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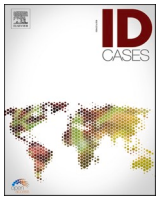

Case report

Rare case of subacute herpetic myocarditis

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A B S T R A C T

Viruses represent the main cause, especially in developed countries. Coxsackie and echoviruses are the most common cardiotropic viruses causing myocarditis. Herpes simplex virus-induced myocarditis is uncommon, and few cases of Herpes simplex virus (HSV) type II have been reported to date. This article presents a rare case of subacute herpetic myocarditis in a 35-year-old male patient

Background

The World Health Organization defines myocarditis as an inflammatory disease of the myocardium that is non-ischemic in origin [1].

The Dallas criteria, published in 1986, provide a standardized system for diagnosing and classifying myocarditis on a histopathologic basis Under the Dallas criteria, active myocarditis on the initial endomyocardial biopsy is defined as the presence of inflammatory infiltrates with adjacent myocyte degeneration or myonecrosis, atypical from ischemic injury. If myocyte degeneration or necrosis is absent, it is considered borderline myocarditis. [2].

Myocarditis represents one of the leading causes of death in patients under 40 years of age (5% of sudden death causes in those under 20 years of age [3]. Viruses represent the main cause, especially in developed countries [4]. Coxsackie and echoviruses are the most common cardiotropic viruses causing myocarditis. Other viral pathogens include the human immunodeficiency virus (HIV), adenovirus, hepatitis B and C, Parvovirus B19, poliovirus, Epstein-Barr virus [5]. Herpes simplex virus-induced myocarditis is uncommon [6] And only one case of HSV type II has been reported to date [7]. We report a case of subacute myocarditis caused by HSV.

Case presentation

Our patient was 35 years old man, a native and resident of Beni Mellal, in Morocco, working as a taxi driver. He had high-risk behaviors such as unprotected sex with multiple partners. He had no personal or family history of heart disease. He was immunocompetent without history of recurrent infections. His blood count showed no neutropenia or lymphopenia, and his HIV serology was negative.

The patient was admitted for retrosternal, constrictive, non-radiating thoracic pain occurring at rest. His pain had no analgesic position and was aggravated by the slightest effort, with a rapidly progressive dyspnea evolving for 15 days.

On admission, the patient was obnoxious, with a blood pressure of 70/46 mmHg, oliguria, cold extremities and a thready pulse. He was polypneic at 30 cycles per minute, with signs of respiratory struggle, and his oxygen saturation was 85%. He had bilateral crackles. The EKG showed atrial flutter (atypical/non-CTI-dependent) at 84 bpm, with a complete left bundle branch (Fig. 1).

On transthoracic echocardiography (Fig. 2), the left ventricle was dilated, with global hypokinesis. The left ventricular ejection fraction was 28% on Simpson biplan. The filling pressures were high. The left atrium was dilated with an indexed volume of 151.44 ml/m2 (Fig. 3).

The mitral valve was thin, with severe mitral insufficiency by mitral annular dilation. The right ventricle was of borderline longitudinal systolic function. The systolic pulmonary artery pressure was 43 mmHg and the inferior vena cava was dilated.

On biological workup:

- Hemoglobin = 15.1 g/l, white blood cells = 9040/mm3, platelets = 238000/mm3, Ultra-sensitive troponin = 3903 ng/l, C-reactive protein = 88 mg/l, SGOT= 1100 IU/l, SGPT = 1200 IU/l, Natremia = 138 meq/l, Kalemia = 3.9 meq/l, urea = 0.23 g/l, creatinemia = 10.2 mg/dl, prothrombin time = 40%, INR = 2.58, Factor V = 40%, activated) partial thromboplastin time = 30.1 s, fibrinogen = 6.36 g/l

The patient was initially admitted to the intensive care unit, where he received full monitoring, central venous line, oxygen therapy, urinary catheterization, analgesic treatment, dobutamine started at a dose of 5 gamma/Kg/min, with boluses of IV furosemide depending on diuresis.

