

Case report

What can hide behind an “idiopathic” dilated cardiomyopathy?

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Abstract

Myocarditis is an infectious–inflammatory disease with viral infections being one of the most common infectious cause. When it is superimposed to an individual genetic background, myocarditis may progress into a chronic heart muscle disorder, most often dilated cardiomyopathy (DCM), with a natural history similar to classic forms of genetic or idiopathic dilated cardiomyopathies. We present the case of a 30-year-old patient, with a persistent infectious episode in the last 8 weeks, pain and swelling in the large joints. At admission the patient had fever, tachycardia and a grade 2/6 systolic mitral murmur. Laboratory findings revealed inflammatory syndrome, hepatocytolysis syndrome and microalbuminuria. The electrocardiogram (ECG) showed possible right atrial tachycardia. The echocardiography revealed a globally enlarged heart with reduced ejection fraction and diffuse hypokinesia. When discussing the etiology of the DCM, the following were taken into consideration: a tachycardiomyopathy, ischemic etiology, genetic component, autoimmune etiology (elevated anti-Ro titer), and myocarditis. The diagnosis of myocarditis was confirmed by the cardiac magnetic resonance imaging which showed diffuse fibrosis of the interstitial space and an important increase of the extracellular volume. This case is distinguished by a particular immunological panel requiring dynamic monitoring in order to diagnose a possible associated autoimmune pathology.

Keywords: dilated cardiomyopathy; myocarditis; heart failure; echocardiography; autoimmune disease.

Introduction

Myocarditis is an infectious–inflammatory disease and viral infection is one of the most common infectious cause. The most frequently implicated viruses include adenoviruses, coxsackie B virus, cytomegalovirus and human immunodeficiency virus [1]. When it is superimposed to an individual genetic background, myocarditis may progress into a chronic heart muscle disorder, most often dilated cardiomyopathy, with a natural history

similar to classic forms of genetic or idiopathic dilated cardiomyopathies. It is still unclear whether in this case the myocarditis is the cause which uncovers myocardial genetic anomalies, or the genetic alterations favor the evolution to end stage myocardial disease.

Case report

We hereby present the case of a 30-year-old patient, with a normal weight (BMI=21 kg/m²), without significant personal or family medical history, with a 10-pack year history of smoking and occasional alcohol use, who addressed to the family doctor for a persistent infectious episode in the last 8 weeks accompanied by pain and swelling in the large joints. On this occasion, tachycardia was

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documented and he was addressed to our clinic for evaluation.

On arrival to our facility, the patient had fever (38°C). The physical examination revealed tachycardia, with a grade 2/6 systolic mitral murmur, mild perimalleolar edema and bilateral basal crackling.

The biological work up revealed inflammatory syndrome (WBC= 10,300/mm³, ESR= 24mm/h, Fibrinogen=610.7 mg/dL,

CRP=41.1 mg/L), hepatocytolysis syndrome (ALT= 45 U/L, AST=73 U/L, GGT=67 U/L), mild hypoproteinemia (58.1g/L) and micro-albuminuria.

The ECG showed supraventricular tachycardia 150/min, inverted P waves in V1, suggestive for right atrial origin, positive P waves in inferior leads suggestive for a superior site of origin- possible right atrial tachycardia (Figure 1).

