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Case Report Open Access

Biopsy Based Diagnosis of Inflammatory Cardiomyopathy in a Patient with Negative Magnetic Resonance Image Finding

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Abstract

This article describes a case of the patient hospitalized for a sudden heart failure with severe left ventricular dysfunction. This case report presents a history of biopsy-proven inflammatory cardiomyopathy with negative MRI findings. Inflammatory Cardiomyopathy (ICM) is a potentially reversible disease, in which targeted treatment may be considered.

Keywords: Inflammatory cardiomyopathy; Heart failure; Endomyocardial biopsy; Immunosuppressive therapy

Introduction

Myocarditis is defined as an acute or chronic inflammation of the myocardium with presence of inflammatory infiltrating leukocytes and/or increased expression of HLA in the myocardium. Myocarditis may present with wide range of symptoms from mild to death [1]. The diagnosis is presumed on clinical presentation and noninvasive diagnostic methods such as cardiovascular Magnetic Resonance Imaging (MRI). Endomyocardial Biopsy (EMB) is the gold standard for diagnosis of myocarditis. Biopsy finding was considered as indicative for myocarditis if number of infiltrating cells was ≥ 7 T-lymphocytes (CD3+ cells)/mm^2 and/or ≥14 mononuclear leukocytes (LCA+ cells)/mm^2 similarly to the TIMIC study inclusion criteria [2], although recently published position statement suggests somewhat different diagnostic criteria [3]. Another part of the examination is the search for the presence of viruses in the myocardium, because viral (or postviral) myocarditis is the most common type in our region [4,5]. Part of the EMB evaluation should be search for the presence of a pathogenic agent in the myocardium using the Polymerase Chain Reaction (PCR).

Case report

44-year-old patient with ankylosing spondylitis without cardiac symptoms until October 2011 was hospitalized for sudden onset cardiac failure with severe Left Ventricular (LV) dysfunction with cardiogenic shock. LV Ejection Fraction (LVEF) was 11% by echocardiographical evaluation. MRI was performed but did not show any signs of a specific cause of dilated cardiomyopathy. Coronarography found no stenosis of coronary arteries, so the diagnosis of recently occurred Dilated Cardiomyopathy (DCM) was established. EMB was not performed at this moment. Standard therapy of heart failure was introduced. Biventricular cardioverter defibrillator implantation was indicated in primary prevention in patient with LV dysfunction and LBBB, but the implantation of LV electrode failed owing to technical problems. No clinical improvement occurred with standard heart failure treatment; therefore the patient was transferred to our centre for consideration of heart transplantation (HTx). At admission, the patient was in cardiogenic shock with hypotension, tachycardia and resting dyspnea. Pharmacological treatment was optimized, and the combination of continuous furosemide and dobutamine resulted in a stabilized condition. Dilatation of the left ventricle (diastolic diameter – LVDD - was 76 mm, systolic diameter - LVSD - 67 mm) and severe impairment of LV function (LVEF about 15%) were present. Other echocardiographic findings were secondary mitral regurgitation (Figure 1), restrictive filling pattern (Figure 2), left atrial dilatation (LA 48 mm) and enlargement of the right ventricle (RV 40 mm) with systolic dysfunction and presence of pulmonary hypertension. No damage of aortic valve and ascending aorta was identified.

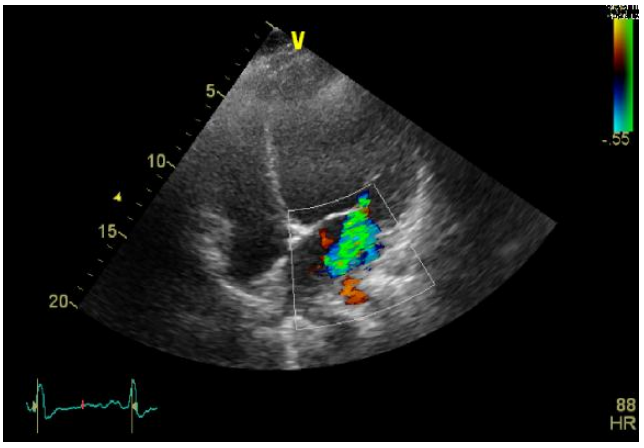

Figure 1: Dilated left vetricle with secondary mitral valve regurgitation.