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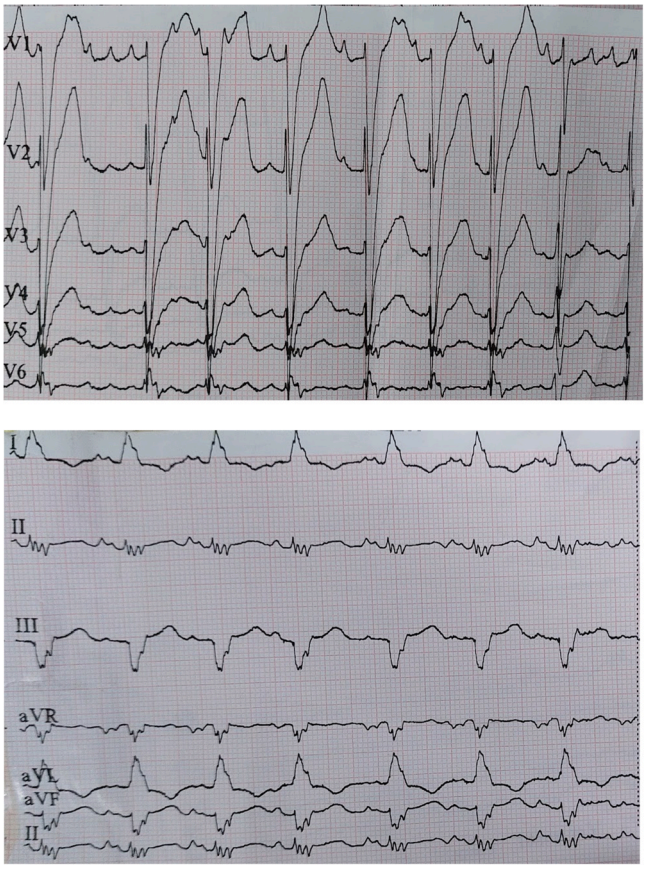

Fig. 1. : EKG showing atrial flutter (atypical/non-CTI-dependent) at 84 bpm, with a complete left bundle branch.

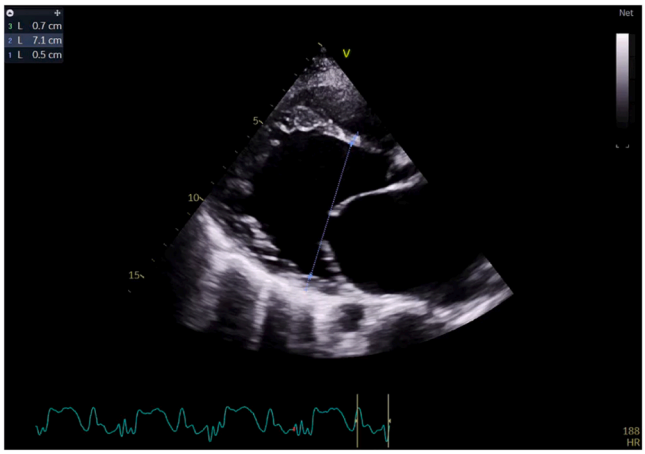

Fig. 2. : Left ventricle dilated to 71 mm.

The patient was anticoagulated with Hbpm in curative dose, then overlapped with VKA with an INR target between 2 and 3.

A coronary angiography was performed showing no abnormalities, followed by a cardiac MRI (Fig. 4) which showed a quasi-transmural myocardial damage predominantly in the lateral wall of the left ventricle, evaluated at 36,2% of the total myocardial mass, with a diffuse inflammatory component, on T2 mapping, and a high ECV of 0.40 + /- 0.03 in favor of active myocarditis, complicated by hypokinetic dilated cardiomyopathy, with bi-ventricular dysfunction, LVEF = 30.6%, RVEF = 26.3%.

