

[ CASE REPORT ]

## Successful Medical Treatment Using Tolvaptan of Ventricular Septal Rupture Following Myocardial Infarction

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### Abstract:

Although improved treatments for acute myocardial infarction (AMI) have considerably reduced the mortality of AMI in the past two decades, the treatment for ventricular septal rupture (VSR)-a rare but life-threatening mechanical complication of AMI-still remains quite challenging. We herein describe the case of a high-surgical-risk patient with VSR after AMI who was successfully treated using tolvaptan (a novel V<sub>2</sub>-receptor antagonist) without any mechanical support.

**Key words:** acute myocardial infarction, ventricular septal rupture, Tolvaptan, heart failure

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### Introduction

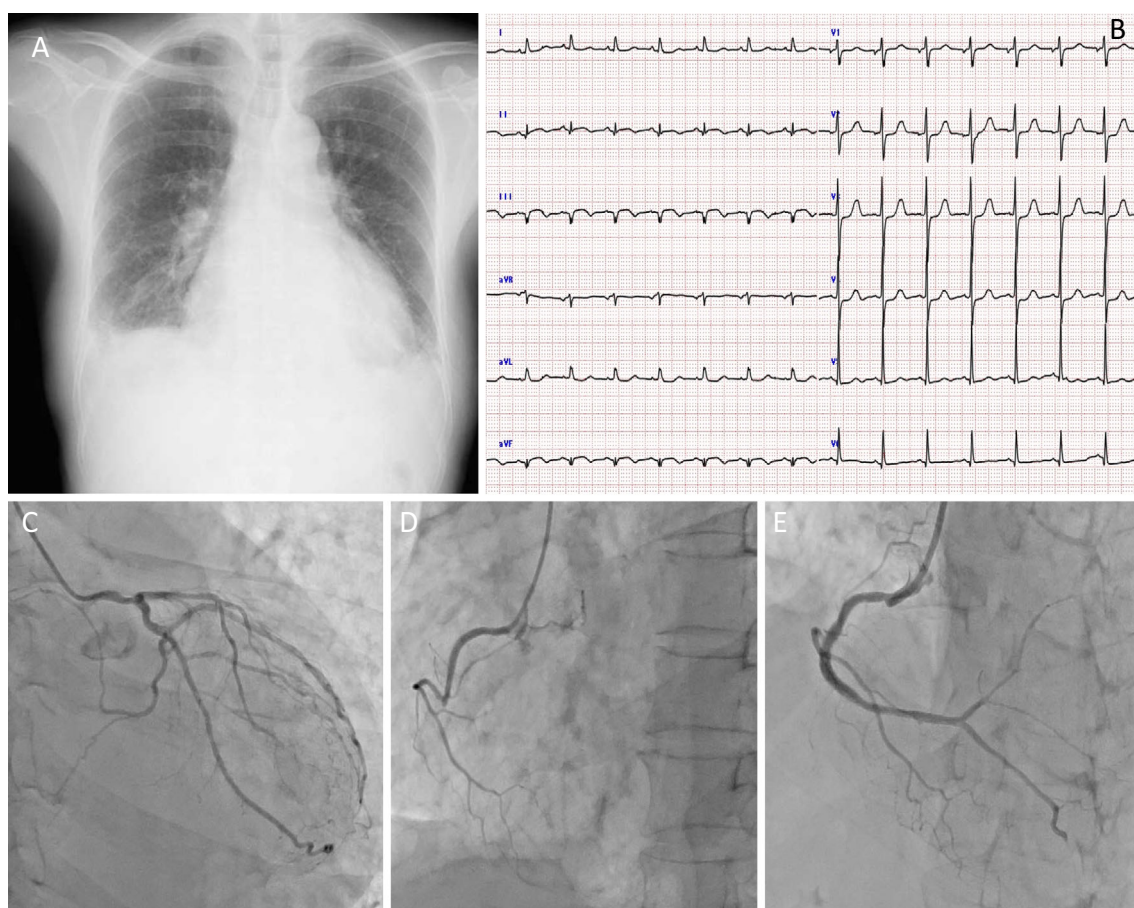
The effectiveness of percutaneous coronary intervention and advances in adjunctive pharmacotherapies for the treatment of acute myocardial infarction (AMI) have considerably reduced the mortality associated with AMI in the past two decades (1, 2). However, treatment for ventricular septal rupture (VSR)-a rare but life-threatening mechanical complication of AMI - still remains extremely challenging.

