

Fulminant Myocarditis Survivor After 56 Hours of Non-Responsive Cardiac Arrest Successfully Returned to Normal Life by Cardiac Resynchronization Therapy : A Case Report

Koichi SUGAMURA, MD

Seigo SUGIYAMA, MD

Hiroaki KAWANO, MD*

Eiji HORIO, MD

Shunichi ONO, MD*

Sunao KOJIMA, MD

Koichi KAIKITA, MD

Katsuyuki SAGISHIMA, MD*

Tomohiro SAKAMOTO, MD

Michihiro YOSHIMURA, MD

Yoshihiro KINOSHITA, MD*

Hisao OGAWA, MD, FJCC

Abstract

A 20-year-old female survived fulminant myocarditis with 56 hr of non-responsive cardiac arrest and was able to resume a normal life with cardiac resynchronization therapy (CRT). On admission, she had developed cardiogenic shock refractory to pharmacological intervention. Percutaneous cardiopulmonary support was initiated with intraaortic balloon pumping. She developed complete cardiac standstill unresponsive to ventricular pacing. After 56 hr of cardiac arrest, ventricular fibrillation occurred and her ventricle started to respond to pacing therapy. She could leave the intensive care unit, although she continued to have severe heart failure refractory to medical intervention. She presented with paradoxical ventricular motion with a low cardiac output, so CRT was performed. After the initiation of CRT, her heart failure symptoms improved and she could return home.

J Cardiol 2006 Dec; 48(6): 345 - 352

Key Words

■Myocarditis (fulminant)

■Cardiac surgery (resynchronization therapy)

■Cardiac arrest (standstill)

INTRODUCTION

Fulminant myocarditis is commonly recognized

as acute myocarditis with cardiogenic shock requiring artificial mechanical support systems.^{1,2)}

Fulminant myocarditis still causes substantial mor-

熊本大学大学院医学薬学研究部 循環器病態学講座, *侵襲制御医学講座: 〒860-8556 熊本県熊本市本荘1-1-1

Department of Cardiovascular Medicine, *Department of Aggressology and Critical Care Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto

Address for correspondence: SUGIYAMA S, MD, Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Honjo 1-1-1, Kumamoto, Kumamoto 860-8556; E-mail: ssugiyam@gpo.kumamoto-u.ac.jp

Manuscript received July 5, 2006; revised August 2, 2006; accepted August 17, 2006

idity and mortality, especially in children and young adults. Before the development of mechanical assist devices, most patients with fulminant myocarditis died in the acute phase because of rapidly progressive cardiac decompensation.³⁾

Acute stage survival of fulminant myocarditis has been improved by the use of mechanical circulatory assist devices, such as intraaortic balloon pumping(IABP), percutaneous cardiopulmonary support(PCPS), and left ventricular assist devices.⁴⁻⁸⁾ Mechanical circulatory support has become the standard method to bridge patients with intractable heart failure to either transplantation or myocardial recovery.

Survivors of the acute phase of fulminant myocarditis have a good long-term prognosis with complete reversal of cardiac dysfunction.⁹⁻¹³⁾ However, some fulminant myocarditis patients have recovered from the critical clinical condition with severe cardiac dysfunction.

We treated a young female who survived the acute phase of fulminant myocarditis with the use of circulatory assist devices and was able to resume a normal life after cardiac resynchronization therapy(CRT).

CASE REPORT

A 20-year-old healthy female developed general fatigue and was admitted to a local hospital. Electrocardiography showed complete atrioventricular block(AV block). She was treated with temporary pacing, but atrioventricular conduction did not recover over 7 days. A permanent pacemaker was implanted at the primary hospital, but then pacing failure occurred because of rising threshold and worsening heart failure. Fulminant myocarditis was suspected, and she was transferred to our university hospital by ambulance because of cardiogenic shock.

On arrival, she was alert and responsive with respiratory distress and signs of central cyanosis. Auscultation detected coarse crackles in the lower bilateral lung fields, and weak cardiac sounds. Her temperature was 38.1 °C, systolic blood pressure was 72 mmHg(under 5 µg/kg/min dopamine infusion), her pulse rate had an irregular rhythm at 105/min, and her respiratory rate was 28/min. Chest radiography indicated cardiomegaly(cardiothoracic ratio 52%), obvious pulmonary edema and no pleural effusion.