An etiological workup of the myocarditis was performed including

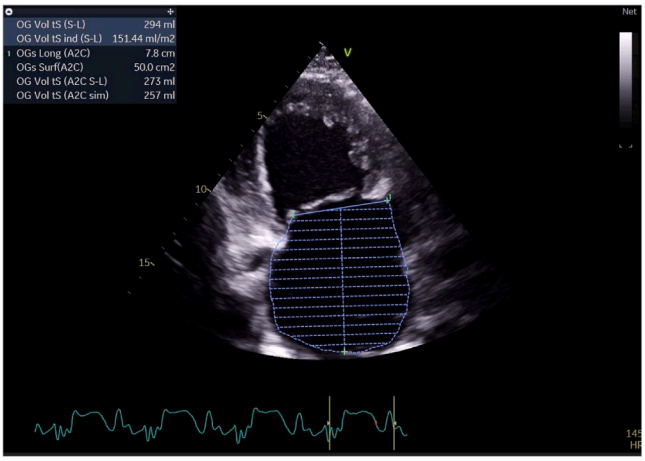

Fig. 3. : Left atrium dilated with an indexed volume of 151.44 ml/m2.

an immunological workup, thyroid workup, blood calcium, conversion enzyme, CPK, blood cultures which were normal, and viral serologies (Technique used: CMIA/MEIA/FPIA on ARCHITECT I10000 (Ablott): Covid 19: IgM (-) IgG = 4.41, HSVI/II: IgM (+) IgG(+), concentration = 70 UR/ml (Positif if > 22 UR/ml, negative if < 16 UR/ml), CMV: IgM (-) IgG (+), EBV VCA IgM (-), IgG (+), Parvovirus B19: IgM (-) IgG (+), Coxackie virus: IgM (-), IgG (-). Serologies for HIV, viral hepatitis B, viral hepatitis C were negative. The myocardial biopsy could not be performed because of technical unavailability. Given these results, a myocarditis of herpetic origin was retained. Treatment was initiated with aciclovir IV at a dose of 5 mg/Kg/8 h for 5 days, followed by valaciclovir 500 mg* 2/day for 7 days.

The short-term clinical course was favorable, and the patient was weaned off dobutamine. Pharmacological treatment of heart failure was introduced progressively (ACE inhibitors, mineralocorticoid receptor antagonists and beta-blockers).

At the 1-month follow-up echocardiography, the left ventricular ejection fraction was 45% and the liver balance has become normal. However, the patient was re-hospitalized for global cardiac decompensation 2 months later, and died after 6 months in his home, probably as a result of arrhythmia. An autopsy could not be performed.

Discussion

Acute myocarditis is defined histologically by the presence of an inflammatory infiltrate (mostly lymphocytic) associated with patches of myocyte necrosis, all in the absence of coronary artery disease [8]. In 1991, Lieberman et al. proposed a classification of myocarditis that distinguishes four subclasses: fulminant myocarditis, acute myocarditis, chronic active myocarditis and chronic persistent myocarditis [9]. It represents a significant etiology of dilated cardiomyopathy (about 16% of biopsies on unexplained dilated cardiomyopathies conclude to myocarditis) [10]. Diagnosis of myocarditis can be difficult in current clinical practice. A 2013 paper from the European Society of Cardiology (ESC) Working Group on Myocardial and Pericardial Diseases [8]. distinguishes between clinically suspicious and definite myocarditis. Clinical suspicion of myocarditis is based on the patient's clinic (primarily chest pain), electrocardiogram (ECG) (often ST-segment elevation), laboratory tests (i.e., increased serum troponin), and imaging findings, including those obtained by echocardiography and MRI. Diagnostic criteria for MRI have recently been updated and include the coexistence of T1- and T2-related criteria indicative of myocardial inflammation [11]. Endomyocardial biopsy confirms the diagnosis of myocarditis and identifies the underlying aetiology and the type of inflammation (e.g. giant cell, eosinophilic myocarditis, sarcoidosis) which imply different treatments and prognosis. Importantly, EMB is also the basis for safe

