharge.
The observed clinical improvements in the present case underscore the value of S/V treatment, and suggest that this drug may have the potential to reduce heart failure-related hospitalization, mortality, and adverse cardiac remodeling in HFREF patients. Neprilysin inhibition may contribute to reductions in pulmonary pressure, mitral regurgitation, and myocardial afterload. The mechanisms whereby S/V treatment achieves antiarrhythmic activity are less clear, but may be linked to complicated interactions between ejection fraction increases, reductions in sympathetic tone, and reverse remodeling.
Previous clinical trials demonstrated that LVEF was enhanced after prolonged treatment with ARNI. Proving short-term effectiveness is controversial, however.

The long-term beneficial outcomes in the present case and our overall experience with this patient suggest that additional large-scale clinical trials evaluating echocardiographic outcomes in S/V-treated patients are warranted to understand the impact of such treatment on ventricular remodeling. In summary, we found that S/V treatment in this patient was safe, feasible, and associated with symptomatic improvement.

Conflicts of interest: All authors have no conflict of financial or non-financial interest in the submission of this manuscript. Moreover, we declare that none of the work contained in this manuscript, in whole or in part, is published in any language or currently under consideration at any other journal. Each named author has read and approved this version of this article, and due care has been taken to ensure the integrity of the work.

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