

Clinical Feature of Japanese Patients with Fulminant Myocarditis

—Myocarditis in Japanese Patients

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ABSTRACT

Fulminant myocarditis is commonly recognized as an acute myocarditis with cardiogenic shock requiring mechanical support systems. Before the development of mechanical assist devices, previous study described that most of patients with fulminant myocarditis die at acute phase because of rapidly progressive cardiac decompensation. To investigate the feature of myocarditis, we checked consecutive 18 patients (10 men, 8 women, (12 yr - 80 yr)) from April in 2001 to September 2008 in University. Of these patients 3 needed intra-aortic balloon pumping (IABP) (2 men, 1 woman), 6 did both IABP and percutaneous cardiopulmonary support (PCPS) (2 men, 4 women). Three patients who need both IABP and PCPS died (2 men, 49 yr and 65 yr, 1 woman, 54 yr) because of uncontrolled bacterial infection. No patients whose age was under 40 yr (5 men, 4 women) died although a man needed IABP and 3 women did both IABP and PCPS. Sixteen patients were able to resume a normal life although 1 male patient needed permanent pacemaker, 1 female did cardiac resynchronization therapy, and a male and a female had left ventricular systolic dysfunction. In conclusion, the young patients had better prognosis than older even if mechanical assist is needed. Although half of patients needed mechanical assist, the prevention of multi-organ complications including bacterial infection is one of the most important keys in the treatment of fulminant myocarditis.

Keywords: Myocarditis, Mechanical Support, Immunosuppressive Therapy, Immunomodulation Therapy

1. Introduction

Myocarditis is one of the most challenging diagnoses for cardiologists. The entity is rarely recognized, the pathophysiology is poorly understood, there is no commonly accepted diagnostic gold standard and all current treatment is controversial. The prevalence of myocarditis has been found to be up to 42% in case of unexplained death in people aged 35 or younger [1,2].

Acute myocarditis, especially fulminant myocarditis, still causes substantial morbidity and mortality, especially in children and young adults. Fulminant myocarditis is commonly recognized as an acute myocarditis with cardiogenic shock requiring artificial mechanical support systems [3,4]. Recently, because of the use of steroids and immunoglobulin as well as mechanical circulatory assist devices, such as intra-aortic balloon pumping

(IABP), percutaneous cardiopulmonary support (PCPS), and left ventricular assist devices, the acute stage survival of fulminant myocarditis have been improved [5-8]. Mechanical circulatory support has become the standard therapy to bridge patients with intractable heart failure to either transplantation or myocardial recovery.

In the present study, we report the feature of Japanese patients with fulminant myocarditis who hospitalized between 2001 and 2008 in our institute.

2. Methods

Before the development of mechanical assist devices, previous study described that a lot of patients with fulminant myocarditis die at acute phase because of rapidly progressive cardiac decompensation [10]. From April in 2001 to September 2008, we had 18 patients with fulmi-

nant myocarditis who had severe heart failure (New York Heart Association IV) in our institute. All had cardiac symptoms and clinical suspicion of myocarditis in the absence of known non-inflammatory causes including coronary artery disease. We did transthoracic Doppler echocardiography, complete heart catheterization and selective coronary angiography in all patients. Ejection fraction (EF) was measured by Simpson methods with echocardiography.

Endomyocardial biopsy is the critical test to confirm the diagnosis. Unfortunately, we were not able to perform endomyocardial biopsy in all patients because of the unstable circulation due to myocarditis. Thus, myocarditis had been diagnosed with clinical symptoms, physical examinations, heart catheterization, electrocardiogram and echocardiography [9]. All subjects gave written, informed consent, and the study was approved by the ethics committee at our institution.

3. Results

The etiology of myocarditis had been suspected viral infection. Of 18 patients, 3 needed intra-aortic balloon pumping (IABP) (2 men, 1 woman), 6 did both IABP and percutaneous cardiopulmonary support (PCPS) (2 men, 4 women) as shown in **Table 1**. Three patients who need both IABP and PCPS died (2 men, 49 yr and 65 yr, 1 woman, 54 yr) because of uncontrolled bacterial infection. No patients whose age was under 40 yr (5 men, 4 women) died although a man needed IABP and 3 women did both IABP and PCPS. Sixteen patients were able to

resume a normal life although 1 male patient needed permanent pacemaker, 1 female did cardiac resynchronization therapy, and a male and a female had left ventricular systolic dysfunction.

4. Discussion

Multiple infectious etiologies had been implicated as the cause of myocarditis, the most common being viral [11]. In the majority of patients, active myocarditis remains unsuspected because the cardiac dysfunction is subclinical and self-limited. In the present study, the etiology of myocarditis had not been able to defined, but been suspected viral infection in all study patients.