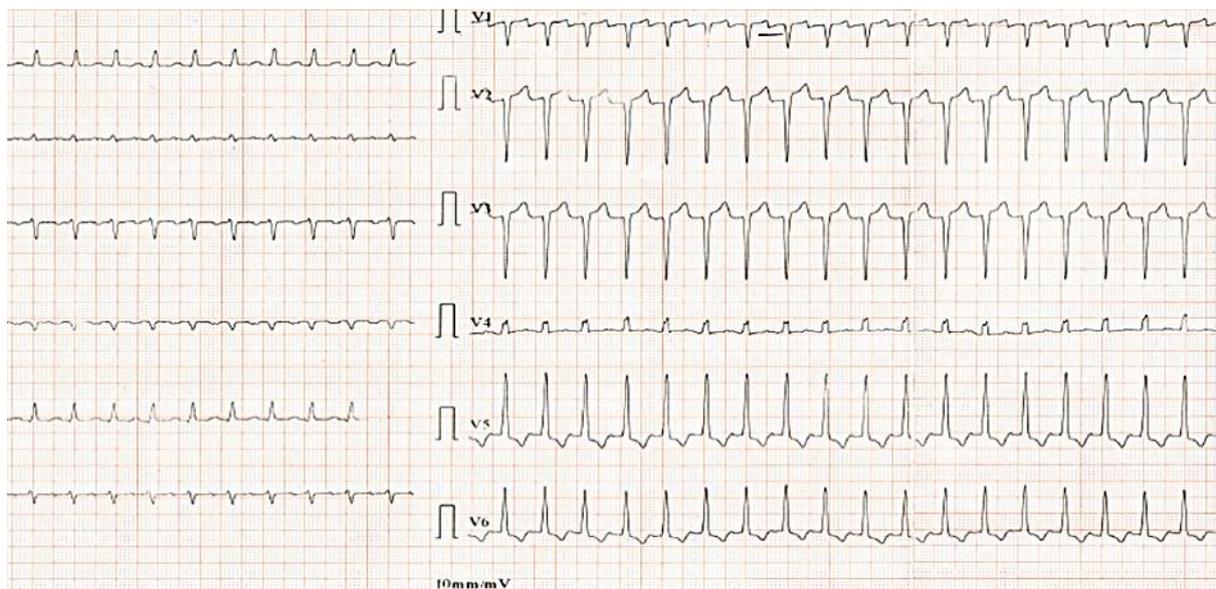


Fig. 1. ECG aspect: Supraventricular tachycardia 150/min, inverted P waves in V1, suggestive for right atrial origin, positive P waves in inferior leads suggestive for a superior site of origin- possible right atrial tachycardia

Transthoracic echocardiography showed a globally enlarged heart, with severe impairment of left ventricular ejection fraction and diffuse hypokinesia (ejection fraction of 20% by the Simpson biplane method) (Figure 2). There

were also moderate mitral and tricuspid regurgitations, with an estimated systolic pulmonary arterial pressure of 30 mmHg and a small posterior pericardial effusion.

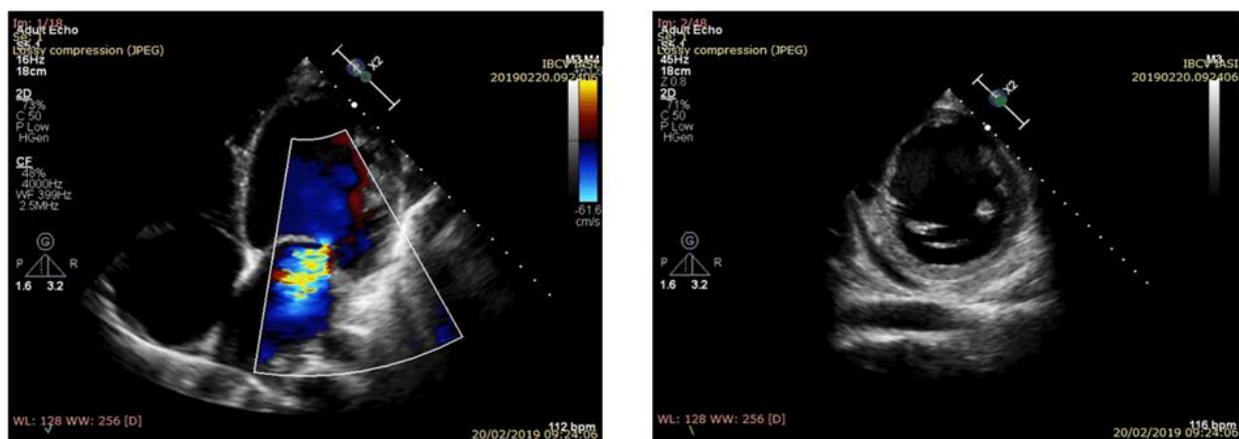


Fig. 2. Transthoracic echo: Enlarged heart with severe impairment of LVEF, moderate mitral regurgitation, small pericardial effusion



Given the initial ECG aspect, a tachycardiomyopathy was taken into consideration. We used beta-blocker (Carvedilol 6.25 mg bid) and Ivabradine 7.5 mg bid, in order to slow down the heart rate and elucidate the ECG aspect. After reaching a more convenient heart rate, the ECG showed sinus rhythm, biphasic P waves with prolonged duration (120ms), which is diagnosis for an advanced interatrial block with left atrial retrograde activation (Bayes syndrome) (Figure 3). As an alternative when the ECG during tachycardia is unclear, adenosine injection and

vagal maneuvers may help in clinical diagnosis [2].