The mortality associated with VSR generally remains high, but it varies (from 19-64%) when surgical repair is performed. In contrast, the mortality consistently reaches 90-95% when VSR is treated conservatively (3). Although delaying surgery in stable patients with VSR may provide better results, conventional medical therapy with such drugs as furosemide, carperitide, and dobutamine is usually futile. Therefore, until now, surgical repair using full mechanical support has been considered the sole option (3). We herein describe the case of a high-surgical-risk patient with VSR after AMI who was successfully treated using tolvaptan (a novel V<sub>2</sub>-receptor antagonist) without any mechanical support.

### Case Report

A 78-year-old man was taken to the emergency room be-

cause he had presented with continued general fatigue and shortness of breath over the previous 2 weeks following an episode of chest pain. On examination, he was ill-appearing and febrile with a temperature of 37.5°C. His blood pressure was 78/52 mm Hg, pulse 112/min, respiratory rate of 22/min with an O<sub>2</sub> saturation of 91% on room air. A heart exam revealed S3 and a holosystolic murmur was noted. His chest exam revealed decreased breath sounds bilaterally. Chest X-rays showed a distinctive pattern of congestive heart failure (CHF) (Fig. 1A). The laboratory data are shown in Table 1. Moreover, a coronary angiogram was immediately acquired as the electrocardiogram demonstrated inferior Q wave and ST elevation (Fig. 1B). The coronary angiogram showed no significant stenosis of the left coronary artery (Fig. 1C) and the subtotal occlusion of the right coronary artery (Fig. 1D), which was successfully treated by the implantation of a bare metal stent (Fig. 1E). After recanalization, transthoracic echocardiography (TTE) showed a preserved left ventricular function and moderate pulmonary artery hypertension with moderate tricuspid regurgitation. Furthermore, TTE revealed aneurysmal dilatation in the inferior and septal myocardial segment concomitant with 4.2 mm of VSR (Fig. 2A, B). The findings on TTE are shown in Table 2. To improve the congestion, carperitide was administered at an initial dose of 0.1 µg/kg/min, and furosemide 20 mg was administered twice a day. However, as hemodynamic instability frequently occurred, repeated saline



**Figure 1.** A) Chest X-ray findings at admission. B) Electrocardiogram findings at admission. C) No significant stenosis in the left coronary artery. D) Total occlusion of the right coronary artery (RCA). E) A bare-metal stent was implanted at the middle part of the RCA.