Electrocardiography showed idioventricular

Table 1 Arterial blood gas analysis, complete blood count and blood chemistry on admission

Arterial blood gas analysis (at O ₂ 15 l/min)		Hb	13.1 g/dl
pH		Hct	38%
PaO ₂	57.7 mmHg	Plt	12.5 × 10 ⁴ µl
PaCO ₂	42.1 mmHg	Blood chemistry	
HCO ₃ ⁻	21.6 mmol/l	AST	1,067 IU/l
BE	- 4.1 mmol/l	ALT	604 IU/l
Complete blood count		LDH	2,147 IU/l
WBC	14,800/ µl	CK	2,866 IU/l
Neu	83.9%	CK-MB	123 IU/l
Lym	8.9%	TnT	16.3 ng/ml
Mon	7.0%	CRP	5.55 mg/dl
Eos	0.1%	BNP	406.4 pg/ml

tachycardia with widened QRS complexes, left axis deviation, and a QS pattern in leads V₁, V₂, V₃, a F and a R (Fig. 1 - A). Echocardiography showed a thickened left ventricular wall, particularly the anterior wall with reduced systolic contraction, and pericardial effusion without left ventricular cavity enlargement(Fig. 2 - A). The results of arterial blood gas analysis, a complete blood count and blood chemistry on admission are shown in Table 1. The arterial blood gas analysis indicated hypoxia and metabolic acidosis under O₂ therapy. The white blood cell count and other biochemical markers were all elevated, especially the creatine kinase (CK)level.

Mechanical ventilatory support, IABP, and PCPS were started promptly according to standard operating procedures. Corticosteroid(125 mg/day)and immunoglobulin(5,000 mg/day)therapy were also started. PCPS was initiated at 3.5 l/min in addition to the conventional treatments(Fig. 3). We suspended the pacemaker because pacing stimulation was not effective due to the rising threshold.

Her myocarditis was resistant to therapy, and her bradycardia progressed to ventricular standstill (Fig. 1 - B). The day after ventricular standstill occurred, P waves disappeared and the electrocardiography showed complete cardiac standstill(Fig. 1 - C). Effective systole was not seen on echocardiography and her heart became non-responsive (Fig. 2 - B). At this time, CK and CK in the myocardial band(CK-MB)reached their peak levels. The value of CK was 9,472 U/l and CK-MB was 169 U/l. Because of cardiac standstill, her circulatory function completely depended on the

