Case Report

Myocarditis in a Patient with *Escherichia coli* Urinary Tract Infection

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Abstract

We report the case of a 40-year-old Taiwanese female, who was initially infected with *E. coli* urinary tract infection, followed by myocarditis during hospitalization. She was discharged after 12 days of antibiotic therapy. Two months later, follow-up echocardiography revealed persistent left-ventricular remodeling. Thus, infectious myocarditis should be suspected in patients with sepsis and ventricular dysfunction, even infected with uropathogen of *E. coli*. Although viral infections are responsible for most cases of infectious myocarditis, aggressive antibiotic therapy is mandatory for the treatment of hidden bacterial infections. (Acta Nephrologica 2011; 25: 192-195)

KEY WORDS: infectious myocarditis, *Escherichia coli*, urinary tract infection

Introduction

Myocarditis is defined clinically as the inflammation of the heart muscle. It may result from a variety of different disorders, most of which are infections. Viral infections due to adenoviruses, parvoviruses, and enteroviruses remain the most common causes of myocarditis in developed countries (1, 2). Less commonly, bacteria may also cause infectious myocarditis in overwhelming sepsis. The possible pathogens include *Corynebacterium diphtheriae*, *Staphylococcus*, and *Haemophilus influenzae* (2, 3). Several bacteria-induced myocarditis had been reported in the literature; but there is no report yet of myocarditis associated with an *Escherichia coli* (E. Coli) infection.

In the current report, we present an immunocompetent patient who suffered from infectious myocarditis with *E. coli* urinary tract infection. She was discharged after 12 days of medical treatment. Therefore, infectious myocarditis should be suspected in patients with sepsis and ventricular dysfunction. When dealing with such patients, aggressive antibiotic therapy is mandatory even though viral infection is the most common cause of myocarditis.

Case Report

A 40-year-old Taiwanese female, without any previous medical illness, complained of urinary frequency, urgency, and hematuria one week prior to admission. Four days later, she experienced lower back pain, nausea, vomiting with intermittent high fever up to 40°C. At the same time; urine output gradually reduced. Owing to persistent symptoms, she came to our emergency room for help.

At the emergency room, the patient’s body temperature was 39°C; respiratory rate was 18 times/min; her pulse was regular, 159 times/min; and blood pressure was 86/49 mmHg. Laboratory findings showed the following: hemoglobin level was 11.5 g/dL; white-blood cell count was 32.6 × 10³/µL with 10% of band form; platelet count was 172 × 10³/µL; blood urea nitrogen (BUN) was 30 mg/dL; and serum creatinine level was 2.9 mg/dL. Urinalysis showed microscopic
hematuria (10 red blood cells per high power field) and pyuria (numerous white blood cells per high power field), with normal chest X-ray. Then, she was admitted under diagnosis of urosepsis with shock hydration and intravenous form of antibiotic (cefotaxime 2 g twice daily) was prescribed initially. Hemodynamic status gradually stabilized. However, on the second day of admission, there was sudden onset of retrosternal chest tightness with diaphoresis. In addition, progressive dyspnea, elevated cardiac enzymes of troponin-I: 52.2 ng/mL; creatine kinase (CK): 3321 U/L; and creatine kinase MB isoenzyme (CKMB): 263.1 U/L were noted. Electrocardiography showed diffused ST segment elevation over limb leads of II, III and aVF, precordial leads of V4, V5 and V6 (Fig. 1), and no elevation of VR4 on the right sided electrocardiography. Echocardiography showed global hypokinesis of the left ventricular contractility and systolic function with an ejection fraction of 45%. Infectious myocarditis was suspected, and acute myocardial infarction was unlikely because she was at low risk for coronary artery disease. Emergent percutaneous transcoronary angiography (PTCA) was not suitable at that time due to severe sepsis, and the patient was transferred to the intensive care unit (ICU).

