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Case report

Giant-cell myocarditis – A case report and a brief review

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ABSTRACT

Giant-cell myocarditis is an extremely rare disease with high morbidity and mortality. In the majority of cases, the course of the disease is in the form of fulminant myocarditis. The cornerstone of the treatment is aggressive immunosuppresive therapy in addition to heart failure treatment, however the need for mechanical circulatory support or heart transplant is high. In our case report, we present a patient suffering from giant cell myocarditis, who, despite rapid diagnosis and prompt aggressive treatment, died shortly after heart transplant.

Introduction and brief review

Giant-cell myocarditis (GCM) is a rare form of myocarditis first described by Saltykow in 1905 [1]. Due to its rarity there is no relevant data in terms of the prevalence of the disease, while autopsy studies report the incidence of approximately 0.007–0.053% of autopsied [2]. The disease is neither age nor sex specific with the average age of first manifestation within the 4th decade of life.

The exact aetiology of the disease is unknown, but it has been hypothesized to be autoimmune in origin with probably very variable trigger. Indeed, it has been suggested to be linked to other autoimmune diseases such as idiopathic bowel disease [3], however the variety of linked immunopathologies is very wide and not organ specific. Interestingly, similar histological findings to GCM can be experimentally induced by myosin immunization in Lewis rats [4], again supporting its autoimmune origin. It has also been suggested in experimental animal studies as well as in clinical practice, that the

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development of the disease is more dependent on cellular rather than antibody-mediated immunity [5,6]. Nevertheless, immunological abnormalities are not the only contributor to the pathogenesis of the disease since a well documented vascular component is present [7]. Finally, a defect of desmosomes of intercalated discs has been described in both GCM and arrhythmogenic cardiomyopathy [8].

The clinical presentation of patients suffering from GCM is rather non-specific. However, very rapid progression of heart failure is common, hence the resemblance with fulminant myocarditis with average time from diagnosis to death or heart transplant being 3 months in patients without treatment. Although not specific, conduction system disturbances are more common compared to lymphocytic myocarditis [9].

Currently, there is no specific non-invasive imaging modality to confirm the diagnosis of GCM. Echocardiography mostly shows diffuse hypokinesis with impaired systolic function not corresponding to coronary territories, while left ventricular dilation is uncommon [10]. Magnetic resonance imaging (MRI), which has become a standard imaging modality for myocarditis, typically shows multiple "patchy" lesions of late gadolinium enhancement (LGE) dispersed throughout myocardial wall without any predilection to myocardial layer and again not corresponding to cardiac vessels anatomy [11]. This pattern may, however, be found in cardiac sarcoidosis as well as in other diseases.

Myocardial autoantibodies are often found in GCM, but their significance still remains dubious since they are also often present in patients suffering from lymphocytic myocarditis and even in healthy controls [12].

The definite diagnosis of GCM can only be established with histological findings of myocarditis with giant multinucleated cells of Langhans type together with the absence of well developed granulomas. The sensitivity of endomyocardial biopsy (EMB) for GCM is somewhat higher than for lymphocytic myocarditis probably owing to the autoimmune nature of the disease with only 15% of specimens being false negative [13].

Considering therapy, the rarity of the disease does not allow to establish an optimal treatment protocol, however, certain assumptions can be made regarding published data. The cornerstone of the pharmacological therapy consists of the combination of immunosuppressive agents targeted on cellular immune response including cyclosporine A or sirolimus in case of proven cyclosporine toxicity [14]. Indeed, it has been shown that corticosteroid therapy alone carries no survival benefit [3]. Despite that, progression of the disease with a need of heart transplant can be anticipated in more than a third of patients during the first year of therapy and, above that, there is a risk of life threatening arrhythmias with the cumulative incidence of sustained ventricular tachycardias/ventricular fibrillation or sudden cardiac death reaching as high as 69% in published case series [15]. Therefore, unlike in lymphocytic myocarditis, implantation of cardioverter/defibrillator (ICD) is common in GCM. Mechanical circulation support as a bridge-to-transplant and subsequent heart transplant is a well established treatment of end-stage heart failure. There has been reported no difference in 3 years mortality in GCM compared to non-GCM patients following heart transplant [3], therefore GCM patients should not be excluded from heart transplant based solely on the risk of disease recurrence in graft [16].

Case report

A 48-year-old Caucasian male sought medical help for progressive shortness of breath and syncopy. During admission, his physical examination was unremarkable except for basal crackles and mild bradycardia with approximately 50 beats per minute. His ECG showed third degree AV block with wide QRS (193 ms) left bundle branch block-like escape rhythm (Fig. 1). His complementary studies showed markedly elevated troponin I, mildly elevated C-reactive protein and interstitial lung oedema Meszarosz IIC on chest X-ray. Bedside transthoracic echocardiography showed hypokinesis of the basis of interventricular septum and akinesis of inferior wall without any dilation of cardiac chambers. Coronary angiography was performed, which ruled out significant coronary artery disease and was administered loop diuretics with rapid improvement of symptoms.

Since the diagnosis of myocarditis seemed likely, we conducted MRI as well as EMB. Magnetic resonance imaging study showed transmural late enhancement in multiple locations (Fig. 2) as well as oedema mostly in septal region (Fig. 3) – in accordance with 2D longitudinal strain echocardiograms (Fig. 4). Endomyocardial biopsy samples were taken from right ventricular septum, apex, basis and outflow tract with marked lymphocytic infiltrate with multiple multinucleated CD68 positive giant cells visible on the sample from right ventricular basis, which confirmed the diagnosis of GCM (Fig. 5). Thereafter, combined immunosuppresive therapy with corticosteroids and cyclosporine was administered which lead to lower need of diuretic therapy and regression of AV conduction abnormality to first degree AV block. Nevertheless, on the fourth day, the patient developed sustained ventricular tachycardia with urgent need of electrical cardioversion (Fig. 6) and soon after progressed to complete AV block, therefore we decided to implant implantable biventricular cardioverter/defibrillator (BiV-ICD). Following a period of mild improvement, the patient deteriorated approximately after 2 months and was readmitted for severe shortness of breath and severe left ventricular dysfunction. The BiV-ICD interrogation revealed multiple long runs of ventricular tachycardias treated with antitachycardia pacing. Redo EMB confirmed the presence of GCM. Despite the addition of mycophenolate mofetil the patient's status was rapidly worsening in terms of the low cardiac output state including progression in renal failure, therefore, the patient was put on extracorporeal membrane oxygenation (ECMO) as a bridge to transplant and was listed for urgent transplantation. Nevertheless, the pretransplant period was complicated with sepsis, consumption coagulopathy and haemolysis and despite the transplant was performed on 15th day on ECMO, termination of cardiopulmonary bypass was difficult and, following several hours of brief stabilization, irreversible circulatory collapse occurred and the patient expired on the transplant day.

Discussion

In our case we illustrate a sinister course and serious prognosis of GCM despite rapid diagnosis and prompt treatment. Our patient presented with non-specific signs and symptoms of

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