At this point in the investigation, we began to search for specific etiologies for the DCM, but only after making sure that we are not facing secondary heart failure etiologies, such as coronary heart disease, hypertensive heart disease or valvular heart disease. Hypertension was excluded and the valvulopathies mentioned above were interpreted as functional. The coronary computed tomography (CT) angiogram excluded an ischemic heart disease (Figure 4).

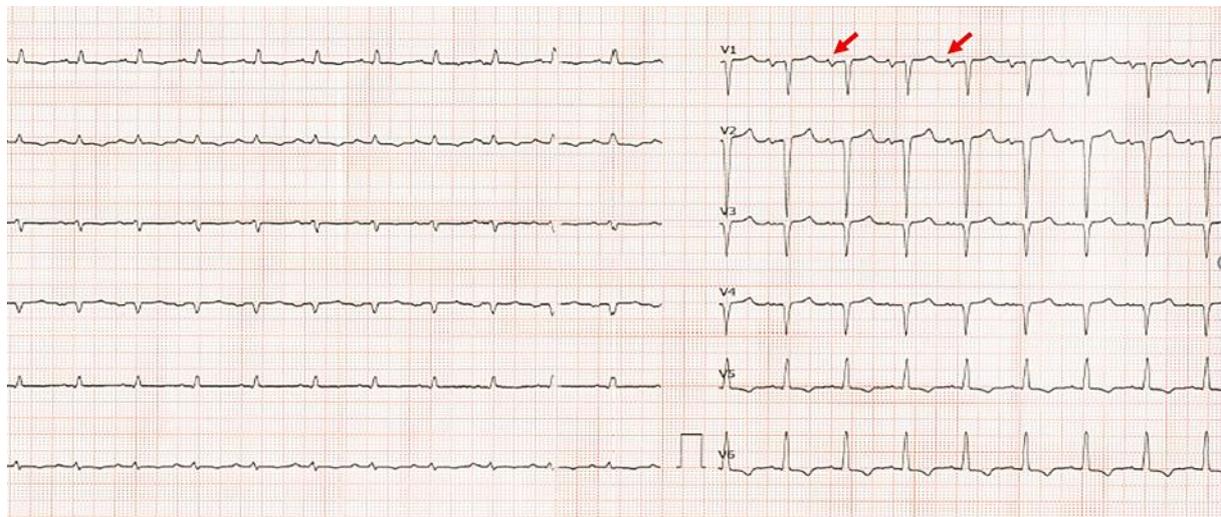


Fig. 3. ECG aspect: Sinus rhythm 80 bpm, biphasic P waves with prolonged duration (120 ms), negative T waves in V5, V6, DII and flattened T waves in DII, aVF

