

Acute Myocarditis and Myopathy as Presenting Manifestations of Human Immunodeficiency Virus Infection

Dan Kiselnik MD¹, Arik Wolak MD², Mahmoud Abu-Shakra MD¹ and Anna Basok MD¹

¹Department of Internal Medicine D and ²Cardiac MRI Unit, Department of Cardiology, Soroka University Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

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Cardiac and skeletal muscle myopathies are not uncommon manifestations of human immune deficiency virus (HIV) infection. However, severe skeletal myopathy occurs in only 0.2% of HIV-infected individuals, and clinically symptomatic cardiomyopathy develops in 1-2% of patients. The damage to muscle cells occurs as a result of direct invasion of the cells by the HIV virus, or by immunological alteration of the cell-mediated immunity. Autoimmune mechanisms have also been reported to have a pathogenic role. We

report here a patient without a past medical history who presented with severe skeletal myopathy and fulminant myocarditis as a presenting manifestation of HIV infection.

PATIENT DESCRIPTION

A healthy 46 year old Caucasian male was admitted with sudden chest pain that appeared at rest. The pain was radiating to the left shoulder and upper abdomen and lasted for 2 hours. He also complained of diffuse muscle pain and weakness of his extremities that had begun 4 weeks earlier. He denied a history of fever, cough and shortness of breath.

His blood pressure was 102/50 mmHg, heart rate 110 beats/minute, and respiratory rate 18 breaths/minute. Physical examination revealed mild muscle wasting of the upper shoulder girdle. His muscle strength was 4/5. Laboratory workup showed creati-

nine kinase (CK) 14,549 IU/ml, troponin T 0.21 ng/ml, creatinine 0.58 mg/dl, lactate dehydrogenase 2501 U/ml, aspartate aminotransferase 560 U/ml and alanine aminotransferase 254 U/ml.

The electrocardiogram recordings revealed ST elevation in the leads referring to anterior and lateral wall with reciprocal ST-T depression in the leads referring to the inferior wall. Coronary angiography disclosed normal coronary arteries. 2D echocardiography study on admission also demonstrated normal left ventricular systolic function.

Cardiac MRI (CMRI) findings were consistent with myocardial inflammation, fulfilling two of the three "Lake Louise" criteria: abnormal T2 ratio (2.6, normal \leq 1.9) [Figure 1] and abnormal early gadolinium enhancement ratio (8.8, normal $<$ 4). Both abnormal findings exhibited a global pattern. The CMRI did not dem-

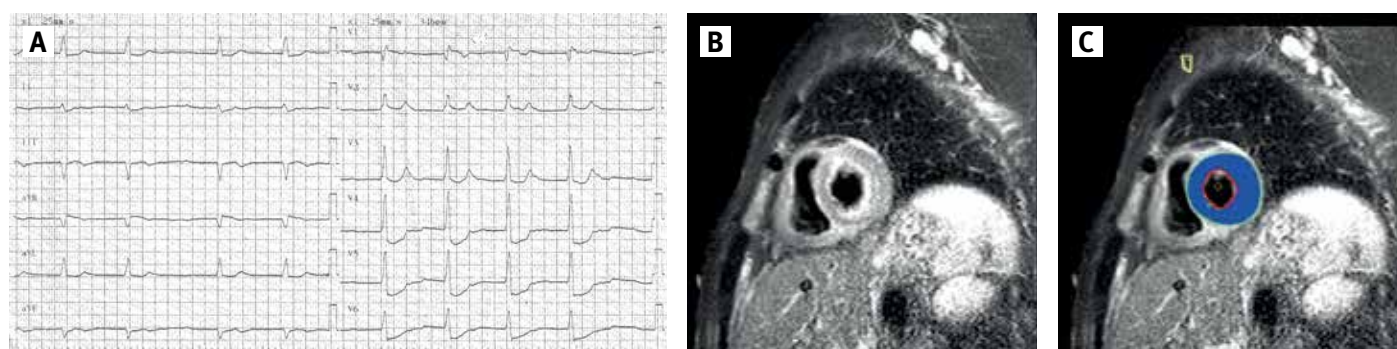


Figure 1. [A] ECG tracing with junctional rhythm. [B] T2-weighted STIR images, representing a slice of the myocardium in short axis view in the mid-left ventricle. The image demonstrates global high intensity signal. The calculated T2 ratio was 2.6 ($>$ 2 considered abnormal). [C] Toggle T2 ratio overlay of the same slice in [B]. The toggle T2 ratio overlay graphically displays the T2 ratio, normalized to skeletal muscle. Colored blue regions represent a T2 ratio $>$ 2 (abnormal reading). The diffuse blue readout demonstrates global abnormal T2 ratio

onstrate a focal late gadolinium enhancement lesion.