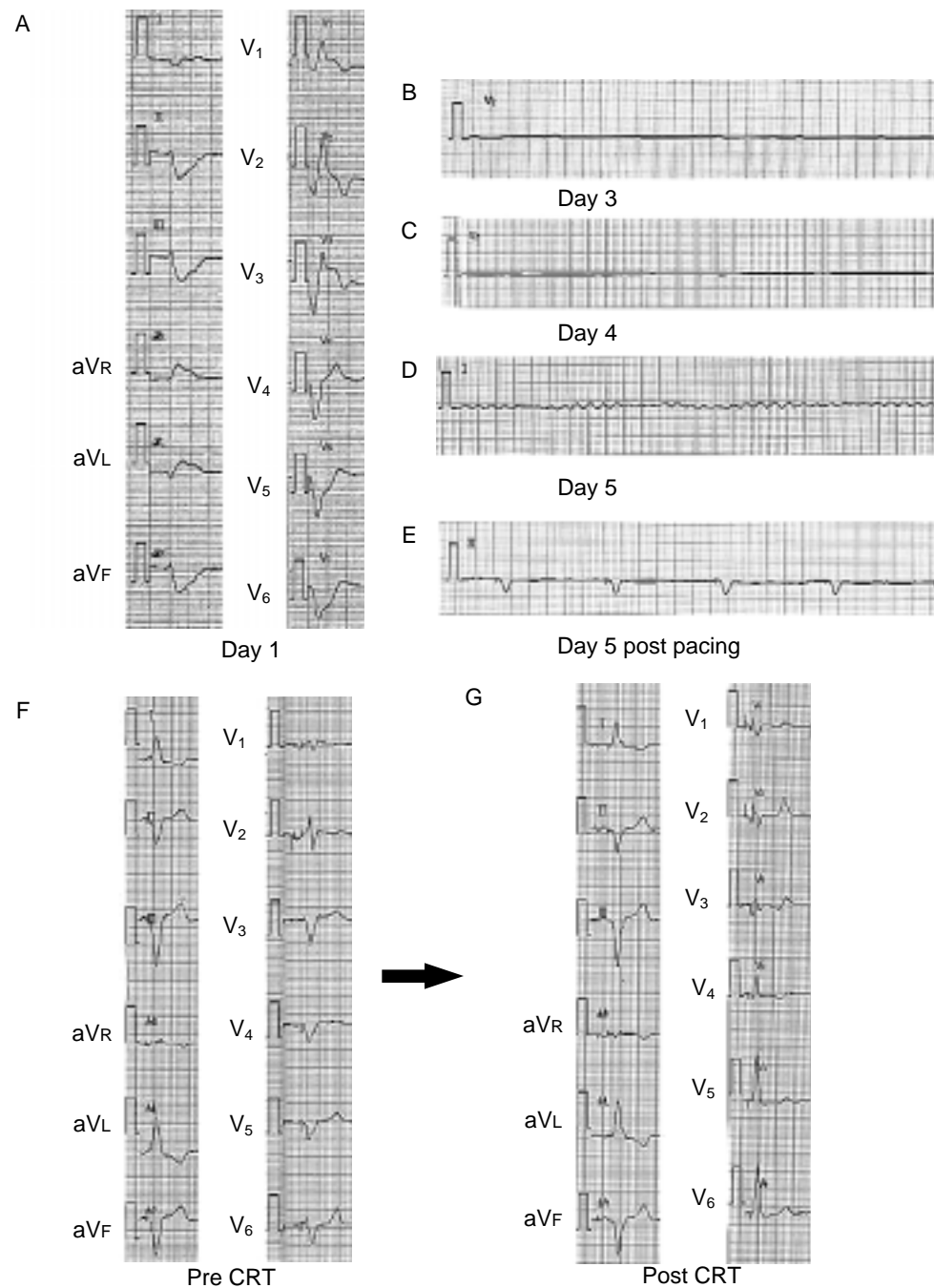


Fig. 1 Time course of the electrocardiographic findings

A: Electrocardiography showed idioventricular tachycardia with widened QRS complexes (160 msec), left axis deviation, and a QS pattern in leads V_1 , V_2 , aVF and V_4 - V_6 on admission.

B: A wide QRS like complex was found in the limb leads and a P-wave like pattern in V_1 - V_2 .

C: Cardiac standstill occurred on day 4.

D: Ventricular fibrillation occurred on day 5.

E: Post VVI pacing on day 5.

F: Pre CRT. QRS width was 220 msec.

G: Post CRT. QRS width decreased to 160 msec.

CRT = cardiac resynchronization therapy.

