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Fulminant Human Herpesvirus 6 Myocarditis in an Immunocompetent Adult

Role of Cardiac Magnetic Resonance in a Multidisciplinary Approach

Golmehr Ashrafpoor, MD; Laurent Andréoletti, MD, PhD; Patrick Bruneval, MD, PhD; Laurent Macron, MD; Arshid Azarine, MD; Antoine Lepillier, MD; Nicolas Danchin, MD, PhD; Elie Mousseaux, MD, PhD; Alban Redheuil, MD, PhD

A 28-year-old immunocompetent man coming back from Brazil was admitted to the coronary care unit after an episode of syncope without chest pain, vomiting, or other symptoms. Physical examination revealed bradycardia and splenomegaly without fever. The ECG showed a complete atrioventricular (AV) block with ventricular escape rhythm at 38 bpm (Figure 1). Biology showed mild elevation of cardiac troponin Ic at 0.7 ng/mL (normal range <0.15 mg/L), an increased white blood cell count at 15.5 G/L (normal range 4–10.0 G/L), and C-reactive protein was 8.1 mg/L (normal range <10 mg/L). Chest x-ray was normal (Figure 2). Transthoracic echocardiography showed a normal left ventricular (LV) ejection fraction with hypertrophy and normal regional wall motion. Intravenous isoprenaline was started with a satisfactory ventricular response (55 bpm; Figure 3).

On day 2, troponin Ic increased to 9.88 ng/mL. Cardiac magnetic resonance (CMR) revealed severe asymmetrical hypertrophy with marked predominance in the anterior basal region of the interventricular septum (22 mm thickness) and systolic anterior motion of the mitral valve (Figure 4A; see Movie I in the online-only Data Supplement), and LV ejection fraction was normal. Furthermore, large areas of edema (Figure 4B) and severe necrosis with areas of microvascular obstruction were seen in the interventricular septum, particularly in the region of the His bundle (Figure 4C).

On day 3, the patient developed fever and an eruption of the face and trunk. AV conduction (2:1) was noted (Figure 5). Extensive viral and bacterial serologies, including HIV, were negative. Intravenous antibiotic therapy was initiated for suspicion of Lyme disease.

On day 4, he complained of severe acute abdominal pain. Troponin Ic increased to 36 ng/mL, and C-reactive protein rose to 120 mg/L. An emergency coronary angiogram showed normal coronary arteries, and a temporary pacing lead was placed. Transthoracic echocardiography showed deterioration of LV function (40% LV ejection fraction). The patient

experienced recurrence of complete AV block and several episodes of sustained ventricular tachycardia (Figures 5 and 6), leading to the discontinuation of isoprenaline and the starting of temporary pacing. Repeat transthoracic echocardiography showed additional alteration of ventricular function (20% LV ejection fraction). The patient suffered from rapid hemodynamic deterioration, followed by cardiopulmonary arrest attributable to pulseless electric activity. Cardiopulmonary resuscitation was performed, and the patient died while being put on extracorporeal life support.

Necropsy confirmed that LV hypertrophy was attributable to massive hemorrhagic myocardial necrosis (Figure 4D and 4E). Classic histological analyses showed, according to the Dallas criteria, a lymphocytic myocarditis with plurifocal lesions along with inflammation and necrosis of the His bundle, which explained the complete AV block (Figure 4F). Molecular detection of the major common cardiotropic viruses, including influenza A H1N1pdm 2009, was performed by use of a combination of classic real-time and multiplex polymerase chain reaction and microarray hybridization assays. The results revealed only the presence of human herpesvirus 6 (HHV6) genome in the myocardium and in the splenic tissues. Moreover, Chagas disease was excluded by a negative trypanosoma detection using a classic polymerase chain reaction assay in cardiac tissues.