The cornerstone of therapy for patients with acute myocarditis is supportive care [11]. Serial echocardiography, right heart catheterization, etc., are all employed determine native cardiac reserve and suitability for device choose. We present the feature of 18 patients with fulminant myocarditis including a 20-year old woman with long term non-responsive cardiac arrest returning to normal life. In many cases with fulminant myocarditis, it is difficult to maintain good circulatory function with mechanical support devices, including ventilation, pacing, IABP, PCPS, etc., because of several critical complications. Thus, it is important to maintain good circulatory support to allow sufficient time for resolution of cardiac inflammation and improvement in ventricular function. We had to pay much attention to prevent multi-organ complications and circulatory insufficiency, and to control bacterial infection control during

Table 1. Patients characteristics.

No.	Age (yr)	Mechanical support	Immunosuppressive & Immunomodulation therapy	EF(%)
man				
1	18			23
2	22			22
3	24		Corticosteroid	23
4	34	IABP (for 4 days)	Corticosteroid + IVIG	12
5	38	IABP (for 9 days)	Corticosteroid + IVIG	11
6	49	PCPS + IABP (for 11 days)		12 (dead)
7	59			23
8	65	PCPS (for 8 days)		20 (dead)
9	68	Pacing (for 3 days)		31
10	80	Pacing → permanent pacemaker		23
woman				
1	12	PCPS + IABP (for 5 days)	Corticosteroid + IVIG (see Figure 1)	24
2	16	PCPS + IABP + Pacing (for 7 days)	Corticosteroid + IVIG	12
3	20	PCPS + IABP + Pacing (for 9 days) → cardiac resynchronization therapy	Corticosteroid + IVIG	13
4	30			20
5	49			21
6	54	PCPS + IABP (for 9 days)	Corticosteroid + IVIG	13 (dead)
7	56			14 (dead)
8	71	IABP (for 7 days)	Corticosteroid + IVIG	19

EF: ejection fraction; IABP: intra-aortic balloon pumping; IVIG: High-dose intravenous immune globulin; PCPS: percutaneous cardiopulmonary support.

the mechanical support in order to resume a normal life. Thus, several specialists, such as cardiologists, anesthesiologists, respiratory doctors, infection control teams, mechanical support technicians, and skilful nurses, were essential to care patients with fulminant myocarditis in intensive care unit.

The treatment of myocarditis is controversial, and no specific therapeutic regimen has been established [11]. All patients with myocarditis should receive standard heart failure therapy. Immunosuppressive therapy has been proposed to treat myocarditis in both children and adults. The results of an international trial, the Myocarditis Treatment Trial in 1995, showed that there was no difference in heart function in the treated with immunosuppressive agents or placebo [12]. Despite the negative results of this trial, the authors indicated that patients who responded to immunosuppressive therapy appeared to have higher initial ejection fraction and shorter duration of illness. High-dose intravenous immune globulin (IVIG) has both immune modulatory and antiviral effects [13-15]. However, there was no difference between placebo and IVIG. Thus, there was no benefit of immunomodulation. In the present study, some patients had immunosuppressive therapy, some had IVIG and some had both. The present small study cannot conclude the effects of the immunosuppressive and the immunomodulation therapy for fulminant myocarditis. Taken as a whole, the present small study together with previous trials, do not support the routine use of immunosuppressive and immunomodulation therapy for fulminant myocarditis [16]. These data suggest that subgroup with ongoing fulminant myocarditis, especially in the patients who need mechanical cardiac support, can be more likely to benefit from immunosuppressive and immunomodulation therapy, although no uniform methodology yet exists to identify them.

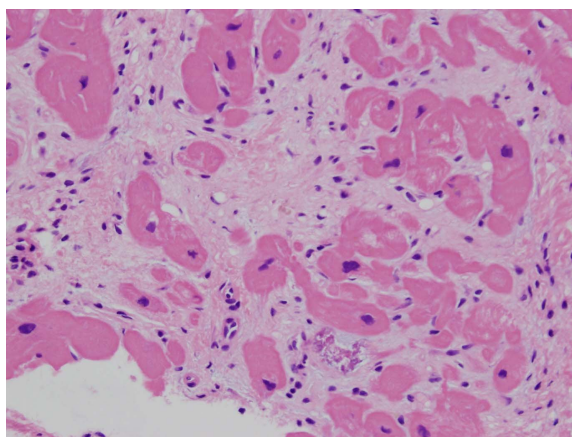


Figure 1. Endomyocardial tissue of 12 yr woman with myocarditis (case 1). (Hematoxylin and Eosin stain).

In conclusion, the young patients had better prognosis than older even if mechanical assist is needed. Although half of patients needed mechanical assist, the prevention of multi-organ complications including bacterial infection is one of the most important keys in the treatment of fulminant myocarditis.

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