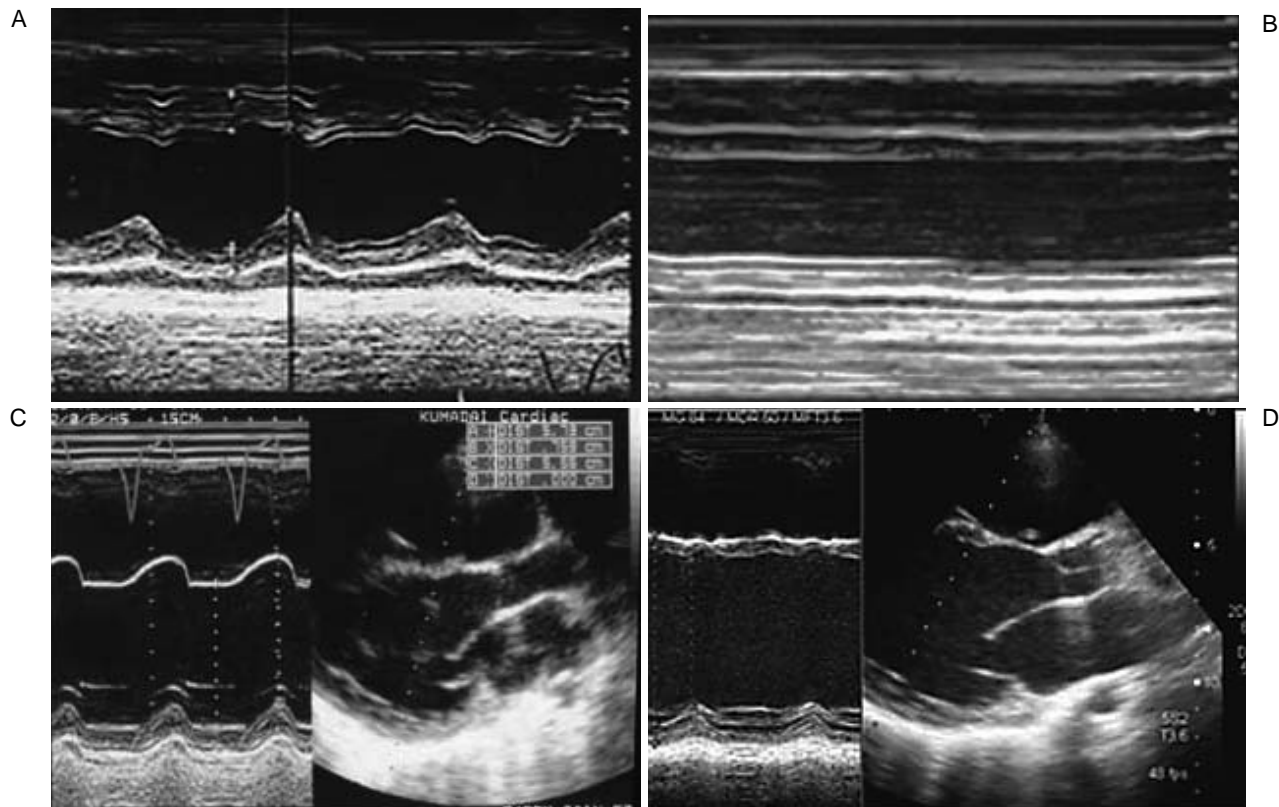


Fig. 2 Time course of the echocardiographic findings

M-mode scans at the mid-ventricular level are shown.

A: On admission, echocardiography showed a thickened left ventricular wall, particularly the anterior (interventricular septum 14mm and posterior wall 9mm) with a slight reduction in systolic performance (ejection fraction 59%). The left ventricular end-diastolic diameter was within normal limits and pericardial effusion was present.

B: After ventricular standstill occurred, effective systole was not seen.

C: The patient had severe left ventricular dysfunction (ejection fraction 28%). The septal wall was thinned and paradoxical motion was observed.

D: After cardiac resynchronization therapy was performed, the ejection fraction increased by 5% and the paradoxical motion disappeared.

mechanical assist devices. Although termination of life support was considered at this time, when we reduced her degree of sedation to check her consciousness level, she awoke and well-preserved central nervous system function was confirmed. We decided to continue the on-going treatment.

During this period, we used only mechanical assist devices without inotropic agents (dopamine, dobutamine or norepinephrine) for the avoidance of cardiac damage. Since 20 hr had passed after her heart stopped, ventricular fibrillation occurred spontaneously and direct current defibrillation was attempted (Fig. 1 - D). Although the ventricular fibrillation was converted back to cardiac standstill, ventricular fibrillation continued to recur, and direct current defibrillation was attempted repeatedly with

the same outcome (cardiac standstill). Since the occurrence of ventricular fibrillation suggested the recovery of cardiac muscle excitability, we attempted ventricular pacing which was successful (Fig. 1 - E). Her heart restarted approximately 56 hr after cardiac arrest.

Although cardiac pacing was restarted, left ventricular motion was still very weak, so mechanical cardiac support was continued until there was more recovery of left ventricular function. On day 9, she was weaned from PCPS and IABP because she met the weaning criteria¹⁰⁾ and pulmonary alveolar hemorrhage occurred as a complication of anticoagulant therapy. However, after weaning, several critical complications (sepsis, pulmonary bleeding, disseminated intravascular coagulation, and acute