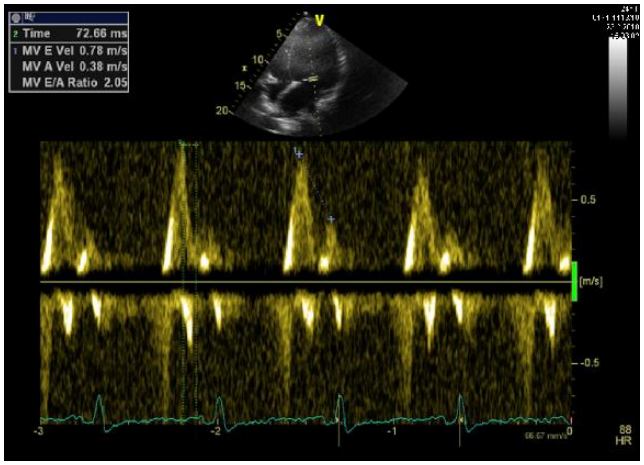

Figure 2: Dilated left ventricle with restrictive filling.

Pre-HTx examination was initiated, no contraindication to surgery was found. However, the inflammatory etiology was suspected because the heart failure was of short duration and refractory to standard heart failure therapy. Despite previous negative results of MRI, EMB from RV was performed in one session together with routine pre-transplant right heart catheterization. The biopsy result showed significant inflammatory infiltration (Figure 3)-11 T-lymphocytes (CD3+ cells)/mm^2 and 25 leukocytes (LCA+ cells)/mm^2. The presence of viral nucleic acids in the myocardium was determined by quantitative polymerase chain reaction (PCR) in real time, for PVB19, CMV, EBV, HSV1/2, HHV6, and adenoviruses, and by reverse transcription followed by real-time PCR for enteroviruses, respectively. No nucleic acid of the pathological agent was detected in the myocardium by the PCR method.

Immunosuppressive therapy – a combination of azathioprine (dose 2 mg/kg/day) and prednisone (initial dose 1 mg/kg/day for 4 weeks, with following reduction to 0.3 mg/kg/day) was started. This treatment was administered for a total of 3 months and then withdrawn. Already after 14 days of this treatment, a significant improvement was observed.

Echocardiographic control was performed before the discharge from hospital (i.e. 3 weeks after the initiation of immunosuppressive therapy) and showed an improvement in LVEF to 25% with persistent LV dilatation (LVDD 72 mm, LVSD 64 mm). The patient was discharged to outpatient care in a clinically stable condition. Next echocardiographic control was done three months after the introduction of immunosuppressive therapy. Systolic function of LV markedly improved and the size of the LV was also reduced (LVEF 40-45%, LVDD 63 mm, LVSD 50 mm). Diastolic dysfunction retreated as well as mitral and tricuspid regurgitation, RV size normalized (RV 30 mm). A significant improvement in the subjective status of the patient was achieved (NYHA class II). The patient was withdrawn from list of HTx candidates. In control EMB after six months a healing myocarditis with remission of inflammatory infiltration (number of cells: 7 CD3+ cells/mm^2, 14 LCA+ cells/mm^2) was described. Simultaneously echocardiographic examination was performed, showing good systolic and diastolic function of nondilated LV (LVEF 55%, LVDD 58 mm, LVSD 44 mm), RV with normal systolic function and no dilatation. The patient was in very good clinical condition (NYHA I), so it was possible to reduce dose of diuretics.

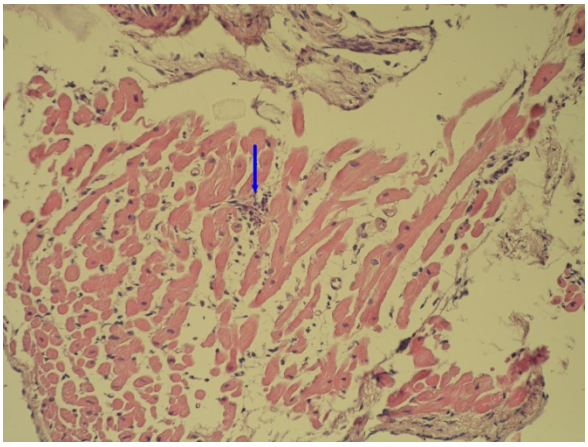

Figure 3: Bioptic finding in myocarditis – leukocytes infiltration in myocardium (arrow).

Discussion

Heart failure is a serious condition with growing incidence in the population [6]. According to the Registry of the International Society of Heart and Lung Transplantation (ISHLT), DCM is the most common cause of end-stage heart failure leading to the HTx [7].

Interesting comorbidity in our case report was ankylosing spondylitis. Ankylosing spondylitis is a seronegative arthritis of mainly young men. The sacroiliac joints and spine are affected especially. The cardiac manifestations including aortitis causing aortic regurgitation, myocarditis causing conduction disturbances, and increased myocardial fibrosis causing abnormalities of left ventricular relaxation and pericarditis. Sinus node dysfunction and atrial and ventricular arrhythmias are described less frequently [8].

