Case Report

Myocarditis Due to Influenza B Virus: The Importance of Early Antiviral Therapy

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Abstract

Myocarditis is usually triggered by medications, toxins, autoimmune disorders as well as bacterial, fungal or protozoal infections, with the viruses being the most common cause. Most of the signs and symptoms are non-specific, ranging from fever, myalgias, palpitations, or dyspnea on exertion to hemodynamic instability, cardiogenic shock and sudden death. Importantly, myocarditis may be the cause of dilated cardiomyopathy through inflammatory autoimmune processes that now have been under investigation. According to the diagnostic procedures, until recently the confirmatory test was endomyocardial biopsy, but has now been replaced by the Cardiac Magnetic Resonance Imaging (MRI). The treatment consists of medications that significantly improve the left ventricular systolic dysfunction such as b-blockers, ACE inhibitors, and the use of positive inotropic agents or vasopressors. Herein, we present an eighty-one years old female patient who was diagnosed with acute myocarditis due to Influenza B infection. Early antiviral therapy with oseltamivir resulted in full and quick recovery of the patient.

INTRODUCTION

A viral infection may affect the human myocardium and cause diffuse inflammation [1]. It has been demonstrated that adenoviruses and enteroviruses, among many other viral species are the commonest culprits [1,2]. They are also called cardiotropic viruses. However, few are the relative clinical cases that have been reported, where the Influenza A and rarely influenza B trigger this inflammatory condition, that ranges from mild asymptomatic to fulminant myocarditis resulting in cardiogenic shock [1,3,4]. The onset may be insidious, with signs and symptoms such as fever, myalgias, palpitations and progressively worsening dyspnea, which either resolves by supportive care or deteriorates no matter any aggressive measure has been used [1].

CASE DESCRIPTION

An eighty-one year-old Caucasian woman presented to the hospital with general weakness and non-productive cough, which began 2 days ago. Her only medication was a dihydropyridine calcium channel blocker due to hypertension. Blood pressure was 120/60mmHg, SaO2 89% (FiO2 21%), heart rate 77bpm, and she had a temperature of 39°C. On cardiac auscultation no murmurs or gallops were noted. Lung auscultation revealed diffuse rales and wheezing bilaterally. On the abdominal examination no pathological findings were noted. Chest x-ray revealed bilateral lung infiltrates. 12-lead ECG revealed flattened ST-segment in I, aVL, V4 to V6. The abnormal laboratory findings were hs-troponin: 2.487 ng/mL, CPK: 535 mcg/L, CPKMB: 174 mcg/L, hs-CRP: 8 mg/L, and ESR: 120mm/h.

The patient was started on bronchodilation, empiric antiviral with oseltamivir and antimicrobial chemotherapy after drawing blood for cultures. Furthermore, diuretics and low dose corticosteroids were added to her treatment. While the viral panel and tests for autoimmune diseases and bacterial infections were pending, she underwent thoracic computed tomography, which revealed lung infiltrates bilaterally, particularly on the left, a pleural effusion on the right and an increased cardiothoracic index. Due to high levels of CK, CKMB and Troponin, without ST segment elevation, she was evaluated by the Cardiologists and she had a transthoracic cardiac ultrasound in order to identify any cardiac wall hypokinesias or functional abnormalities. The imaging of the heart revealed a normal left ventricle with a left ventricular ejection fraction of 60%, with mild systolic dysfunction and mild diastolic dysfunction, as well as mild mitral and aortic regurgitation. At the same time she underwent a cardiac MRI, which revealed increased intake of the paramagnetic substance in the posterior-lateral wall of the left ventricle, which was indicative of acute inflammation, specifically myocarditis (Figure 1).
The patient had an excellent clinical outcome and she was discharged, with diuretics and an ACE-inhibitor, while the IgM antibodies against Influenza type B came out to be positive. The IgM antibodies against influenza A (H1N1), echoviruses, coxsackie viruses and parainfluenza viruses were negative.