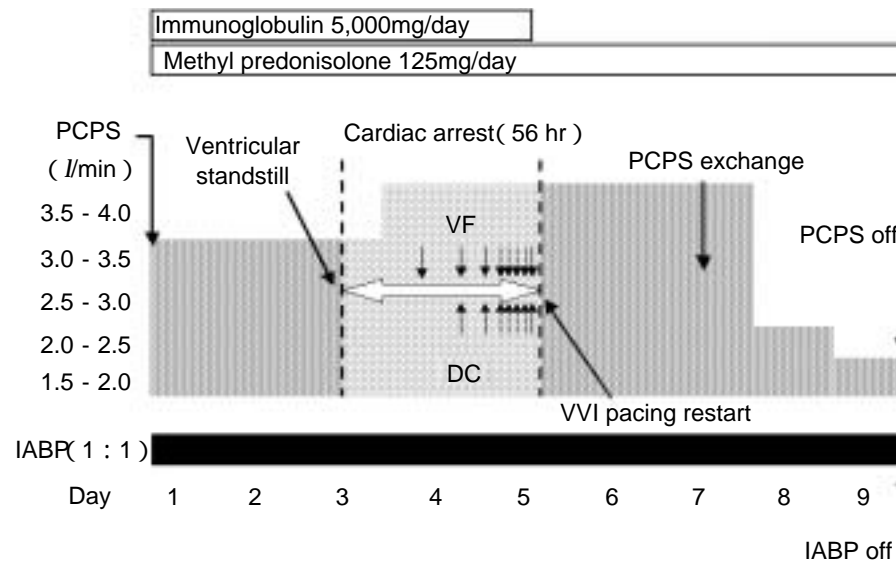


Fig. 3 Clinical course, treatment and circulatory assist

PCPS was initiated at 3.5 l/min. After cardiac standstill occurred, effective systole was lost and we had to increase the flow of PCPS. Ventricular fibrillation occurred intermittently (down arrows) and direct current defibrillation was attempted (up arrows). However, cardiac standstill was sustained, so we tried cardiac pacing again on day 5, which was successful and cardiac beats were restarted approximately after 56 hr of cardiac arrest. On day 9, PCPS and IABP were stopped.

PCPS = percutaneous cardiopulmonary support; VF = ventricular fibrillation; DC = direct-current counter-shock; IABP = intraaortic balloon pumping. Other abbreviation as in Fig. 1.

renal failure) occurred sequentially. Continuous hemodialysis filtration was necessary because of anuria, but she recovered from these complications and her condition was stabilized.

She was moved from the intensive care unit. Her consciousness was clear and there was no neurological disorder except for peripheral neuropathy in the lower left leg, which was caused by long-term recumbency. At that time, her left ventricular ejection fraction was only 28%, plasma brain natriuretic peptide levels were elevated (1,740 pg/ml), complete AV block was still present, and she was pacemaker dependent. Electrocardiography showed a left bundle-branch block pattern due to the right ventricular pacing and the QRS width was 220 msec (Fig. 1 - F). The septal wall was thinned and paradoxical motion was observed (Fig. 2 - C). She had drug-refractory severe heart failure and New York Heart Association (NYHA) class symptoms. Although all possible medications were administered, congestive heart failure was still present and she could not be discharged from the hospital.

After she left the intensive care unit, there was no further elevation of troponin T or CK levels.

Endomyocardial biopsy of the left ventricle revealed extensive fibrosis and a few remaining lymphocytes, which indicated that she was in the healing phase of myocarditis. In this period, lethal arrhythmia did not appear. The absence of any signs of continuous myocardial inflammation suggested that the chronic myocarditis had resolved. We examined all indicators of secondary myocarditis as far as possible, but the possibility of the secondary myocarditis including sarcoidosis could be excluded. Repeated measurement of several virus antibody titers disclosed no evidence of recent viral infection.

Because of her wide QRS complex, we thought that left ventricular dys-synchrony may have been a contributing factor to her severe heart failure. Therefore, she was considered a good candidate for CRT.

Since a permanent pacemaker had already been implanted, a new coronary venous pacing lead was added from the coronary sinus and the generator was exchanged to the Insync (Model 8040, Medtronic, Inc; mode DDD, Lower rate 70 beats/min, AV delay 200 msec). After CRT was initiated, the QRS width decreased to 160 msec