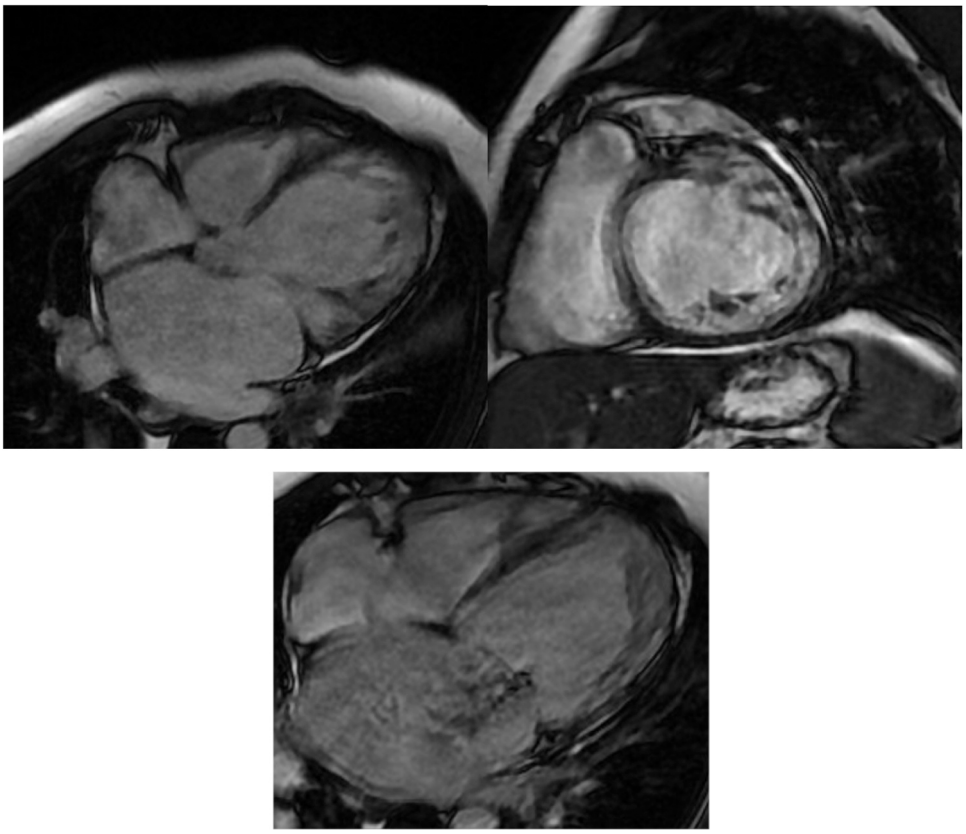

Fig. 4. : LGE sequence: Transmural late enhancement: Near-transmural myocardial damage predominantly in the lateral wall of the left ventricle.

(infection negative) immunosuppression and antiviral treatment. If EMB is performed byexperienced teams, its complication rate is low. The recent scientific statement on EMB gave highest levels of recommendations in the life-threatening clinical presentations [8].

Viruses are the leading cause of acute myocarditis, particularly in developed countries. On the basis of serological studies, Adenovirus and EBV have long been considered the most common cardiotropic viruses causing myocarditis, but recent studies using PCR for viral diagnosis in cardiac biopsies have indicated that PVB19 and HHV6 are the most common pathogens in patients with acute myocarditis [4].

Herpes simplex virus-induced myocarditis is uncommon. Few cases have been reported in the literature. We can mention one case of fulminant myocarditis due to primary HSV-2 infection, without genital involvement, in a 41-year-old woman. The patient was considered immunocompetent before the onset of HSV-2 infection. The disease rapidly progressed to fulminant myocaditis, coma and liver failure. The diagnosis was made post mortem [12].

Bowles et al. reported that PCRs were positive for HSV in 5 of 624 (0.8%) specimens obtained from patients with myocarditis [6]. It has also been reported that viral myocarditis can be associated with hepatitis, which was the case of our patient, pancreatitis, nephritis, and encephalitis, but the majority of these reports have used postmortem biopsies [13].