**DISCUSSION**

Several factors may cause myocarditis, a diffuse inflammation of the myocardium, which can be life-threatening. Viral and bacterial infections together with autoimmune diseases and hypersensitivity reactions to drugs, may provoke the disease. Hypersensitivity myocarditis, a form of eosinophilic myocarditis is an autoimmune reaction in the heart, which is drug-related and usually characterized by acute rash, fever, peripheral eosinophilia, and ECG abnormalities, such as nonspecific ST segment changes. It is usually related to a recently initiated drug, but there are cases of hypersensitivity myocarditis that occur years after the use of a drug [4]. Among the potential viruses, that trigger the inflammatory response, most frequently listed are the adenovirus, coxsackievirus, cytomegalovirus, HIV and Parvovirus B19, while at the same time, Epstein-Barr virus, Hepatitis C and Influenza A and B may less frequently be the culprit of a devastating course [5]. Until lately, endomyocardial biopsy was considered the gold standard method for the right diagnosis, but due to its serious, even fatal complications, this test has markedly been replaced by more specific imaging techniques such as the Cardiac MRI, which is performed by appropriately skilled medical stuff [1]. Cardiac MRI can distinguish between myocarditis and myocardial infarction [6]. Delayed-enhancement imaging is the most important technique for evaluation of myocardial infarction, quantifying the scar, assessing viability, and evaluating thrombus. Myocarditis is characterized by nodular delayed enhancement in a diffuse, predominantly infero-lateral sub-epicendial location in non-vascular territories, while acute myocardial infarction is associated with early sub-endocardial perfusion defects and sub-endocardial or transmural delayed enhancement of a smaller number of segments, all in a vascular distribution [6].

Influenza B myocarditis is an unusual cause of this condition, due to the low affinity of virus to the heart [5]. In 1918, influenza spread from Spain on a worldwide scale and in this pandemic form that killed over a 50 million people there was a first association between myocarditis and Influenza A infection, based on autopsy studies [1,7]. Characteristics are the patchy infiltrates, mainly in the lateral free wall of the left ventricle [2]. Literally, myocarditis caused by influenza B infection has rarely been reported. When this is noticed, it ranges from mild asymptomatic to fulminant myocarditis or cardiomyopathy, resulting in cardiogenic shock [5,7]. There are a few data that couple influenza B with fulminant myocarditis or cardiomyopathy in children. In Japan, clinicians described, a case of a 15-years old boy with influenza B myocarditis. The adolescent had the typical clinical course; flu-like symptoms, as well as ECG abnormalities similar to that we see in a myocardial infarction. His symptoms responded well on nitrates and diuretics while the cardiac MRI showed no inflammation at the time the symptoms subsided [7]. Furthermore, similar presentations that affect adults were documented in 1958, in a group of four patients with myopericarditis due to Influenza B [5,7]. In addition Ray et al., as well as Mc Carthy et al., described one case each with severe heart failure and cardiogenic shock preceded by a virus infection with influenza B, in previously healthy adults [7].

Influenza, a common febrile illness during winter season, may affect the myocardium, through several mechanisms, in approximately 10% of cases [1]. There are four phases of viral myocarditis; initially, a) receptor-mediated binding and endocytosis of virus in cardiomyocytes, together with infiltration of inflammatory cells into myocardium lead to b) cardiomyocyte necrosis. Due to c) ongoing cytokine production, there is d) further activation and recruitment of cell-mediated immunity [1,2]. Most of the cases are self-limited, with a short course of the disease, some other cases end-up to chronic inflammation; fibrosis, dilated cardiomyopathy, or even end-stage heart failure, and there is a limited number that progresses to culminant disease [1,2]. The disease course either will not be clinically apparent or its outcome will be fatal, with a high mortality rate of 28% among myocarditis patients. It has been reported, that repetitive infection by influenza A or B leads to a detrimental course, including dilated cardiomyopathy and end-stage heart failure [1,5]. However, administering the appropriate circulatory supportive therapy, such as diuretics, ACE-inhibitors, b-blockers, the neuraminidase inhibitor oseltamivir, and if needed, percutaneous extracorporeal membrane oxygenation support at the first 48-hours from the onset of symptoms, truly improves the survival [1,7]. Interestingly, the worst outcome is seen with influenza A infection compared to B. Importantly, this can be even seen in patients with previously intact cardiovascular...
system. It has been documented that a patient with insignificant past medical history suffering from a viral myocarditis may have an ejection fraction of 10% and after receiving the appropriate treatment the ejection fraction may goes up to 55% [5,7].

To our knowledge, only a few cases of Myocarditis caused by Influenza B virus have been documented. Early antiviral treatment may substantially contribute to a successful and quick recovery. To conclude, in cases of fever together with elevation of cardiac enzymes, clinicians should rule out the presence of myocarditis, as prompt therapy may protect against a devastating course of the disease and against the late onset appearance of dilated cardiomyopathy.

REFERENCES