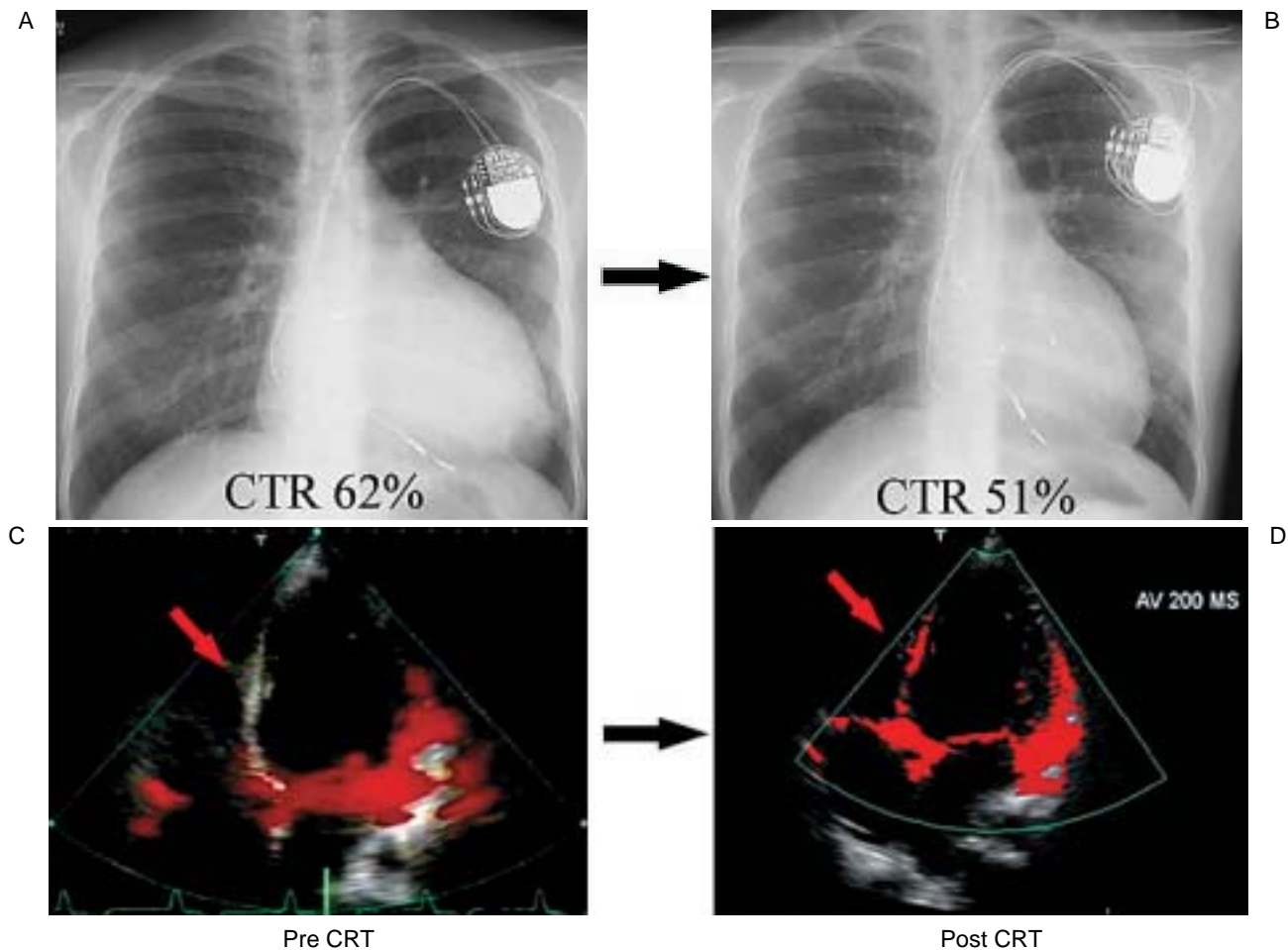


Fig. 4 Chest radiographs and tissue Doppler echo images

Chest radiograph showed the cardiothoracic ratio decreased from 62% (A) to 51% (B) after CRT was initiated. Comparison of the tissue Doppler echo images before (C) and after (D) CRT shows synchronization of the septal wall (red arrows indicated) at the lateral wall after CRT.

CTR = cardiothoracic ratio. Other abbreviation as in Fig. 1.

(Fig. 1 - G), left ventricular ejection fraction increased by 5%, and paradoxical motion disappeared (Figs. 2 - D, 4 - C, D). The cardiothoracic ratio decreased from 62% to 51% (Figs. 4 - A, B). Plasma brain natriuretic peptide levels also markedly decreased from 555 to 152 pg/ml. NYHA class improved from to , and she recovered enough to return to normal life. She has been in good health with normal activity of daily life for 10 months since her discharge.

DISCUSSION

The present 20-year-old female survivor of fulminant myocarditis with 56 hr non-responsive cardiac arrest was able to return to normal life by CRT. Cardiac arrest is one of the most fatal and severe

complications occurring in patients with fulminant myocarditis. This case is remarkable for the recovery after a long-lasting (56 hr) period of asystole with neurological function intact. In many cases with fulminant myocarditis, good circulatory function was difficult to maintain with mechanical support devices because of several critical complications. In this case, although the 56 hr period of cardiac arrest was complicated, the patient was saved by maintaining suitable circulatory assistance and periodically retrying cardiac pacing. CRT improved the cardiac insufficiency and served as a bridge to help the patient return home and resume a normal life.