The patient was diagnosed with myocarditis and skeletal muscle myopathy. Further laboratory studies demonstrated normal levels of complement and rheumatoid factor, and antinuclear antibody was not detected in the serum. Serology for HIV was positive on enzyme-linked immunosorbent assay (ELISA) and confirmed by Western blot. Viral load was 16,000 copies/ml, and the count of CD4 T cells was 264/ml. Therapy was initiated with Truvada® (emtricitabine/tenofovir disoproxil fumarate, Gilead, USA) and Kaletra® (lopinavir and ritonavir, Abbot, USA).

During his hospitalization, the patient developed severe congestive heart failure and arrhythmia including episodes of atrial fibrillation, multiple bigeminy, non-sustained ventricular tachycardia (VT) and subsequently monomorphic VT at 180 beats/min. A 2D echocardiography study revealed moderately decreased left ventricular systolic function and dilatation and akinesia of right ventricle. Mitral and tricuspid regurgitation was observed without elevated pulmonary pressure.

Despite intensive medical therapy, the patient developed severe bradycardia with nodal rhythm, and electromechanical dissociation was recorded with eventual asystole. There was no response to resuscitation measures and the patient died. Autopsy limited to the heart and lungs revealed lymphocytic myocarditis and dispersed fibrosis involving mainly the cardiac apex with mild pericardial effusion (50 ml). Pulmonary edema with pulmonary congestion and bilateral pleural effusion were also disclosed.

COMMENT

We present the case of a patient with acquired immune deficiency syndrome (AIDS) who presented with chest pain and CK elevation. He was further diagnosed with fulminant myocarditis and skeletal

muscle myopathy. A muscle biopsy was not performed. The diffuse myalgia and the very high levels of CK suggest HIV-associated inflammatory myopathy. The CMRI findings and autopsy report were consistent with myocarditis. Myopathies associated with HIV include necrotizing non-inflammatory myopathy, rhabdomyolysis, nemaline rod HIV myopathy, polymyositis, drug-induced myopathy, inflammatory myopathy, inclusion body myositis, and HIV-associated polymyositis. HIV-associated polymyositis is relatively rare and clinically and histologically indistinguishable from autoimmune polymyositis [2]. Since muscle biopsy was not performed and because of the fulminant course of the disease, the type of myopathy could not be determined.

HIV-associated myocarditis is a relatively common pathological finding among patients with HIV infection and is characterized by a lymphocytic infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of the ischemic damage associated with coronary artery disease [3]. Autopsy studies have found myocardial inflammation in up to 50% of AIDS patients. In the GISCA autopsy series (Gruppo Italiano per lo Studio Cardiologico dei pazienti affetti da AIDS), a histological diagnosis of myocarditis was reached in 30 of 82 patients (37%) with cardiac involvement [4]. In addition, echocardiographic findings of cardiomyopathy were reported in 1.59% of asymptomatic HIV-positive patients as a result of myocarditis in the majority of cases [5]. Of 20 autopsy patients with dilated cardiomyopathy, 10 (50%) had active myocarditis on histological examination of myocardial tissue specimens [5].

Infection with HIV is the primary pathogenic cause of AIDS-related myocarditis. However, since myocytes do not express receptors for CD4, it is not clear how the virus invades cardiac muscle cells. It has been proposed that dendritic cells and injury of myocytes by other viruses may

facilitate the entry of HIV virus into CD4 receptor-negative cells. HIV infection leads to T cell-mediated immune suppression, which in turn increases the risk of myocarditis from other infectious causes. HIV may have been the cause of myocarditis in our patient since no other specific pathogens were identified.

Myocarditis in HIV-infected patients may be asymptomatic or present with various clinical manifestations, including congestive heart failure, dilated cardiomyopathy, malignant arrhythmia and symptoms of associated pericarditis, or it may mimic acute coronary syndrome. CMRI has a major role in determining the mechanism of cardiac symptoms among patients infected with HIV [5].

In conclusion, HIV myocarditis and severe myopathy may be the first manifestations of HIV infection, and HIV serology should be included in the workup of unexplained myopathy and myocarditis.

Correspondence

Dr. M. Abu-Shakra

Dept. of Medicine D, Soroka University Medical Center, P.O. Box 151, Beer Sheva 84101, Israel

Phone: (972-8) 640-0601

Fax: (972-8) 638-3632

email: mahmoudS2@clalit.org.il

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“It’s a shallow life that doesn’t give a person a few scars”

Garrison Keillor (born 1942), American author, storyteller, humorist and radio personality