**Table 1.** Laboratory Data at Admission.

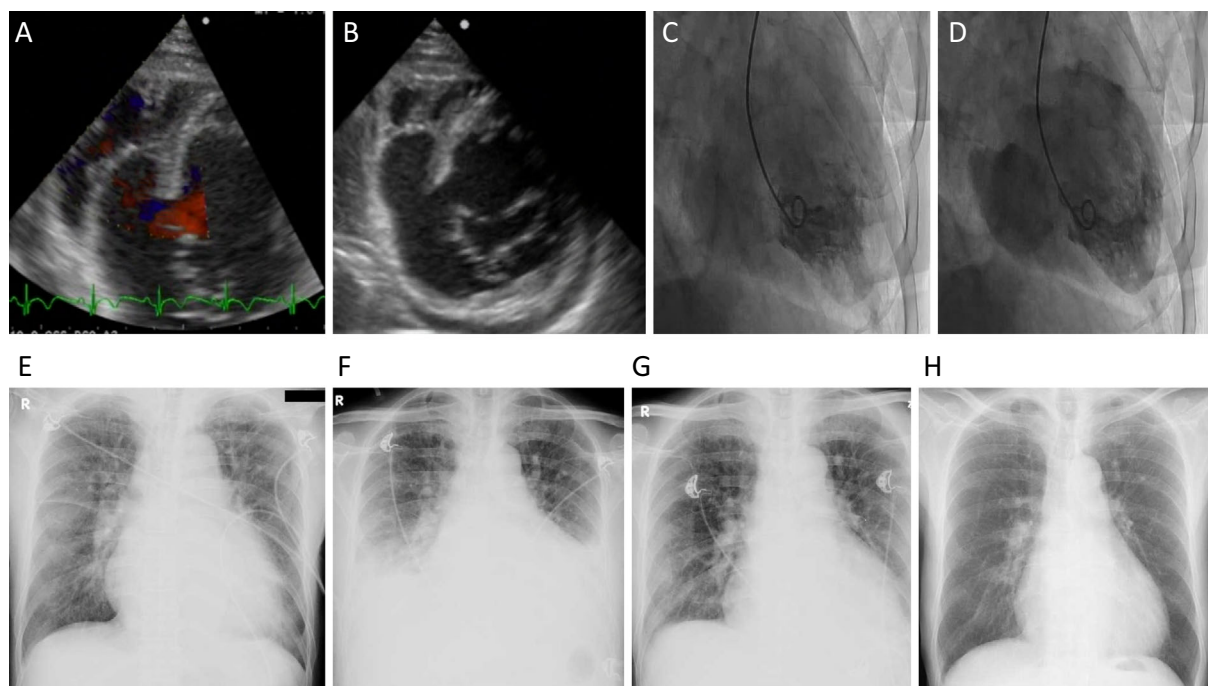
AST	54	IU/L	K	3.8	mEq/L
ALT	71	IU/L	CL	99	mEq/L
r-GTP	17	IU/L	CA	8.1	mg/dL
T-BIL	1.4	mg/dL	BS	169	mg/dL
ALP	189	IU/L	CRP	4.68	mg/dL
LDH	510	IU/L	WBC	6,100	$\mu$ L
CPK	288	IU/L	RBC	$371 \times 10^4$	
BNP	1,069.4	pg/mL	Hb	12.3	g/dL
UA	9.4	mg/dL	Plt	$30.3 \times 10^4$	
UN	28.3	mg/dL	PT	16.4	sec
CRE	1.03	mg/dL	PT %	48	%
TP	5.6	g/dL	PT_INR	1.44	
ALB	3.3	g/dL	APTT	41.1	sec
T-CHO	157	mg/dL	APTT%	55	%
TG	87	mg/dL	D-Dimer	4.3	$\mu$ g/mL
AMY	86	IU/L	CK-MB	10	IU/L
NA	134	mEq/L	Troponin I	2.672	ng/mL

infusions were necessary to restore his blood pressure. At 6 days after admission, tolvaptan 7.5 mg was introduced because of hemodynamic instability and increased pleural effusion. The administration of tolvaptan dramatically increased the patient's urinary output, thus reducing the pleural effu-

sion.

At 12 days after admission, cardiac rehabilitation was started due to hemodynamic stability. At 22 days after admission, left and right cardiac catheterization was performed to assess the indications for surgical repair. A coronary angiogram revealed the right coronary artery to have no significant stenosis. Right heart catheterization revealed an elevated pulmonary capillary wedge pressure and a significant oxygen saturation step-up in the right ventricle. Left ventriculography showed a significant left-to-right shunt, and the right ventricle was enhanced in a delayed fashion (Fig. 2C, D). The calculated ratio of the volume of the pulmonary flow and systemic flow was over 6.0. The findings on right and left heart catheterization are shown in Table 3.

Based on these results, surgical repair was considered. However, his state of dementia worsened due to long-term hospitalization; owing to tolvaptan administration, the patient's hemodynamic stability improved the surgical repair threshold and surgery was therefore no longer required. Finally, he was discharged at 32 days after admission. The chest X-ray changes are illustrated in Fig. 2E-H. Furthermore, the patient's hemodynamic status and urine volume are summarized in Fig. 3.



**Figure 2.** A) Transthoracic echocardiography (TTE) showed aneurysmal dilatation in the inferior and septal myocardial segment concomitant with 4.2 mm of VSR, B) with color doppler. C) Left ventriculography showed a significant left-to-right shunt. D) The right ventricle was enhanced in a delayed fashion. E) Chest X-ray findings at 1 day after admission. F) Chest X-ray findings at 6 days after admission—shortly before introduction to vaptan. G) Chest X-ray findings at 12 days after admission. H) Chest X-ray findings at discharge.