Asystole, a complete rest period of the heart, may be necessary to allow the damaged myocardi-

um to heal and recover adequate function.¹⁴⁾ At the beginning of asystole in our patient, the pacing pulses failed to capture the ventricles because of extensive myocardial inflammation. However, myocardial excitability recovered with the onset of ventricular fibrillation, and her ventricles could be captured by the pacing pulses. It is important that we do not overlook signs of recovery of cardiac muscle excitability during cardiac arrest in patients with fulminant myocarditis.

After becoming asystolic, her circulatory function completely depended on the assist devices, and we continued circulatory support because her central nervous system function was well preserved. Therefore, good circulatory support is important to maintain to allow sufficient time for resolution of cardiac inflammation and improvement in ventricular function in such cases. We should pay special attention to prevent multi-organ complications and circulatory insufficiency.

Although our patient survived the acute phase of fulminant myocarditis, her severe cardiac insufficiency (left ventricular ejection fraction 28%) made

it difficult to return home. One-year, 5-year, and cumulative survivals after fulminant myocarditis are dependent upon ejection fraction and pulmonary capillary wedge pressure.^{15,16)} CRT is known to cause clinical improvement in patients with moderate-to-severe heart failure.¹⁷⁾ Moreover, the Cardiac Resynchronization-Heart Failure (CARE-HF) trial showed that CRT reduces morbidity and mortality regardless of the cause of heart failure.¹⁸⁾ We determined that she fit the enrollment criteria for CARE-HF. This is the first case in which CRT was used successfully in a patient with fulminant myocarditis. After the initiation of CRT, her cardiac function improved and she was able to return home and resume a normal life.

Acknowledgements

This study was supported by a Research Grant for Cardiovascular Disease (17C-2) from the Ministry of Health, Labor, and Welfare, Japan, a Grant-in-aid for Scientific Research (B-17390232 and C-17590753) from the Ministry of Education, Science and Culture, Japan, and the Smoking Research Foundation Grant for Biomedical Research, Japan.

要 約

56時間の心停止から回復し心臓再同期療法により社会復帰しえた 劇症型心筋炎の1例

菅村 公一 杉山 正悟 河野 宏明 堀尾 英治 小野 俊一 小島 淳
海北 幸一 鷺島 克之 坂本 知浩 吉村 道博 木下 順弘 小川 久雄

今回我々は、急性期に56時間の心停止を合併しながらも救命でき、慢性期に残存した重度の心機能障害を心臓再同期療法によって改善、社会復帰可能となった劇症型心筋炎症例を経験した。症例は20歳、女性。薬物治療抵抗性の心原性ショックとして当院集中治療部へ紹介入院となった。臨床経過から劇症型心筋炎と診断し、直ちに大動脈内バルーンポンピング法と経皮的心肺補助法を開始したが、心室ペーシングに反応しない完全な心静止に陥った。56時間の心停止期間中に心室細動が起こり、それを契機として右室ペーシングに反応がみられ心拍を再開しえた。しかし、慢性期に重度の心機能障害が残存し、薬物治療不応性の心不全が持続した。自己心拍は出現せずペーシングに依存しており、ペーシングによる奇異性運動と心拍出量の低下を認め、心臓再同期療法の適応と考えられた。心臓再同期療法施行後、心不全症状は改善され、社会復帰可能となった。

J Cardiol 2006 Dec; 48(6): 345 - 352

References

- 1) Kawahito K, Murata S, Yasu T, Adachi H, Ino T, Saito M, Misawa Y, Fuse K, Shimada K: Usefulness of extracorporeal membrane oxygenation for treatment of fulminant myocarditis and circulatory collapse. *Am J Cardiol* 1998;

82: 910 - 911

- 2) Kato S, Morimoto S, Hiramitsu S, Nomura M, Ito T, Hishida H: Use of percutaneous cardiopulmonary support of patients with fulminant myocarditis and cardiogenic shock for improving prognosis. *Am J Cardiol* 1999; 83: 623 - 625, A10