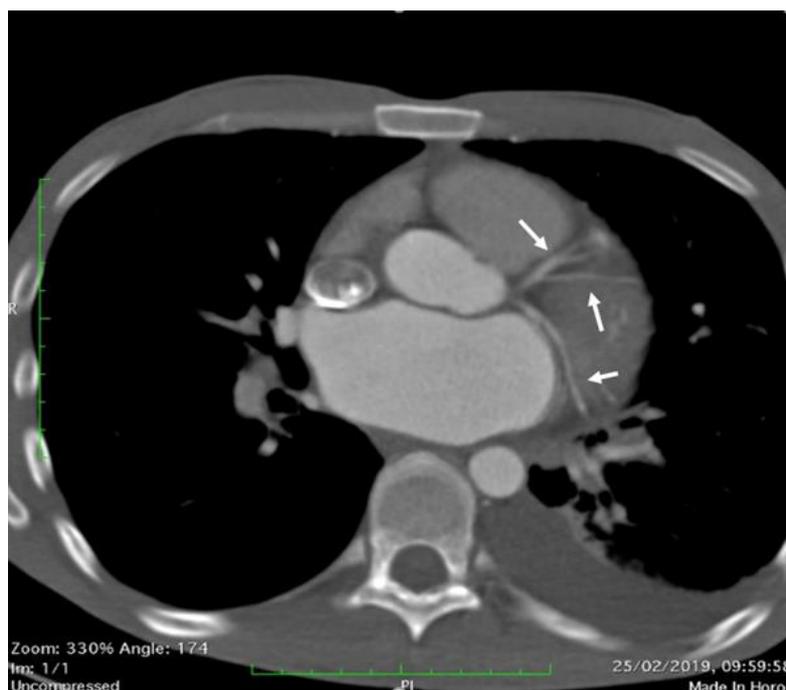


Fig. 4: Coronary CT angiogram: normal epicardial coronary arteries

When discussing the underlying cause of the DCM, the following were taken into consideration: a genetic etiology, an infection leading to myocarditis, a systemic immune-mediated disease, toxic and overload, drugs, as well as a possible endocrine/metabolic etiology [3].

The genetic consultation ruled out a genetic condition. The cultures from the blood, urine, sputum, as well as the pharyngeal exudate were negative. The patient tested negative for acquired immune deficiency syndrome, syphilis and viral hepatitis. Surely, the possibility of a previous viral infection leading to myocarditis remained strong, therefore a cardiac magnetic resonance imaging was performed, showing severe enlargement of the left ventricle

(diastolic diameter 72 mm, systolic diameter 64 mm), moderate to severe systolic dysfunction (LVEF 26%), with diffuse hypokinesia and impairment in both longitudinal and circumferential strain (-9% and -7%).

There were significant diffuse fibrosis of the interstitial space and an important increase of the extracellular volume, without edema, all of this being suggestive for chronic myocarditis (T2Map: 42ms, T1pre: 1280ms; T1post: 482ms, ECV: 33%). The right ventricle was slightly dilated with normal systolic function (EDV 203 ml, ESV 102 ml, EF 50%), but with impairment in both longitudinal and circumferential strain (-11 % and -6%). The left atrium was moderately dilated (56/47/51 mm, area 28 cm²) (Figure 5).

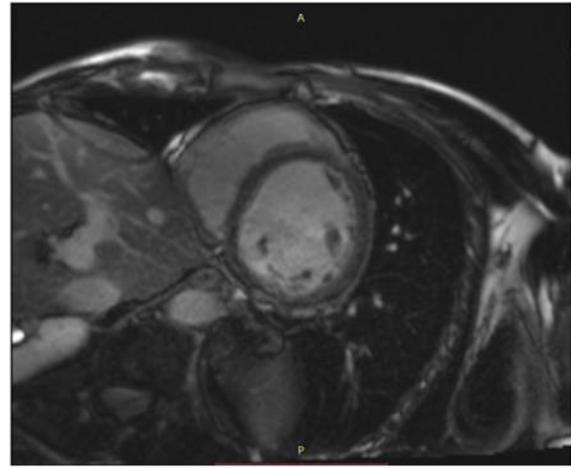
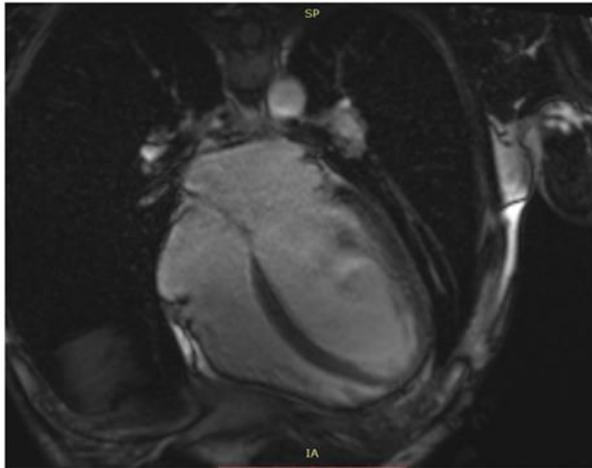


