福岡大医紀（*Med. Bull. Fukuoka Univ.*）：44(2)，91–96，2017

Ventricular Septal Perforation after Acute Myocardial Infarction with Severe Inflammation: Three Case Reports

Keisuke OKAMURA [1),2)], Etsuo MORI [1),3)], Toshihiro NAKAMURA [1)]

1) *Department of Cardiology, National Kyushu Medical Center*
2) *Department of Cardiovascular Diseases, Fukuoka University Chikushi Hospital*
3) *Chihaya Heart Clinic*

Abstract

Ventricular septal perforation（VSP）is one of the severe mechanical complications associated with acute myocardial infarction（AMI）. Although it is rare, VSP has a high mortality rate. VSP is characterized by biventricular volume overload due to left-to-right shunt. Combined with cardiac dysfunction due to AMI, it rapidly leads to heart failure.

This report presents three AMI patients with VSP who were treated at National Kyushu Medical Center. Urgent cardiac catheterization was performed for definite diagnosis, followed by emergency surgery, but two patients died.

In General, advanced age, female sex, initial onset, and diabetes were risk factors for VSP, while the risk factors for postoperative death were shock, advanced age, catecholamine use, low cardiac output, and percutaneous cardiopulmonary support. The one of the fatal case for VSP had many of these risk factors, as well as high levels of inflammatory parameters.

Early diagnosis is important for management of the mechanical complications of AMI. In patients with high levels of inflammatory parameters, it should be remembered that the risk of VSP is elevated.

Key words: Acute myocardial infarction, Ventricular septal perforation, Inflammation, Cardiac catheterization, Mechanical complication

Introduction

The important mechanical complications of acute myocardial infarction（AMI）include left ventricular aneurysm, ventricular septal perforation（VSP）, mitral valve insufficiency, and cardiac rupture（left ventricular free wall rupture）. Although the incidence rate of these complications varies, a common feature is a rapid decline of cardiac function that affects the prognosis. Among them, VSP has a high mortality and is characterized by biventricular volume overload due to left-to-right shunt. Severe heart failure occurs rapidly when the effects of VSP are added to cardiac dysfunction resulting from AMI. It has been reported that advanced age, female sex, initial onset, and diabetes are risk factors for the occurrence of VSP, while the risk factors for postoperative mortality after repair of VSP are shock, advanced age, catecholamine use, low cardiac output, and percutaneous cardiopulmonary support（PCPS）. The mortality rate is high in patients with VSP and the prognosis is poor. Since pharmacotherapy is not effective, urgent surgical intervention is required. Therefore, early diagnosis of mechanical complications is important in patients with AMI. If patients have evidence of severe inflammation, it should be remembered that the risk of VSP is increased.

In this article, 3 cases of VSP are presented together with a literature review.

Correspondence to: Keisuke Okamura, MD, Department of Cardiovascular Diseases, Fukuoka University Chikushi Hospital, 1-1-1, Zokumyoin, Chikushino-shi, Fukuoka, 818-8502, JAPAN.
TEL：81-92-801-1011　Fax: 81-92-928-3890　E-mail: okamurakmd@cis.fukuoka-u.ac.jp

Case Reports

Case 1

A 78-year-old woman.

She was known to have hypertension, but medications had not been prescribed. She felt sudden onset of sustained chest pain when straining on the toilet. When she visited a local doctor one hour later, auscultation revealed a generalized systolic murmur (Levine 4/6) and there was ST segment elevation in leads II, III, and aVF of the ECG. Ultrasound cardiography (UCG) demonstrated akinesis of inferior posterior ventricular wall and cardiac enzymes were elevated. AMI was diagnosed and the patient was urgently transferred to our hospital.

Urgent coronary angiography revealed complete occlusion of the right coronary artery (RCA) at segment 3 (Figure 1). After aspiration of the thrombus, Plain