Herpes simplex virus has rarely been reported in myocardial tissue and these cases represented reactivation of latent infection and complications of organ transplantation and/or immunosuppression. Late diagnosis of HSV-2 infection can rapidly progress to death following fulminant hepatitis [7].

HSV can also cause ventricular arrhythmias, but not as frequently as other viruses such as parvovirus, SARSCOV2 or adenovirus. The most common arrhythmias are: VF, sinus node dysfunction and atrial fibrillation [14].

When seroconversion (low IgG, high IgM and IgA) occurs at the time of cardiac symptoms, it may suggest a viral cardiac event. However, these tests do not prove the direct presence of a viral infection in the heart.

Mahfoud and al [15] reported that the sensitivity for serological detection of a virus that was found in endomyocardial biopsy was 9% and the specificity was 77%. The PPV and NPV were 25% and 49%, respectively.

In our case, the diagnosis of herpetic myocarditis was made on the basis of a series of arguments, as well as on the high level of antibody (IgM and IgG).

The management of myocarditis is primarily symptomatic. Loop diuretics are indicated for congestive signs. Converting enzyme inhibitors (CEIs) or angiotensin-2 antagonists (ARBs) have a beneficial effect (reduction in the progression of LV dysfunction, control of inflammation, fibrosis and myocardial necrosis). Beta-blockers are also indicated, notably for the prevention of rhythmic complications but also for their benefits on LVEF and remodeling. They should be maintained as long as signs of myocarditis activity persist (persistence of kinetic disorders, LV dysfunction, persistence of edema on T2 sequences, etc.). Anti-aldosterones may be discussed, especially in case of persistent congestive symptoms. In case of cardiogenic shock, it is essential to hospitalize the patient in a facility with a surgical unit, to start positive inotropic therapies (dobutamine) and, in case of refractory cardiogenic shock, to have recourse to circulatory assistance (extracorporeal membrane oxygenation [ECMO] in the first instance), potentially with a view to a cardiac transplant [16]. Antivirals such as acyclovir, famciclovir, and valacyclovir are the most effective drugs for people infected with the herpes virus. They help reduce the severity and frequency of symptoms but cannot cure the infection [17].

The treatment of herpetic myocarditis is not codified.

In our case, the treatment was given for 12 days (5 days of Acyclovir IV followed by 7 days of valacyclovir oral). We noticed an improvement in symptoms and EF of LV with acyclovir and valacyclovir. However, the

prognostic was bad attesting by the sudden death of our patient, probably as a result of arrhythmia.

Kuchynka P and al. [18] report the case of a 46-year-old patient whose diagnosis of HSV was confirmed by myocardial biopsy, and who was treated with acyclovir. The protocol was the administration of acyclovir (Herpesin®) intravenously for the first 5 days (500 mg every 8 h) and then 9 days orally (400 mg every 4 h except one dose at night) after hospital discharge. One month after the end of therapy with acyclovir the patient was completely asymptomatic.

The immunosuppression was also proposed by Kalim U et al. [19]. It is concluded that immune suppression with prednisolone, administered at 3 months of the onset of acute myocarditis, is effective in significantly bringing about improvement and cure in persistent left ventricular failure.

Ethical approval

Ethical approval for the study was obtained from the relevant local ethics committees.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompany ingimages

CRediT authorship

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing, others, who have contributed in other ways should be listed as contributors.

CRediT authorship contribution statement

Acquisition of data: Errami Amine. Analysis and/or interpretation of data: Errami Amine. Drafting the manuscript: Errami Amine. Critical revision: Drighil Abdenasser.

Declaration of Competing Interest

We do not have and have not had a financial interest or other relationships in which the individual benefits by receiving a salary, royalty, intellectual property rights, consulting fee, honoraria, ownership interest, or other financial benefit..

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.idcr.2023.e01828.

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