HHV6 is reported as 1 of the most frequent viral causes of myocarditis, found in up to 23% to 36% of cases in series with endomyocardial biopsies.^{1,2} It is associated frequently with acute and chronic heart failure.² Clinically, HHV6 myocarditis may be preceded by upper respiratory tract infection. As opposed to other viral causes of myocarditis, HHV6 infection, although rarely symptomatic in the early stage, is likely to have a worse prognosis. However, only a few cases of acute fulminant HHV6 myocarditis in immunocompetent patients have been reported. The association of HHV6 myocarditis with marked septal thickening by echocardiography and complete AV block has been reported previously.³ CMR has

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emerged as an important tool in the diagnosis of human myocarditis by uniquely combining assessment of cardiac anatomy and dynamics with noninvasive tissue characterization. The present case underlines the diagnostic value of CMR to assert the presence of acute regional myocardial necrosis and microvascular obstruction (late gadolinium enhancement), edema, and hemorrhage (T2-weighted imaging), explaining the unusually severe anteroseptal hypertrophy and the complete AV block. In this case, tissue characterization by CMR allowed to rule out hypertrophic cardiomyopathy despite the presence of typical anatomic features, such as severe asymmetrical and obstructive hypertrophy of the basal septum (22 mm) with systolic anterior motion of the mitral valve. Moreover, CMR can assess the severity and extension of myocardial inflammation as well as necrosis, which is potentially useful for prognostic stratification and endomyocardial biopsy guidance. Newly available multiplex polymerase chain reaction–microarray assay allows consistently robust qualitative detection of cardiac HHV6 infection.⁴ Together, these recent developments in both imaging and virology may suggest that early image-guided endomyocardial biopsy and perhaps early LV assistance should be considered in severe forms of myocarditis confirmed by CMR, such as in the present case.

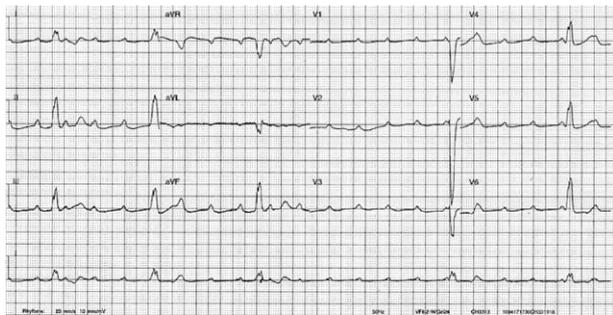


Figure 1. ECG at admission showing a complete atrioventricular block with a ventricular escape rhythm of \approx 38 bpm.

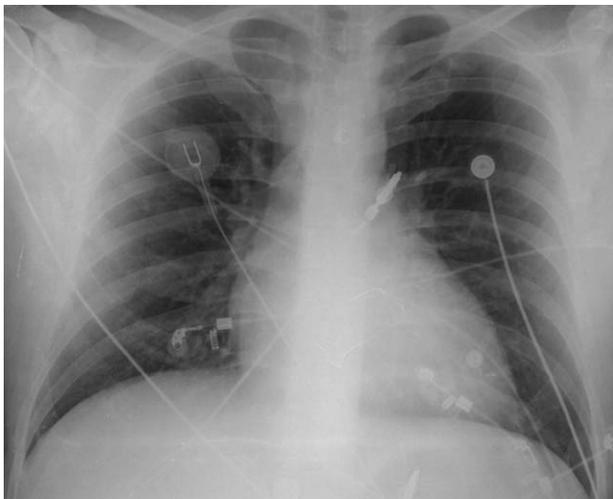


Figure 2. Chest x-ray was normal. In particular, there were no signs of pulmonary edema.

This report should hopefully raise awareness of the usefulness of CMR to diagnose unusual forms of viral myocarditis as well as the utility of endomyocardial biopsies to characterize histological lesions and identify the viral cause of inflammation. Such a multidisciplinary diagnostic approach might constitute the first step to improve the clinical management and possibly the treatment of severe infectious myocarditis in immunocompetent adult patients.

Disclosures

None.