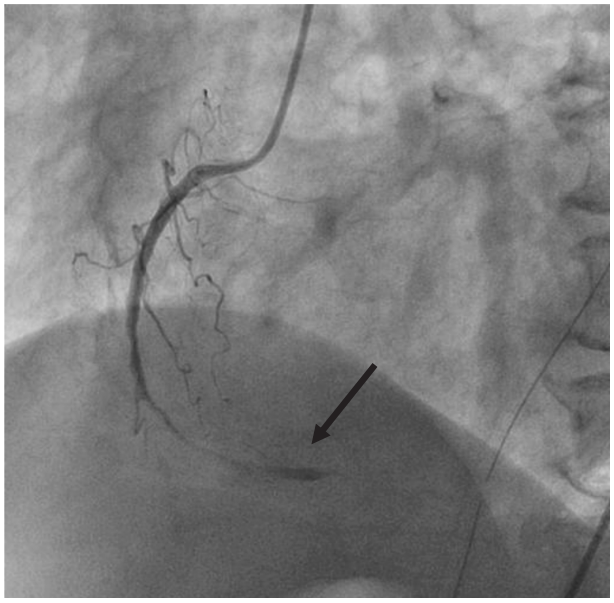

Fig. 1 Complete occlusion is seen in the right coronary artery (segment 3).

Old Balloon Angioplasty (POBA) was conducted for revascularization and blood flow improved to TIMI grade 2. Soon after she entered the angiography laboratory, her blood pressure declined gradually and intravenous catecholamine infusion was started. Contrast imaging of the left ventricle also showed the right ventricle and pulmonary artery (Figure 2) and step-up of oxygenation was observed from the right atrium to right ventricle. Although the VSP was missed by echocardiography, we could notice VSP by the left ventriculography. Because our hospital basically performed the left ventriculography

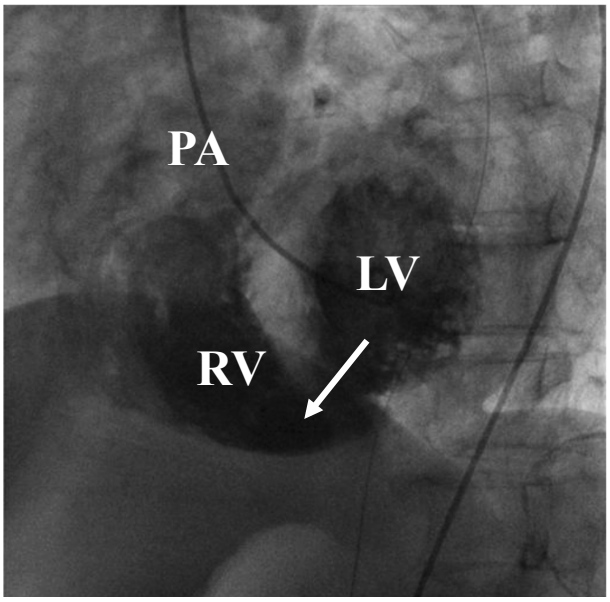

Fig. 2 Contrast medium flows from the left ventricle (LV) to the right ventricle (RV). The pulmonary artery (PA) is also enhanced.

on the case of AMI at the time, this worked well. An intra-aortic balloon pump (IABP) was inserted and emergency closure of the defect was conducted under PCPS at cardiac surgery department by David's infarct exclusion method.

After surgery, UCG showed virtually no left ventricular systolic contraction under PCPS activation. And the patient was confirmed dead.

Case 2

An 86-year-old woman

The patient was on medication for hypertension, diabetes mellitus, and dyslipidemia. She developed back pain and vomiting, but rested at home. On the next day, she developed dyspnea and visited her local doctor. Auscultation demonstrated a generalized systolic murmur (Levine 3/6), while there was ST segment elevation in leads I, aVL, and V2-6 on the ECG. Cardiac enzymes were increased and the chest X-ray film suggested pulmonary congestion. AMI and congestive heart failure were diagnosed and the patient was transferred to our hospital.

UCG revealed akinesis at the anterior septum and blood flow through a VSP. Urgent coronary angiography showed 75% stenosis of segment 2 and complete occlusion of segment 7. Although the left ventricular ejection fraction was maintained, the hemodynamics was broken easily by high Qp/Qs with VSP. An IABP was inserted and under PCPS, and a VSP located about 2 cm from the apex was

closed by the infarct exclusion method of David. PCPS was removed on postoperative Day 3, and tracheotomy was conducted on Day 12. Thereafter, recovery went smoothly for some time.

However, intestinal obstruction with multiple organ failure occurred on Day 28 and the patient died on Day 62. Autopsy demonstrated intestinal perforation and peritonitis, which was considered to be the cause of death.

