

## CASE REPORT

# Bacterial myocarditis as a cause of fatal septic shock

DJF Nieuwenhuijs<sup>1</sup>, DF Zandstra<sup>2</sup>

<sup>1</sup> Department of Anaesthesiology and Intensive Care, St. Antonius Hospital, Nieuwegein, The Netherlands

<sup>2</sup> Department of Intensive Care, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

**Abstract.** Clinical presentations of myocarditis range from nonspecific systemic symptoms, fever, myalgias, palpitations, or exertional dyspnoea, to fulminant haemodynamic collapse and sudden death. We report a case of a fatal septic shock in a 47-year-old man with bacterial myocarditis confirmed at autopsy. Current diagnosis and management of bacterial myocarditis is discussed.

**Keywords:** myocarditis, bacterial myocarditis, severe sepsis, septic shock.

## Introduction

Septic shock is a complex, dynamic and heterogeneous clinical syndrome caused by various organisms. Despite continuous progress in the development of antibiotics and other supportive care therapies, sepsis remains a leading cause of morbidity and mortality in the intensive care unit [1]. The reported mortality remains as high as 35–75% [1] in critical care.

Rapid recognition of the causative pathogen is essential for optimal treatment but can be challenging given the expanding spectrum of organisms associated with septic shock. Myocarditis is clinically characterized by a variety of symptoms ranging from fatigue, difficult breathing, murmur, and rapid heartbeat to sudden death from fatal arrhythmia. The classification, diagnosis, and treatment of myocarditis continue to prompt considerable debate. We report a case of fatal septic shock due to bacterial myocarditis. Current diagnosis and treatment will be discussed

## Case report

A 47-year-old man was admitted to our hospital. His medical history included alcoholic liver cirrhosis with ascites and oesophageal varices. He had a one-week history of abdominal pain. On admission he was lethargic but responded to commands. Examination revealed tachycardia (120 bpm), hypotension (75/40 mmHg), and a body temperature of 33.7 °C. His abdomen was diffusely tender with ascites. Electrocardiography showed sinus tachycardia with non-specific ST segment changes. Chest X ray showed no infiltrates or pleural effusion. Laboratory examination showed  $8.9 \times 10^9$  litre<sup>-1</sup> leucocytes, elevated C-reactive protein, 72 mg litre<sup>-1</sup>. Haemoglobin was 5.3 mmol litre<sup>-1</sup> and  $27\,000 \times 10^9$  litre<sup>-1</sup> platelets. Arterial blood gases revealed metabolic acidosis, pH 7.09 with a high base deficit of 19.6 mmol litre<sup>-1</sup>, Lactate was 14.6 mmol litre<sup>-1</sup>. The creatine kinase enzymes were elevated, CK was 954 IU litre<sup>-1</sup> and CKmb was 19 IU litre<sup>-1</sup> and troponin-T was also elevated, 0.08 ng ml<sup>-1</sup>. A tracheal tube was inserted and mechanical ventilation was started. Four sets of blood cultures were drawn and empiric treatment with cephalexin (4g per day) and ciprofloxacin (800mg per day) was initiated. As standard treatment for severe sepsis, intravenous immunoglobulin therapy

was started and 1 mg kg<sup>-1</sup> dexamethasone intravenously was given as immunosuppressive therapy. He rapidly developed multiple organ failure with acute renal failure and acute on chronic liver failure. Continuous veno-venous haemofiltration with replacement fluid of 35 ml kg<sup>-1</sup>, considered to be high volume haemofiltration, was started within 6 hours of admission. During the subsequent hours his condition deteriorated rapidly and in spite of cardiopulmonary resuscitation and high doses of vasopressors and inotropes he died within 24 hours of admission.

*Staphylococci aureus* were found in throat cultures taken on admission. There were no pathogens isolated from blood cultures. Post-mortem microscopy of the heart revealed focal micro-abscesses containing gram-positive cocci, suggestive for *Staphylococci aureus*, throughout the myocardium (see Figure 1). No abnormalities were observed on the valves. The coronary arteries were normal. Micro-abscesses containing *Staphylococci aureus* were found in the spleen. The liver was steatotic and cirrhotic and the oesophageal varices were not bleeding.

## Discussion

Clinical presentations of bacterial myocarditis range from nonspecific systemic symptoms, fever, myalgias, palpitations, or exertional dyspnoea, to fulminant haemodynamic collapse and sudden death. The extreme diversity of clinical manifestations has made the true incidence of bacterial myocarditis difficult to determine. Recent prospective post-mortem data have implicated myocarditis in sudden cardiac death of young adults at rates of 8.6% to 12% [2].

Although a broad array of aetiologies have been implicated as causes of myocarditis, the majority of cases of myocarditis result from viral infection. Bacterial myocarditis is a rare cause of infectious myocarditis. It is usually seen in the context of overwhelming sepsis and the potential pathogens are many: streptococci, staphylococci, pneumococci, gonococci and mycobacterium among others [3].

