What's new in myocarditis?

Charles-Edouard Luyt, Guillaume Hékimian, Fredric Ginsberg²

► To cite this version:

Charles-Edouard Luyt, Guillaume Hékimian, Fredric Ginsberg². What's new in myocarditis?. Intensive Care Medicine, 2016, 42 (6), pp.1055-1057. 10.1007/s00134-015-4017-5 . hal-01196308

HAL Id: hal-01196308

<https://hal.science/hal-01196308>

Submitted on 9 Sep 2015

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

What's new in myocarditis?

Charles-Edouard Luyt¹, Guillaume Hékimian¹, Fredric Ginsberg²

¹Service de Réanimation Médicale, Institut de Cardiologie, Groupe Hospitalier Pitié-Salpêtrière, 47-83 boulevard de l'Hôpital, 75013 Paris, Assistance Publique-Hôpitaux de Paris Sorbonne Universités, UPMC Université Paris 06, INSERM, UMRS_1166-ICAN, Institute of Cardiometabolism and Nutrition, F-75013 Paris, France; ²Cooper Medical School of Rowan University, Camden, New Jersey, USA

Word count: 1082 words

Myocarditis is an illness characterized by myocardial infiltration with inflammatory cells and non-ischemic myocyte necrosis. Typical histological finding is lymphocytic infiltration, but other forms involving eosinophilic or giant-cell inflammation exist. Coronary vasculitis is another pathogenic mechanism in some instances. The leading causes are infectious diseases, most commonly viral; immune-mediated injury (triggered by viral infection, allogenic agents such as drugs or associated with autoimmune disease); and toxins.

Acute myocarditis is defined by the recent onset of severe symptoms including chest pain or dyspnea. In some patients the disease can be fulminant, with acute onset and rapid progression to cardiogenic shock. Recent advances include the widespread use of cardiac magnetic resonance imaging (MRI) for diagnosis; and the increasing use of circulatory

support (mainly extracorporeal membrane oxygenation – ECMO) with good results in the most critically ill patients.

Diagnosis

The diagnosis of myocarditis remains a clinical one, although histological examination of the myocardium is the gold standard for the diagnosis. It allows the confirmation of the diagnosis and, in some cases, to identify its cause. The 2007 American Heart Association – American College of Cardiology - European Society of Cardiology (ESC) guidelines recommended that an endomyocardial biopsy (EMB) should be performed in the following circumstances: 1) new-onset heart failure of under 2 weeks duration associated with a normal-sized or dilated left ventricle and hemodynamic compromise, or 2) new-onset subacute heart failure of 2 weeks to 3 months duration associated with a dilated left ventricle and new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual heart failure pharmacologic care [1]. More recently, the ESC has proposed diagnostic criteria for clinically suspected myocarditis and recommended that all these patients should be considered for EMB [2]. However, although the reported rate of complications is low, given its risk/benefit ratio in patients without severe myocarditis, we think EMB should be performed only in patients with severe disease who do not improve, or in patients in whom giant-cell or eosinophilic myocarditis is suspected (i.e., those with severe ventricular arrhythmia or high-grade heart block) (Figure). EMB should not be performed in patients in whom the diagnosis of the causal disease is evident (e.g. auto-immune disease) and in patients without severe disease who quickly recover (Figure). In order to obtain information on the aetiology and pathogenesis of the disease, specimen analysis should include standard histology, immunohistochemistry and detection of viral genome by PCR [3].

Whereas histology is the gold standard for the diagnosis of myocarditis, MRI is becoming indispensable for the diagnosis of acute myocarditis. Current diagnostic recommendations on the basis of Lake Louise criteria rely on a combination of T1-weighted imaging (relative enhancement ratio) to detect myocardial inflammation and hyperaemia, T2-weighted imaging to detect myocardial oedema (oedema ratio >1.9 , regional increase in T2 signal intensity), and late gadolinium enhancement (LGE) imaging to detect myocardial necrosis or fibrosis. LGE alone is highly specific but not sensitive for diagnosis. The positive findings of 2 or 3 imaging criteria confirm the diagnosis [4]. Using a combination of all 3 parameters increased the diagnostic accuracy up to 85% [5]. A recent large study of 165 patients with viral myocarditis showed that acute myocarditis can be independently identified by native T1 of >5 standard deviation higher than the mean of the normal range, whereas convalescence is best defined by either abnormal native T1 (>2 standard deviation) or presence of late gadolinium enhancement [4]. Because of its relative safety, we think MRI should be systematically performed in patients with suspected myocarditis (Figure) [2]. When MRI is difficult to perform at the acute phase of the disease, it can be performed during recovery since findings persist for several weeks [4]. Another potential interest of MRI is its prognostic value as the presence of late gadolinium enhancement has been reported to be an independent predictor of cardiac mortality [6]. Finally, MRI could be useful by guiding EMB [2].

Treatment

Aside from supportive treatment of heart failure and arrhythmia, no specific medical therapy is available in acute myocarditis. The use of antiviral treatment for viral myocarditis cannot be recommended. In the acute phase of the disease, the virus is rapidly cleared and except in specific situations (oseltamivir for influenza for example), antiviral treatment is ineffective in

acute myocarditis [7]. Immunosuppressive drugs have been tested, but with disappointing results. A recent meta-analysis showed that intravenous immunoglobulin is not useful for presumed viral myocarditis [8]. Steroids may worsen prognosis in patients with viral myocarditis, whereas they are the cornerstone of the treatment in patients with autoimmune diseases-associated myocarditis. Recently, cases of successful treatment with various regimens of immunosuppressive drugs in patients with giant-cell myocarditis have been reported, reinforcing the need for EMB [9]. Despite these negative results, research on treatment continues. A randomized, placebo controlled trial of 85 patients showed significant improvement in patients treated with immunosuppressives if EMB showed active inflammation but no evidence for persistent viral infection [10].