Case 3

A 73-year-old man

The patient was being treated with oral medications for hypertension and diabetes mellitus by his family doctor. He developed chest pain, but it was tolerable. On the next day, respiratory distress occurred and he visited his doctor. On auscultation, a generalized systolic murmur was heard（Levine 2/6）. The ECG showed ST segment elevation in leads I, aVL, and V1-6. Cardiac enzymes were elevated and UCG demonstrated septal wall akinesis and VSP flow. Urgent coronary angiography displayed complete occlusion of segment 6 and 90% stenosis of segment 14, while step-up of oxygenation was observed in the right ventricle. Left ventricular ejection fraction was low, but the hemodynamics was relatively undamaged.

An IABP was inserted and the patient was transferred to our hospital. Emergency closure of the VSP（about 3 cm from the anterior wall and running through the posterior wall at 1/3 of the distance from atrium to apex）was done by the infarct exclusion method of David. Coronary artery bypass grafting was also conducted to segment 14 using a saphenous vein graft. Before surgery, the patient went into shock, but his hemodynamics were stabilized by catecholamines. Postoperative hemodynamics remained stable, although an inotropic agent was needed. Prerenal renal failure occurred, but responded to continuous hemodiafiltration（CHDF）for 2 days. The IABP was removed on postoperative day 4.

Subsequently, the patient recovered smoothly and was discharged for outpatient follow-up.

Discussion

We recently experienced 3 patients with VSP and their features are summarized in Table 1. All 3 patients developed VSP after the onset of AMI and the diagnosis was confirmed by urgent cardiac catheterization, followed by emergency surgery. All 3 patients presented to our hospital one day after the onset of symptoms, allowing treatment to be initiated.

For surgical repair of VSP, the infarct exclusion method of David [1] was adopted in all 3 patients. With this method, a large patch is sutured to the normal left ventricular myocardium to cover the infarcted area. This is expected to reduce pressure on the perforated site and also to reduce stress on the infarcted myocardium, as well as inhibiting late remodeling. Right ventricular incision or plasty is not performed. In general, the base of the ventricular septum is supplied by the RCA, while the apex of the septum is supplied by the septal branch of the left coronary artery. Thus, if the culprit lesion is in the RCA, VSP tends to occur at the base of the septum, while it is most frequently found at the septal apex if the culprit lesion is in the left anterior descending artery. VSP can be divided into simple and complex types [2]. Compared with VSP caused by a left anterior descending artery lesion, VSP due to an RCA lesion is more likely to be complex and penetrate the myocardium in an irregular manner. Since this type of VSP tends to cause right heart failure, hemodynamics is easily affected. Furthermore, posterior septal perforations tend to have a larger diameter and surgical treatment is more difficult.

Among the present 3 patients, 1 survived and 2 died. Intestinal obstruction and perforation led to one of the two deaths. In Japan, the incidence rate of VSP was reported to be 0.77%（37 out of 4,824 patients with AMI）at Kokura Kinen Hospital [3]. It has also been reported that the incidence of VSP was about 1-2% prior to introduction of thrombolytic therapy and 0.2% after its introduction [4]. The SHOCK registry study [5] was initiated after introduction of thrombolytic therapy and percutaneous coronary angioplasty for AMI. Among 939 patients with myocardial infarction complicated by cardiogenic shock in that registry, 55 patients（5.9%）had VSP and it was detected at an average of 16 hours after the onset of myocardial infarction. All of our patients had a confirmed diagnosis of VSP within 24 hours after the onset of myocardial infarction.

Recently, risk factors for VSP associated with AMI have identified. According to the SHOCK registry, factors associated with VSP include advanced age, female sex, initial onset, diabetes mellitus, and smoking [5]. The average age of our 3 patients was 79 years and 2 patients were female. It was the first AMI in all 3 patients. Two patients had diabetes mellitus and one patient was a smoker. One of the reasons why females are more likely to develop VSP is that the collagen structure of the myocardium is different and it is more susceptible to