References

1. Kühl U, Pauschinger M, Seeborg B, Lassner D, Noutsias M, Poller W, Schultheiss HP. Viral persistence in the myocardium is associated with progressive cardiac dysfunction. *Circulation*. 2005;112:1965–1970.
2. Mahrholdt H, Wagner A, Deluigi CC, Kispert E, Hager S, Meinhardt G, Vogelsberg H, Fritz P, Dippon J, Bock CT, Klingel K, Kandolf R, Sechtem U. Presentation, patterns of myocardial damage, and clinical course of viral myocarditis. *Circulation*. 2006;114:1581–1590.
3. Fukae S, Ashizawa N, Morikawa S, Yano K. A fatal case of fulminant myocarditis with human herpesvirus-6 infection. *Intern Med*. 2000;39:632–636.
4. Andréoletti L. Viral myocarditis. Physiopathology and diagnosis. In: Cihakova D, ed. *Myocarditis*. Rijeka, Croatia: InTech Publishers; 2011:87–104.

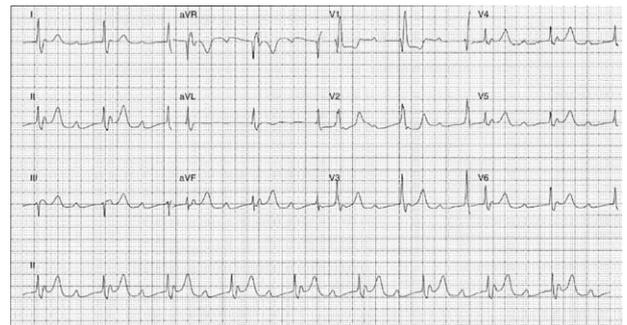


Figure 3. After administration of intravenous isoprenaline, the patient showed 2:1 atrioventricular block, with a ventricular response of 55 bpm.

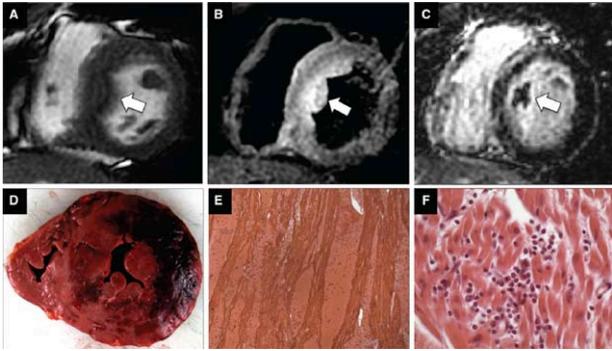


Figure 4. **A**, Cardiac magnetic resonance (CMR): severe asymmetrical hypertrophy with marked predominance of wall thickening in the anterior basal region of the interventricular septum (22 mm thickness) in mid-left ventricular short-axis steady-state free precession cine image. **B**, CMR: massive myocardial inflammation and edema seen as high myocardial intensity on triple inversion recovery T2-weighted images with fat saturation. **C**, CMR: large areas of severe necrosis with areas of microvascular obstruction were seen in the interventricular septum (hypointense areas within high-intensity delayed enhancement in inversion recovery images acquired 10 minutes after gadolinium contrast injection). **D** and **E**, Necropsy: macroscopic and microscopic observation revealed left ventricular hypertrophy attributable to massive hemorrhagic myocardial necrosis. **F**, Necropsy: microscopic observation showed lymphocytic myocarditis with plurifocal lesions.

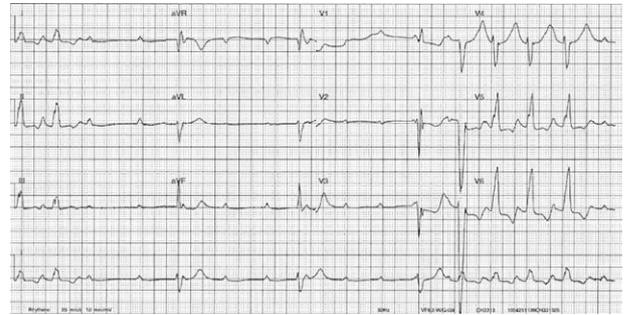


Figure 5. ECG showing recurrence of complete atrioventricular block.



Figure 6. Sustained ventricular tachycardia on ECG monitor.