Supportive therapy is the mainstay of acute myocarditis treatment. Most recent advance in the management of fulminant myocarditis is the use of circulatory support in patients with refractory cardiogenic shock, ECMO being the preferred first-line method [11-13]. No consensus exists on the optimal timing and criteria for providing circulatory support in patients with fulminant myocarditis. However, persistence or appearance of signs of low cardiac output despite maximal medical treatment should trigger a discussion for ECMO support: clinicians should be aware that abdominal pain, nausea, vomiting, worsening lactic acidosis, hepatic cytolysis or acute renal failure are signs of poor hemodynamic status and low cardiac output that may progress rapidly to death. Echocardiography can offer a noninvasive hemodynamic assessment. Finding of a low cardiac output (aortic VTI below 8-10 cm/s) should alert the clinician for a potential need of circulatory support. The use of ECMO has been associated with good outcomes in patients with fulminant myocarditis, with a 60-85% survival to hospital discharge [11, 12, 14]. Moreover, long-term quality of life of patients having being supported by ECMO for fulminant myocarditis seems to be favorable [11]. Other devices either seem to be less effective when used alone (the Impella device is mostly

used in combination with ECMO in this setting) [13], or are not superior to ECMO and are more invasive [15].

In conclusion, diagnosis of myocarditis is based on clinical findings, EMB histology and immunologic testing, and cardiac MRI, the latter showing increasing utility in the diagnostic workup. The main advance in management is the use of circulatory support in the most severe cases, which is associated with good outcome.

Figure: Diagnostic workup in patients with acute myocarditis. EMB, endomyocardial biopsy.

* refers to patients in whom a diagnosis can be made without endomyocardial biopsy.

Conflict of interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

1. Cooper, L.T., K.L. Baughman, A.M. Feldman, A. Frustaci, M. Jessup, U. Kuhl, et al., The role of endomyocardial biopsy in the management of cardiovascular disease: a scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. *Circulation*, 2007. **116**: 2216-33.
2. Caforio, A.L., S. Pankuweit, E. Arbustini, C. Basso, J. Gimeno-Blanes, S.B. Felix, et al., Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J*, 2013. **34**: 2636-48, 2648a-2648d.
3. Kindermann, I., C. Barth, F. Mahfoud, C. Ukena, M. Lenski, A. Yilmaz, et al., Update on myocarditis. *J Am Coll Cardiol*, 2012. **59**: 779-92.
4. Hinojar, R., L. Foote, E. Arroyo Ucar, T. Jackson, A. Jabbour, C.Y. Yu, et al., Native T1 in discrimination of acute and convalescent stages in patients with clinical diagnosis of myocarditis: a proposed diagnostic algorithm using CMR. *JACC Cardiovasc Imaging*, 2015. **8**: 37-46.
5. Yilmaz, A., V. Ferreira, K. Klingel, R. Kandolf, S. Neubauer, and U. Sechtem, Role of cardiovascular magnetic resonance imaging (CMR) in the diagnosis of acute and chronic myocarditis. *Heart Fail Rev*, 2013. **18**: 747-60.
6. Grun, S., J. Schumm, S. Greulich, A. Wagner, S. Schneider, O. Bruder, et al., Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. *J Am Coll Cardiol*, 2012. **59**: 1604-15.
7. Kuhl, U. and H.P. Schultheiss, Viral myocarditis. *Swiss Med Wkly*, 2014. **144**: w14010.

8. Robinson, J., L. Hartling, B. Vandermeer, and T.P. Klassen, Intravenous immunoglobulin for presumed viral myocarditis in children and adults. *Cochrane Database Syst Rev*, 2015. **5**: CD004370.
9. Suarez-Barrientos, A., J. Wong, A. Bell, H. Lyster, G. Karagiannis, and N.R. Banner, Usefulness of Rabbit Anti-thymocyte Globulin in Patients With Giant Cell Myocarditis. *Am J Cardiol*, 2015. **116**: 447-51.
10. Frustaci, A., M.A. Russo, and C. Chimenti, Randomized study on the efficacy of immunosuppressive therapy in patients with virus-negative inflammatory cardiomyopathy: the TIMIC study. *Eur Heart J*, 2009. **30**: 1995-2002.
11. Mirabel, M., C.E. Luyt, P. Leprince, J.L. Trouillet, P. Leger, A. Pavie, et al., Outcomes, long-term quality of life, and psychologic assessment of fulminant myocarditis patients rescued by mechanical circulatory support. *Crit Care Med*, 2011. **39**: 1029-35.
12. Diddle, J.W., M.C. Almodovar, S.K. Rajagopal, P.T. Rycus, and R.R. Thiagarajan, Extracorporeal membrane oxygenation for the support of adults with acute myocarditis. *Crit Care Med*, 2015. **43**: 1016-25.
13. Abrams, D., A. Combes, and D. Brodie, What's new in extracorporeal membrane oxygenation for cardiac failure and cardiac arrest in adults? *Intensive Care Med*, **2014**. **40**: 609-12.
14. Combes, A., P. Leprince, C.E. Luyt, N. Bonnet, J.L. Trouillet, P. Leger, et al., Outcomes and long-term quality-of-life of patients supported by extracorporeal membrane oxygenation for refractory cardiogenic shock. *Crit Care Med*, 2008. **36**: 1404-11.
15. Pages, O.N., S. Aubert, A. Combes, C.E. Luyt, A. Pavie, P. Leger, et al., Paracorporeal pulsatile biventricular assist device versus extracorporeal membrane oxygenation-extracorporeal life support in adult fulminant myocarditis. *J Thorac Cardiovasc Surg*, 2009. **137**: 194-7.