**Table 2.** Findings on Transthoracic Echocardiography at Admission.

AODs	22.6	mm
LAD	33.7	mm
IVST	7.4	mm
PWT	5.9	mm
LVDd	51.0	mm
LVEDV	162.1	mL
LVESV	77.1	mL
SV	85.0	mL
EF	52	%
IVC	17	mm
AR	trivial	
MR	trivial	
TR	Mild-moderate	
TR-PG	26	mmHg
pericardial effusion(+)		

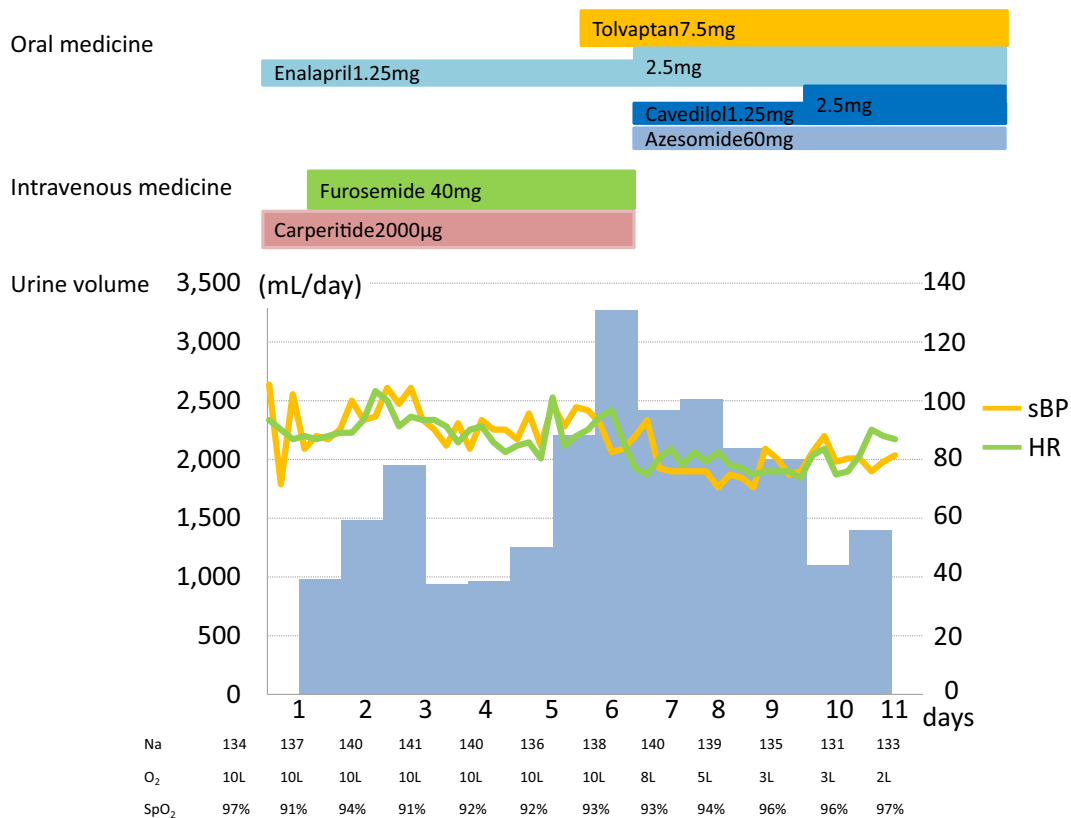
AODs: aortic root diameter, LAD: left atrial dimension, IVST: interventricular septum thickness, PWT: posterior LV wall thickness, LVDd: left ventricular end-diastolic dimension, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, SV: stroke volume, EF: ejection fraction, IVC: inferior vena cava, AR: aortic regurgitation, MR: mitral regurgitation, TR: tricuspid regurgitation, PG: pressure gradient

## Discussion

VSR is a rare but well-known complication after AMI. In the prethrombolytic era, VSR was thought to complicate 1-2% of AMI presentations (1). After percutaneous coronary intervention became a common practice for AMI, however, more contemporary series show it to be increasingly rare, complicating between 0.17 and 0.31% of the patients presenting with AMI (4-6). Therefore, the frequency of VSR has decreased as a result of the wide acceptance of early reperfusion therapy as it prevents extensive myocardial necrosis and preserves the left ventricular function (1, 3-6).