Myocardial dysfunction is one of the key manifestations in clinical sepsis that contributes to significant morbidity and mortality in patients in intensive care units [4]. Postulated causative mechanisms of myocardial dysfunction include myocardial ischaemia, myocardial oedema due to inflammation-induced vascular leakage, and release of myocardial depressant substances [5].

In our patient, microscopic post-mortem investigation showed gram-positive cocci and inflammation of the heart. This bacterial

## Correspondence

D Nieuwenhuijs  
Email: d@nieuwenhuijs.org

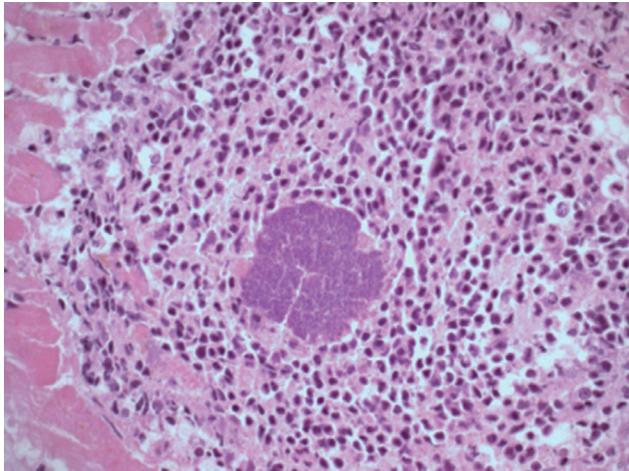


Figure 1. High-power magnification of endomyocardial biopsy showing mixed inflammatory infiltrate containing mononuclear and polymorphonuclear neutrophils encircling gram-positive cocci in association with myocyte damage (hematoxylin-eosin stain; original magnification X 400).

myocarditis presumably caused the contractility failure of the heart in our patient and ultimately the death of this patient.

At present, the definitive diagnosis of bacterial myocarditis requires endomyocardial biopsy [3]. In 1987, the Dallas histologic classification was introduced as a means to establish criteria for the diagnosis of myocarditis [6]. The presence under light microscopy of an inflammatory infiltrate associated with necrosis is required for the histological diagnosis of myocarditis. These criteria are highly specific but have only a 10% to 22% sensitivity for myocarditis [7].

### Diagnostic Evaluation

In the absence of a positive biopsy, differentiating acute coronary syndrome or sepsis-induced myocardial depression from bacterial myocarditis is challenging. These conditions share common features such as ventricular dysfunction and elevated cardiac biomarkers [3]. Non-invasive myocardial imaging that can improve the diagnostic precision to detect myocarditis are:

#### Echocardiography

The most common echocardiographic features of acute myocarditis are quite nonspecific. Segmental wall motion abnormalities that can simulate acute myocardial infarction are quite common [8]. Increased sphericity and left ventricular volume occur in acute myocarditis. Echocardiography is useful for detecting LV thrombus, transient LV aneurysm, right ventricular involvement, and pericardial effusion.

The acoustic properties of myocardium can be defined using ultrasonic backscatter and infer the physical state of cardiac muscle. The myocardial density and elasticity are influenced by the extent of oedema and cell infiltration. However, the diagnostic accuracy is not known and ultrasonic tissue characterization cannot differentiate between idiopathic dilated cardiomyopathy and acute myocarditis [8].

Tissue Doppler has also been used to assess acute myocarditis. Urhausen et al. [9] reported a case of biopsy-proven myocarditis in which no abnormalities were shown using 2-dimensional echocardiography and colour and pulsed-wave Doppler. However, a net loss of systolic regional wall velocity was evident on cardiac TD.

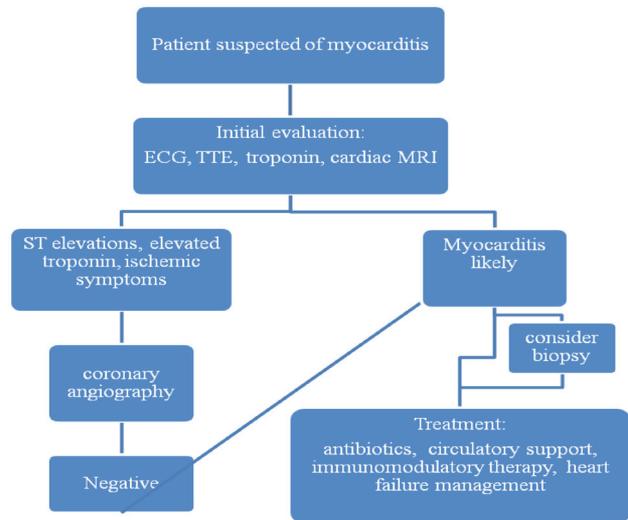


Figure 2. Algorithm of diagnostic and therapeutic approach for patients suspected for myocarditis. TTE = transthoracic echocardiogram.