Fig. 5: Cardiac MRI: the presence of diffuse fibrosis of the interstitial space and an important increase of the extracellular volume of the LV (T2Map 42 ms, T1 pre 1280 ms, T1 post 482 ms, ECV 33%)

Given the AST/ALT =1.6, hypoproteinemia and microalbuminuria, a systemic pathology was suspected and therefore an autoimmune work-up was pursued. The serum antinuclear antibody (ANA) was positive (22.3 UA/ml) based on the anti-Ro/SSA antibodies (394 U/mL), but at that moment, neither the criteria for Sjogren's syndrome nor for systemic lupus erythematosus (SLE) were fulfilled. Both toxic/overload and drug induced etiologies for dilated cardiomyopathy were excluded. The patient had no clinical/ paraclinical criteria for acromegaly or pheochromocytoma, and the thyroid work up was within normal limits (TSH= 3.509 μ UI/ml, FT4=1.37 ng/dl, Anti-TPO=16.2 UI/ml).

Therefore, the final diagnosis was DCM secondary to chronic myocarditis, and the patient received the treatment for heart failure with reduced ejection fraction, according to the current guidelines [4], with Furosemid 40 mg qd, Spironolactone 25 mg qd, Ramipril 2.5 mg qd, Carvedilol 6.25 mg bid and Ivabradine 7.5 mg bid.

During the first follow-up visit at 3 months, the patient described palpitations and the ECG revealed atrial fibrillation. In this context, we decided to stop the treatment with Ivabradine and initiate antiarrhythmic treatment with Amiodarone, with the restoration and maintenance of sinus rhythm. The reevaluation

of the left ventricle function showed no significant difference.

At 6 months distance from the initial diagnosis, the patient developed typical discoid lupus lesions localized on the bridge of the nose and the upper cheeks and the dermatological evaluation established the diagnosis of systemic lupus erythematosus (SLE) and treatment with Azathioprine 50 mg bid, Hydroxychloroquine 200 mg bid was initiated.

The echocardiographic reevaluation at 9 months distance from the initial diagnosis showed little improvement of the ejection fraction (ejection fraction of 36% by the Simpson biplane method). The patient was asymptomatic.

Discussion

Myocarditis usually manifests in patients without comorbidities and it can be caused by viral, fungal or bacterial infections, drugs, toxins, as well as autoimmune or systemic diseases [5]. Despite these various causes, the etiology remains unclear in a large number of cases and it is said that the viral etiology is the most frequent one, with almost 20 known cardiotropic viruses [6]. Myocarditis is encountered in ~10% cases of sudden death [7] and it is said that men are more inclined to develop DCM and chronic heart failure [8]. While cardiovascular magnetic resonance should be performed in all patients, endomyocardial biopsy (EMB) is strongly recommended in unstable patients because it offers the possibility to administrate targeted therapy [9].

The presented case highlights a myocarditis which was diagnosed in a young patient directly in its final stage of DCM and it is distinguished by a particular immunological panel, which later on led to the diagnosis of SLE. Myocarditis secondary to SLE has a

prevalence of about 9% and usually requires EMB for confirmation. However, because of the focal nature of the disease, the biopsy has a low sensitivity. Moreover, until the present moment, there are no clear cut-offs for the sensitivity or specificity of the available diagnostic modalities in lupus myocarditis [10].

Conclusion

Thus, when facing a young patient with myocarditis, it is important to maintain a high suspicion for systemic immune-mediated diseases, because a correct diagnosis and a pathogenic treatment can sometimes lead to the improvement of the ejection fraction. Moreover, because of the nonspecific clinical and paraclinical presentation, myocarditis is often a diagnosis of exclusion, and in this scenario, a multimodality imaging approach plays an essential role. Contrast-enhanced cardiovascular magnetic resonance is the most extensive imaging tool for both the diagnosis and prognosis of patients with suspected myocarditis. The Lake Louise Criteria are established diagnostic CMR criteria and include hyperemia, edema and necrosis. The presence of 2 criteria indicate the diagnosis of active myocarditis. In addition, the presence of scar or necrosis play an important role in the prognosis of patients with myocarditis [11].

Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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