In the ICU, pulmonary artery catheterization was inserted and the results were as follows: cardiac index: 2.84 L · min⁻¹ · m⁻²; pulmonary artery wedge pressure: 16 mmHg; and systemic vascular resistance index (SVRI): 1265 DSm⁻²/cm⁻⁵. These data were compatible with sepsis and inotropic agent (nor-epinephrine) was prescribed with dosage of 0.25 µg · kg⁻¹ · min⁻¹ for maintaining mean arterial pressure at 65 mmHg. To cover the possible extended-spectrum β-lactamases strain of bacteria, we changed the antibiotic to flomoxef 0.5 g thrice daily. However, progressive dyspnea and pulmonary edema were noted on the next day, we supported respiration with noninvasive bi-level positive airway pressure ventilator and gave intravenous form of furosemide 20 mg thrice daily. At the same time, serial examinations of Swan-Ganz catheter showed gradual reduction of cardiac index from 2.8 to 2.5 with increased SVRI to 2141 DSm⁻²/cm⁻⁵, and ejection fraction reduced to 33%. These data collectively implied that we should change the inotropic agent to dopamine with dosage of 6.9 µg · kg⁻¹ · min⁻¹ because there were both septic and cardiogenic shock. No microorganisms were isolated from two sets of blood culture, viruses such as herpes simplex virus, adenovirus, respiratory syncytial virus, cytomegalovirus, enterovirus, influenza virus, and parainfluenza virus were not detected. Moreover, immunological markers such as antinuclear factor, anti-double stranded DNA, extractable-nuclear-antigen screening, serum C3, C4 levels were all negative. Throughout her hospital stay, only E. coli was isolated from urine culture. After aggressive antibiotic and supportive therapy, her condition improved gradually and PTCA was performed on the ninth day of admission, which revealed a patent coronary artery. She was discharged on the twelfth day of admission with oral ciprofloxacin 500 mg twice daily and perindopril 2 mg once daily. Two months
later, echocardiography revealed improvement of contractility with persistent regional wall motion abnormality at the anterior wall of the left ventricle, and restored systolic function with an ejection fraction of 53%.

**Discussion**

The present case is the first report of infectious myocarditis associated with *E. coli* urinary tract infection in an immunocompetent patient. The presumptive diagnosis was made in view of [1] new onset of ventricular dysfunction, [2] acute myocarditis, which was diagnosed on the basis of morphological ventricular dysfunction, elevated cardiac troponin level, and persistent ventricular remodeling after resolution of sepsis, [3] patent coronary artery, [4] positive urinary culture, and [5] negative findings from viral culture and autoimmune disease screening.

A definitive diagnosis of myocarditis requires endomyocardial biopsy along with evidence of bacterial invasion or positive tissue cultures (2, 4). However, it is an invasive procedure, and cannot conducted at most institutions due to lack of facilities. Therefore, Dr. Arthur suggested that the diagnosis of myocarditis should not only be made on the basis of histology alone. Instead, it should also be made largely on the basis of clinical suspicion (2).

Myocardial dysfunction, but not myocarditis, is commonly identified in patients with severe septic shock (6). Approximately 50% of sepsis seems to be associated with some degree of left ventricular systolic dysfunction (6, 7). Right ventricular dysfunction usually follows left ventricular dysfunction (8) and is not directly related to sepsis. Myocardial dysfunction during sepsis is probably multi-factorial. Many mediators, such as cytokines (e.g., lipo-polysaccharides, tumor necrosis factor-α, interleukin-1β, and interleukin-6), prostanooids, endothelin-1, nitric oxide, and adhesion molecules (6, 9, 10) are pathways seem to be involved, but the precise mechanism remains unclear. Apart from morphological myocardial dysfunction, elevated cardiac troponin level, which was the regulatory protein of thin actin filaments of myocyte (11), is also noticed during severe sepsis. Electrocardiogram may show normal results in both myocarditis and myocardial dysfunction, but in some cases, there may be regional ST segment elevation as in acute myocardial infarction (12). Thus, without an endomyocardial biopsy, it would be difficult to differentiate between the two conditions because their clinical presentations are similar. The major difference is the presence of cardiomyocytes in the myocarditis and significant ventricular remodeling, which persists after resolution of sepsis, as seen in our patient.