Table 1 Detailed preoperative and postoperative data of each patient

	Case 1	Case 2	Case 3
Age (Years)	78	86	73
Sex	Female	Female	Male
HT	(+)	(+)	(+)
DM	(–)	(+)	(+)
DL	(–)	(–)	(–)
History of AP	(–)	(–)	(–)
History of MI	(–)	(–)	(–)
Smoking	(–)	(–)	(+)
Systolic BP (mmHg)	88	120	106
Diastolic BP (mmHg)	50	80	80
PR (bpm)	60	110	80
Killip Classification	4	3	4
Forrester Classification	Ⅳ	Ⅰ	Ⅳ
MI area	Inferior posterior	Antero septal	Antero septal
Culprit Lesion	RCA (Seg3)	LAD (Seg7)	LAD (Seg7)
Number of Vessels	1	1	2
Coronary Revascularization	POBA to Seg3	Medication only	CABG to Seg14
LVEF (UCG / LVG)	50 / 51	50 / 56	21 / not performed
MR	none	trivial	Ⅰ
VSP Length (cm)	1.5	2.0	3.0
Interval to VSP Diagnosis after MI onset	within one day	within one day	within one day
Qp / Qs	2.9	3.6	1.8
Medical Treatment for VSP	Operation	Operation	Operation
Operative Method	Infarction exclusion (Komeda-David)	Infarction exclusion (Komeda-David)	Infarction exclusion (Komeda-David)
Time under Artificial Cardiopulmonary Device (minutes)	226	135	257
Usage of Catecholamine	(+)	(+)	(+)
Usage of IABP	(+)	(+)	(+)
Usage of PCPS	(+)	(+)	(–)
CK (U/L)	781	3941	4160
CKMB (U/L)	52	491	468
CRP (mg/dL)	8.59	0.87	0.26
WBC (/μL)	13400	11000	14900
Prognosis	Dead (15days, Heart failure)	Dead (62days, Ileus)	Alive

HT, hypertension; DM, diabetes mellitus; DL, dyslipidemia; AP, angina pectoris; MI, myocardial infarction; BP, blood pressure; PR, pulse rate; bpm, beats per minute; RCA, right coronary artery; LAD, left anterior descending artery; POBA, plain old balloon angioplasty; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; UCG, ultrasound cardiography; LVG, left ventriculography; MR, mitral regurgitation; VSP, ventricular septal perforation; Qp / Qs, pulmonary blood flow / systemic blood flow ratio; IABP, intra-aortic balloon pump; PCPS, percutaneous cardiopulmonary support; CK, creatine kinase; CKMB, creatine phosphokinase-MB isozyme; CRP, C-reactive protein; WBC, white blood cell;

ischemic injury[6]. In addition, compared to patients with multiple severe coronary lesions, those with a few lesions are reported to be at higher risk of developing VSP due to poor collateral blood flow. In fact, 2 of our patients only had 1 branch lesion.

According to a report by Poulsen et al. [7], in 64 patients with myocardial infarction complicated by VSP, the average interval from onset to diagnosis of VSP was 5 days. The mortality rate at 30 days, 1 year, and 5 year was 62%, 72%, and 95%, respectively, while the 30-day mortality rate of patients who only received pharmacotherapy（n=19）was 100%. Thus, mortality is very high if surgery is not performed. In contrast, for 45 patients who underwent surgery, the survival rate at 30 days, 1 year, and 5 years was 71%, 48%, and 32%, respectively. Risk factors for death were hypertension, heart failure（Killip class >1）, and advanced age. All of our patients had a history of hypertension and they all developed heart failure. In addition, they were elderly. According to a report by Menon et al.[5], the survival rate of VSP patients was 19% after surgical intervention while it was 4% with pharmacotherapy alone.

Risk factors for death after VSP surgery include preoperative shock, advanced age of 70 years or older, preoperative catecholamine use, low cardiac output, right heart failure, inferior infarct, prolonged cardiopulmonary bypass, and postoperative PCPS [8]. The two VSP patients who died at our hospital were older than 70 years and required pressor agents prior to surgery due to low cardiac output. In addition, PCPS was used during and after surgery. Finally, Qp/Qs was 2.9 and 3.6 in these patients, which was higher than in the surviving patient. However, patients with large shunt（Qp/Qs >3.0）need emergency surgery after IABP insertion, since it was reported that medical therapy alone may result in early death due to multiple organ dysfunction. Mueller et al. [9] reported that among patients with non-ST elevation acute coronary syndrome, a C-reactive protein（CRP）level ≥10 mg/dl was associated with a significantly higher in-hospital mortality rate. Anzai et al.[10] reported that in patients with initial Q wave myocardial infarction, the peak CRP level is an important risk factor for cardiac rupture including VSP. Furthermore, Katayama et al. studied patients with myocardial infarction and elevation of serum inflammatory marker（CRP and amyloid A protein）, who underwent revascularization within 24 hours of the onset（n=433）, and reported 9 free wall rupture and 2 VSP. The incidence of cardiac rupture was higher in female patients, patients with a history of diabetes mellitus patients with anterior wall infarction, and CRP was significantly higher in the patients with cardiac rupture than in those without cardiac rupture [11]. On the other hand, the risk of VSP is not related to the peak level of creatine kinase（CK）[12]. In short, it seems that occurrence of VSP not only depends on the extent of infarction but also on the severity of inflammation. Our case 1 had a CRP of 8.59（mg/dl）on arrival at hospital. There were no other inflammatory findings such as pneumonia. Low CRP was observed in case 2 and 3. Although the measurement time is similar with case 1, the reason why CRP is not high is unknown.