The conventional mechanism of VSR involves coagulation necrosis of the ischemic tissue with neutrophilic infiltration, eventually causing thinning and weakening of the septal myocardium (1). This sub-acute process takes 3-5 days—an interval that likely accounts for the traditional timing reported in the early surgical literature. It has recently been proposed that a rupture occurring within 24 hours of presentation is more likely due to dissection of an intramural hematoma or a hemorrhage in the ischemic myocardium (3).

When reperfusion therapy is delayed, then perfusion therapy may lead to myocardial hemorrhage and dissection in the zone of necrotic myocardium, subsequently resulting in a worsening VSR. Therefore, whether reperfusion therapy should be performed in patients with delayed MI still remains controversial. However, this patient was treated using



**Figure 3.** Highlights of the hemodynamic status and urine volume.

**Table 3.** Findings on Left and Right Cardiac Catheterization.

SVC	0-14 (7)	mm Hg
RA	0-16 (8)	mm Hg
Main PA	15-42 (25)	mm Hg
Right PA	12-39 (24)	mm Hg
PCW	20-39 (20)	mm Hg
RV	0-38 (19)	mm Hg
LV	4-70 (34)	mm Hg
LVEDP	12	mm Hg
Aorta	52-74 (62)	mm Hg
EF	51	%
LVEDV	121	mL
LVESV	59	mL
CO	4.9	L/min

SVC: superior vena cava, RA: right atrium, PA: pulmonary artery, PCW: pulmonary capillary wedge pressure, RV: right ventricle, LV: left ventricle, LVEDP: left ventricular end-diastolic pressure, EF: ejection fraction, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, CO: cardiac output

erate the continuous use of IABP because of his moderate dementia. Despite advances in pharmacotherapies, coronary intervention, and surgical techniques, the mortality of patients treated with a surgical repair of VSR remains high (3). The most important predictors of early mortality are reported to be the deterioration of patient's condition before surgical repair and cardiogenic shock on admission. As conservative therapy is associated with an extremely high mortality rate of 94-100%, the timing of surgical repair is critical. It was previously reported that the patients undergoing an early operation for VSR have a more adverse outcome compared with those undergoing late surgery (3). Society of Thoracic Surgeons data showed that patients who underwent surgery within 7 days of presentation had a 54.1% mortality compared with 18.4% mortality if repair was delayed until after 7 days. Mortality was highest (60%) in patients who underwent operation in the first 24 hours, consistent with other investigators (7). Thus, adjunctive pharmacotherapies are important to delay surgical repair. The goals of immediate management include maintaining the coronary artery blood flow, a reduction of systemic vascular resistance with the aim of left-to-right shunt reduction, and maintaining the cardiac output and mean arterial blood pressure to ensure adequate end-organ perfusion. Among the common pharmacotherapies, tolvaptan (a drug that exerts aquaretic effects by blocking the V<sub>2</sub> receptor in the renal collecting ducts and consequently results in the inhibition of water reabsorption) may potentially benefit such patients. According to experts, tolvaptan is recognized as the only novel agent tested in pa-

a bare-metal stent to improve hemodynamic stability, although 2 weeks had already passed after the onset of AMI. Although the use of IABP (intra-aortic balloon pump) has been suggested in this setting (3), our patient could not tol-



tients hospitalized for acute CHF syndrome to reach short-term efficacy without causing deleterious side effects (8). Recently, Jujo et al. demonstrated that the initiation of tolvaptan therapy in acute CHF patients exerted potent dehydration effects and preserved the renal function and the renin-angiotensin-aldosterone system without any adverse effects as compared to furosemide therapy (9). Furthermore, Suzuki et al. revealed that less adverse events, such as worsening heart failure and hypotension requiring drug discontinuation, were observed in the tolvaptan group as compared to carperitide (10). Therefore, tolvaptan has a potential to reduce the patient's edema, improve dyspnea, correct hyponatremia, and to be well-tolerated without adversely affecting the blood pressure, heart rate, electrolyte levels, or renal function when combined with standard therapy (11). Indeed, tolvaptan can be an effective and safe option, particularly in patients with VSR with low cardiac function and low blood pressure. Concomitant with a conventional approach, tolvaptan can help improve congestive heart failure in these cases, and may thus have the potential to become a groundbreaking treatment.

**The authors state that they have no Conflict of Interest (COI).**

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