There are multiple causes leading to development of myocarditis, such as infections (e.g., viral, bacterial, and parasitic infections), systemic disease, drugs, and toxins (5). In developing countries, viral infection is the major cause of myocarditis. The detection of viral genomes in endomyocardial tissue by polymerase chain reaction has been suggested. It may provide both diagnostic and prognostic information (2) and persistent detection of viral genome in patients with dilated cardiomyopathy may be reflective of poor prognosis (13). However, this method is not available at most institutions. Bacterial infections are less commonly associated with myocarditis in immunocompetent patients. In the literature, a variety of bacterial infections have been reported, but *E. coli*-related myocarditis has not been elucidated. In addition, human immunodeficiency virus type 1 (HIV-1), autoimmune diseases (e.g., scleroderma, lupus erythematosus, and polymyositis) should also be screened in myocarditis (2).

In our case, myocarditis with ventricular dysfunction was diagnosed after severe urosepsis, and only *E. coli* was cultured from urine sample. All autoimmune markers were negative, and she had a normal sexual history. Even though coincidental viral infection cannot be completely ruled out, it is less likely in view of the negative viral cultures as well as the dramatic recovery after antibiotic therapy. There was also no evidence of toxic myocarditis. After excluding these possible causes listed above, *E. coli* infection of the urinary tract was found to be the most plausible explanation for infectious myocarditis.

Bacterial myocarditis, which can result from direct bacterial invasion or toxin mediation, is produced by the pathogens. The most famous toxin-mediated myocarditis is diphtheritic infection. The toxin released by * Corynebacterium diptheriae* inhibits elongation factor-2 activity during protein synthesis and causes DNA fragmentation and cytolysis, leading to widespread damage in the heart, kidneys, and nervous system (14). *E. coli* also produces many toxins such as shiga-like toxins, secreted serine proteases, C1 esterase inhibitor, hemolysin, and lysozyme C (15). β-Hemolysin has been suggested to cause a rapid loss of cardiomyocyte viability and function during group B streptococcal infections (16). Specific secreted serine proteases may selectively damage potassium channels of cardiomyocytes (16, 17). Lysozyme C, a bacteriolytic agent, that is produced mainly by disintegrating neutrophilic granulocytes and monocytes, also mediates cardiodepressive effects (18). The interaction of these toxins lead to myocarditis and ventricular dysfunction. It is not clear whether these mechanisms are involved in the present case and further evidence is required to determine the exact mechanism of *E. coli* infection-associated myocarditis.

Aggressive antibiotic and/or anti-toxin therapy...
are the most promising in the management of infections myocarditis (3). Other treatment strategies include the surgical removal of the infection focus, early goal-directed fluid resuscitation, vasopressor for hypotension, mechanical ventilator support, renal replacement therapy, and treatment of complications such as purulent pericarditis and arrhythmias. Without adequate therapy, bacterial myocarditis may undergo a grave or fatal course. The long-term prognosis probably depends on the degree of ventricular dysfunction and remodeling. Thus, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, and aldosterone antagonists should be prescribed and favorable effects have been proven. Combination of these therapies will reduce hospitalization and increase the survival rate (19).

In conclusion, infectious myocarditis should always be suspected in the patients with sepsis and ventricular dysfunction even they were infected with E. coli urinary tract infection. Although viral infection is the main cause of infectious myocarditis, aggressive antibiotic therapy is mandatory even without obvious bacterial infections. In patient of sepsis with cardiac dysfunction, in addition to the well known sepsis related reversible myocardial depression, the possibility of myocarditis should also be kept in mind and follow up echocardiogram may be necessary.

References