Dilated cardiomyopathy is not a homogeneous group of diseases. Biopsy-based diagnosis showed that myocardial inflammation and also viral presence in myocardium are more frequent than it was expected in the past [9]. Viruses are detected in more than a half of the cases of dilated cardiomyopathy [10]. Parvovirus B19 and human herpesvirus 6 HHV6 are currently the most often detected viruses in myocardium, previously enteroviruses and adenoviruses were considered the most important agents causing myocarditis [11]. In this field a number of questions remains - especially in the case of PVB19 it is sometimes difficult to determine whether PVB19 is the etiological agent of the present inflammation or only so-called innocent bystander [5]. The search for etiological agent by serological methods showed no diagnosis significance [12]. Furthermore, it was found that up to half of patients with chronic DCM had the presence of inflammation in myocardium, i. e. myocarditis [13]. In a previous study by our group, the inflammation was detected in 56% of recent DCM patients [14], so the diagnosis should be reclassified to inflammatory cardiomyopathy (ICM) in such cases. Prognosis of myocarditis varies, depending on the histological findings in EMB samples, but in 50%-70% of cases it tends to improvement or even normalization of LV function [15]. The most common manifestation of myocarditis is dyspnea (72% patients), followed by chest pain (32%

patients) or arrhythmias (18%) [3]. In the case of our patient, dyspnea due to severe LV dysfuntion was the main symptom.

Confirmation of the diagnosis of myocarditis is quite difficult. It is based on a comprehensive cardiac examination including echocardiography, coronarography (to exclude ischemic heart disease), with simultaneous ruling out endocrinopathy (mainly thyreopathy) or other possible causes of DCM (alcoholic cardiomyopathy, LV dysfunction after chemotherapy, tachycardia-induced cardiomyopathy). None of these tests is diagnostic; however, importance of these examinations lies in the exclusion of alternative causes of heart failure. All this tests except echocardiography were negative in the described case. Echocardiography is usually used as first examination method; however, findings may vary in a wide range as mentioned by Caforio [3]. Patients with fulminant myocarditis may have normal LV dimensions, but myocardial wall hypertrophy, which is a consequence of myocardial edema. Despite sudden onset, in our case were severe LV systolic dysfunction and LV dilatation present. The most important non-invasive diagnostic method is MRI [16]. In MRI examination, T1, T2 weighted images and late gadolinium enhancement have to be used such as is recommended in JACC white paper [16,17]. Very important part of the assessment is detection of possible myocardial tissue edema as well. The disadvantage of this method is that small changes cannot be noticed because of the MRI resolution. This was probably the case in our patient; MRI was performed at the time of initial presentation of the disease but failed to demonstrate specific changes suggestive of an inflammatory etiology of DCM.

Endomycardial Biopsy (EMB) is considered the gold standard for diagnosis of ICM [3]. This method is the only procedure enabling to show directly an inflammation in vivo and simultaneously detect the presence of a virus (or other agents) in the myocardium [9,18,19]. The main advantage of EMB is its high specificity; its drawback is lower sensitivity due to possible sampling error, and of course, its invasivity as well as a lower availability. Optimal diagnostic approach is the combination of endomyocardial biopsy and MRI [17].

Treatment of myocarditis depends not only on the type of histological and immuno-histological findings but also on the presence of the possible etiologic agent. When the inflammation is present and viruses are absent, immunosuppressive therapy could be considered [3,20]. Results of two randomized monocentric trials with immunosuppressive therapy in patients with biopsy-proven myocarditis showed echocardiographic improvement in patients treated with combined immunosuppressive therapy [2,21]. In the case of detection of a pathogen in the myocardium, targeted therapy, i.e. antimicrobial (mostly antiviral) therapy may be introduced. This approach is still rather empirical-data is largely experimental and clinical studies are not unequivocal [13,22,23]. In contrast, in active myocarditis with evidence of viral genome by the PCR method, immunosuppressive therapy could lead to deterioration of LV function, and is therefore not recommended [18]. So the result of EMB is absolutely essential for indication of specific therapy, such therapy cannot be recommended solely on the basis of noninvasive examinations such e.g. MRI.

Conclusion

We described a case of a recently occurred non-ischemic LV dysfunction with negative MRI results, where the standard treatment of heart failure did not lead to stabilization of the patient. The EMB proved the presence of myocarditis. No nucleic acid of the pathological agent was detected in the myocardium using PCR method. Immunosuppressive therapy was introduced, subsequent improvement in echocardiographic and clinical finding was observed. ICM is a potentially reversible disease so it is appropriate to postpone any major decisions such as device therapy and/or HTx a few weeks or months because of possible improvement of LV function.

Acknowledgements

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