After myocardial infarction, monocytes and macrophages are activated by ischemic tissue injury and these cells release interleukin-6 and tumor necrosis factor. CRP is an acute phase reactant produced by the liver in response to interleukin-6. Infiltration of neutrophils into infarcted myocardium is also considered to be related to the onset of VSP. Severe localized inflammation may increase susceptibility to myocardial injury. Accordingly, if inflammatory markers are relatively high in the early phase after onset of AMI, it is necessary to consider the possibility of a mechanical complication.

Conclusion

The prognosis of VSP is very poor with a high mortality rate. Medical treatment is not effective, and surgical intervention is necessary. All 3 patients at our hospital underwent surgery, but the mortality rate（including death due to complications）was very high. Risk factors for postoperative death are shock, advanced age, catecholamine use, low cardiac output, inferior infarction and use of PCPS. Our patients who died had many of these risk factors.

Since VSP requires rapid surgical intervention, early diagnosis of this mechanical complication by frequent auscultation and UCG is important in patients with AMI.

Moreover, in AMI acute phase, if CRP shows a relatively high value with respect to elevation of cardiac enzyme, we should keep in mind the possibility of VSP.

Acknowledgments

We thank Dr Kazuyuki SHIRAI and Hidenori URATA for their excellent correction of manuscript.

References

1. T. E. David, L. Dale, Z. Sun, Postinfarction ventricular septal rupture: repair by endocardial patch with infarct exclusion. J Thorac Cardiovasc Surg 110 : 1315-1322, 1995.
2. Y. Birnbaum, M. C. Fishbein, C. Blanche, R. J. Siegel, Ventricular septal rupture after acute myocardial infarction. N Engl J Med 347: 1426-1432, 2002.
3. T. Arita, Emergency situation after the onset of acute myocardial infarction. Journal of Clinical Echocardiography 9: 304-313, 2008.
4. O. Topaz, A. L. Taylor, Interventricular septal rupture complicating acute myocardial infarction: from pathophysiologic features to the role of invasive and noninvasive diagnostic modalities in current management. Am J Med 93: 683-688, 1992.
5. V. Menon et al., Outcome and profile of ventricular septal rupture with cardiogenic shock after myocardial infarction: a report from the SHOCK Trial Registry. SHould we emergently revascularize Occluded Coronaries in cardiogenic shocK? J Am Coll Cardiol 36: 1110-1116, 2000.
6. R. C. Becker et al., Fatal cardiac rupture among patients treated with thrombolytic agents and adjunctive thrombin antagonists: observations from the Thrombolysis and Thrombin Inhibition in Myocardial Infarction 9 Study. J Am Coll Cardiol 33: 479-487, 1999.
7. S. H. Poulsen et al., Ventricular septal rupture complicating acute myocardial infarction: clinical characteristics and contemporary outcome. Ann Thorac Surg 85: 1591-1596, 2008.
8. H. Sugiki et al., [Risk factors for the surgical repair of ventricular septal perforation; an 8-year multiinstitutional analysis]. Kyobu Geka 58: 278-283, 2005.
9. C. Mueller et al., Inflammation and long-term mortality after non-ST elevation acute coronary syndrome treated with a very early invasive strategy in 1042 consecutive patients. Circulation 105: 1412-1415, 2002.
10. T. Anzai et al., C-reactive protein as a predictor of infarct expansion and cardiac rupture after a first Q-wave acute myocardial infarction. Circulation 96: 778-784, 1997.
11. T. Katayama et al., Serum amyloid a protein as a predictor of cardiac rupture in acute myocardial infarction patients following primary coronary angioplasty. Circ J 70: 530-535, 2006.
12. U. Ikeda et al., Serum interleukin 6 levels become elevated in acute myocardial infarction. J Mol Cell Cardiol 24: 579-584, 1992.

（平成 29. 2. 22 受付，平成 29. 4. 3 受理）

「The authors declare no conflict of interest.」