#### FAS/FAS ligand system

Fas is a transmembrane cell surface receptor that plays a critical role in apoptosis. The levels of serum Fas and Fas ligand system are increased in myocarditis and correlate with the severity of heart failure and may provide important prognostic information [10].

#### Gallium-67 imaging

Gallium-67 is considered an excellent imaging agent for diagnosing several autoimmune chronic inflammatory conditions. Clinical studies have indicated the usefulness of gallium-67 scintigraphy in detecting myocarditis [8]. However it lacks specificity, therefore it is now rarely used for detecting myocarditis.

#### Indium-111 antimyosin antibody

Indium-111 radiolabelled monoclonal antibody fragments (directed against heavy chain myosin) bind to cardiac myocytes that have lost the integrity of their sarcolemmal membranes. Indium-111 antimyosin antibodies have been shown to detect myocardial necrosis in animal studies and human myocarditis. It has a high sensitivity (91% to 100%) and a high negative predictive value (93% to 100%). However the specificity is low (31% to 58%) [8].

#### Cardiac magnetic resonance imaging

Contrast-enhanced MRI appears to be the most promising noninvasive technique for diagnosing myocarditis on the basis of small observational clinical studies [2,8]. Besides providing anatomical and morphological information, MRI can provide accurate tissue characterization by measuring relaxation times. Because active myocarditis is typically associated with myocyte injury, including oedema and cellular swelling, assessment of relaxation times provides a sensitive measure for its detection. MRI may not only be useful in identifying those patients who should undergo biopsy but can also facilitate a guided approach to the abnormal region of myocardium. This may improve the sensitivity of EMB for establishing a correct histological diagnosis. Serial MRI studies may also be used for tracking the natural history of the disease and could allow noninvasive reassessment of the myocardial response to therapy.

### Summary of diagnostic evaluation

Comprehensive initial workup including a careful history, physical exam, blood work with cardiac biomarkers (creatinine kinase, troponin I and T), ECG, chest X ray and transthoracic echocardiogram should be performed in all patients if myocarditis is suspected. Patients presenting with ST elevations, elevated cardiac markers, and ischaemic symptoms should undergo prompt coronary angiography if the condition of the patient permits. Myocarditis should be considered in patients who lack evidence of coronary atherosclerosis or other pathophysiological aetiologies. Contrast-enhanced cardiac MRI may be the most powerful noninvasive tool for diagnosing myocarditis [8] and, if available, is warranted for initial diagnostic evaluation. Endomyocardial biopsy should be considered for a highly selected group of patients, particularly those with increased myocardial enhancement on cardiac MRI or rapidly progressive cardiomyopathy (see Figure 2) [2,8].

### Management

The management of bacterial myocarditis consists of aggressive treatment of the infectious process with antibiotics and appropriate circulatory support including vasopressors and positive inotropic agents. A ventricular assist device, intra-aortic balloon pumping or extracorporeal membrane oxygenation may be required to sustain patients with refractory cardiogenic shock. In selected cases heart transplantation is necessary.

A few cases of fulminant myocarditis in which intravenous immunoglobulin therapy or immunosuppression with corticosteroids was beneficial have been described [2,11]. However double-blind randomized trials which demonstrate the superiority of immuno-

suppression over conventional heart failure management are lacking.

Continuous veno-venous haemofiltration is often used in critically ill patients with acute renal failure as it was in this patient. Ronco et al. [12] have demonstrated that continuous veno-venous haemofiltration with replacement fluid of 35 ml kg<sup>-1</sup> improves survival in critically ill patients, so called high-volume haemofiltration. Further investigations have demonstrated that cytokines are removed by ultrafiltration during CVVH and significant clinical benefits in terms of haemodynamic improvement have been achieved.

After initial haemodynamic stabilization, heart failure management including an angiotensin-converting enzyme inhibitor and  $\beta$ -adrenergic blocking agent is recommended for all patients [2]. Diuretics and vasodilators such as nitroglycerin and angiotensin-II receptor blocking agents may be beneficial in selected patients.

The patient in this case report was treated with broad-spectrum antibiotics, renal replacement therapy with high-volume haemofiltration, received intensive circulatory support and immunomodulatory therapy with dexamethasone and intravenous immune globulin. Despite all the intensive care the bacterial myocarditis in this patient ran a fulminant and fatal course.

In conclusion bacterial myocarditis is a rare diagnosis. However, it should be suspected in septic patients with ventricular dysfunction and elevated cardiac biomarkers without coronary pathology. ECG, echocardiography, measurement of serum troponin, and noninvasive cardiac MRI, are warranted for initial diagnostic evaluation. Aggressive treatment of the infectious process with antibiotics, appropriate circulatory support, immunomodulatory therapy, and heart failure management is needed (see Figure 2).

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