- 3) Lieberman EB, Hutchins GM, Herskowitz A, Rose NR, Baughman KL: Clinicopathologic description of myocarditis. *J Am Coll Cardiol* 1991; **18**: 1617 - 1626
- 4) Inoue Y, Kaneko H, Yoshizawa Y, Morikawa A: Rescue of a child with fulminant myocarditis using percutaneous cardiopulmonary support. *Pediatr Cardiol* 2000; **21**: 158 - 160
- 5) Kohno K, Aoyama N, Shimohama T, Yoshida M, Machida Y, Fukuda N, Aizaki T, Suzuki K, Kurosawa T, Izumi T: Resuscitation from fulminant myocarditis associated with refractory ventricular fibrillation. *Jpn Circ J* 2000; **64**: 139 - 143
- 6) Arima M, Kanoh T, Kawano Y, Okazaki S, Oigawa T, Yamagami S, Matsuda S: Recurrence of myocarditis presenting as pacing and sensing failure after implantation of a permanent pacemaker at first onset. *Jpn Circ J* 2001; **65**: 345 - 348
- 7) Izawa A, Kinoshita O, Shiba Y, Takahashi W, Uchikawa S, Imamura H, Owa M, Kubo K: Percutaneous cardiopulmonary support aids resuscitation from sustained ventricular tachycardia. *Circ J* 2003; **67**: 1061 - 1063
- 8) Abe S, Okura Y, Hoyano M, Kazama R, Watanabe S, Ozawa T, Saigawa T, Hayashi M, Yoshida T, Tachikawa H, Kashimura T, Suzuki K, Nagahashi M, Watanabe J, Shimada K, Hasegawa G, Kato K, Hanawa H, Kodama M, Aizawa Y: Plasma concentrations of cytokines and neurohumoral factors in a case of fulminant myocarditis successfully treated with intravenous immunoglobulin and percutaneous cardiopulmonary support. *Circ J* 2004; **68**: 1223 - 1226
- 9) Felker GM, Boehmer JP, Hruban RH, Hutchins GM, Kasper EK, Baughman KL, Hare JM: Echocardiographic findings in fulminant and acute myocarditis. *J Am Coll Cardiol* 2000; **36**: 227 - 232
- 10) Aoyama N, Izumi T, Hiramori K, Isobe M, Kawana M, Hiroe M, Hishida H, Kitaura Y, Imaizumi T; Japanese Investigators of Fulminant Myocarditis: National survey of fulminant myocarditis in Japan: Therapeutic guidelines and long-term prognosis of using percutaneous cardiopulmonary support for fulminant myocarditis (special report from a scientific committee). *Circ J* 2002; **66**: 133 - 144
- 11) Maejima Y, Yasu T, Kubo N, Kawahito K, Omura N, Katsuki T, Tsukamoto Y, Sugawara Y, Hashimoto S, Tsuruya Y, Hirahara T, Takagi Y, Kobayashi N, Funayama H, Ikeda N, Ishida T, Fujii M, Ino T, Saito M: Long-term prognosis of fulminant myocarditis rescued by percutaneous cardiopulmonary support device. *Circ J* 2004; **68**: 829 - 833
- 12) McCarthy RE, Boehmer JP, Hruban RH, Hutchins GM, Kasper EK, Hare JM, Baughman KL: Long-term outcome of fulminant myocarditis as compared with acute (nonfulminant) myocarditis. *N Engl J Med* 2000; **342**: 690 - 695
- 13) Kodama M, Oda H, Okabe M, Aizawa Y, Izumi T: Early and long-term mortality of the clinical subtypes of myocarditis. *Jpn Circ J* 2001; **65**: 961 - 964
- 14) Moreno-Cabral CE, Moreno-Cabral RJ, McNamara JJ, Dembitsky WP, Adamson RM: Prolonged extracorporeal circulation for acute myocarditis. *Int J Artif Organs* 1992; **15**: 475 - 480
- 15) Magnani JW, Danik HJ, Dec GW Jr, DiSalvo TG: Survival in biopsy-proven myocarditis: A long-term retrospective analysis of the histopathologic, clinical, and hemodynamic predictors. *Am Heart J* 2006; **151**: 463 - 470
- 16) Magnani JW, Dec GW: Myocarditis: Current trends in diagnosis and treatment. *Circulation* 2006; **113**: 876 - 890
- 17) Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, Kocovic DZ, Packer M, Clavell AL, Hayes DL, Ellestad M, Trupp RJ, Underwood J, Pickering F, Truex C, McAtee P, Messenger J; MIRACLE Study Group: Multicenter InSync Randomized Clinical Evaluation: Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002; **346**: 1845 - 1853
- 18) Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L; Cardiac Resynchronization-Heart Failure (CARE-HF) Study Investigators: The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005; **352**: 1539 - 1549