Autoimmunity Reviews xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Cardiac involvement in polymyositis and dermatomyositis

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ARTICLE INFO

Article history:
Received 12 January 2016
Accepted 22 January 2016
Available online xxxx

Keywords:
Polymyositis
Dermatomyositis
Cardiac involvement
Echocardiography
Cardiac magnetic resonance

Contents

1. Introduction

Idiopathic inflammatory myopathies (IIM) constitute a group of skeletal muscle diseases characterized by symmetrical, proximal muscle weakness, with a histopathological correlate of inflammatory infiltrates. They comprise, according to distinct clinic–pathologic features, different subtypes: dermatomyositis (DM), polymyositis (PM), necrotizing autoimmune myositis (NAM), cancer-associated myositis, and sporadic inclusion body myositis [1]. New histopathological and clinical entities are emerging, such as overlap myositis, characterized by the occurrence of two or more autoimmune diseases in the same patient [1].

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http://dx.doi.org/10.1016/j.autrev.2016.01.015
1568-9972/

In all cases, the pathogenesis of the disease reflects an immune dysregulation; thus, IIM can be considered as a matter of fact autoimmune disorders. Autoantibodies in myositis are distinguished according to myositis-specific antibodies (MSA) or myositis-associated antibodies (MAA) and can help physicians in better defining myositis subtypes, prognosis, and therapy responsiveness. Recent knowledge of immunogenetics and autoantibodies defines more homogeneous subsets in both PM and DM [2,3]. Among the MAA, the cortactin is a new target antigen, mainly documented in PM and NAM [4]. A possible correlation between MSA such as -anti-TIF1γ and anti-NXP2, anti-SAE and anti-MDA5 and disease manifestations was described [5]. The autoimmune response can be triggered by several factors, such as infection and drugs in NAM and eosinophilic myositis [6] and vaccine adjuvants in macrophagic myofascitis [7].

Extramuscular features in IIM are common, and include cutaneous manifestations in DM, interstitial lung disease, and involvement of heart, articular, and vascular system thus emphasizing the systemic nature of such diseases. This review is focused upon cardiac involvement in IIM, with particular interest in the two main subtypes of myositis: DM and PM.

2. Epidemiology

Even though heart involvement in PM and DM was firstly reported in the late nineteenth century, it was considered to be rare in IIM. Most papers were published between 1980 and 1998 and were mainly devoted on histopathological aspects. More recently, other papers have appeared between 2000 and 2015 with new data [2,8]. According to the current literature, cardiac involvement in patients with myositis varies between 6% and 75%, and this depends on patients selection modalities, definition of heart involvement, and methods used to detect cardiac abnormalities [9,10].

Generally, echocardiographic and/or electrocardiogram alterations are present in 15%–20% of patients in the absence of other possible causes of heart disease (e.g., coronary artery disease, history of myocardial infarction or congenital heart disease, and arterial hypertension) [11].

3. Pathophysiology

Histopathologically, each kind of myositis has its own characteristic features. DM is a microangiopathy with capillary damage and secondary ischemic alterations in muscle fibers, whereas PM has cellular infiltrates at predominant endomysial localization with MHC Class I positive muscle fibers invaded by CD8 + lymphocytes [3]. As the myocardium represents a modified skeletal muscle, it is assumed that immune-mediated inflammation might occur also in this tissue. This is supported by reports describing mononuclear inflammatory infiltrates localized to the endomysium and to the perivascular areas with degeneration of cardiac myocytes [12,13]. Even the cardiac conducting system could be affected by the same immunologistic process. Histologic samples of cardiac tissue revealed the presence of myocarditis, fibrosis (involving the sino-atrial node and conducting system) with lymphocytic infiltration and contraction band necrosis [12,13]. Vascular alterations in coronary arteries have also been reported, especially in patients with Raynaud's phenomenon, such as vasculitis, intimal proliferation, and medial sclerosis of vessels. Severe atherosclerosis has been described in some cases [14,15].

4 Clinical manifestations

4.1. Subclinical heart involvement

Subclinical cardiac manifestations are reported in about 70% of cases in the literature and comprise biochemical and instrumental alterations [16].

4.1.1. Biomarkers of myocardial damage

The measurement of cardiac troponins I and T (cTnI/cTnT) has dramatically changed the management of acute coronary syndromes, stratifying patients with a potential acute myocardial damage for a prompt revascularization. However, cTnT is also released by regenerating skeletal muscle, as occurs for CK-MB, so these two markers are not specific for cardiac involvement in patients with myositis and they can be misleading [17]. CK-MB was increased in 51% and cTnT in 41% of patients without clinical evidence for myocardial damage [18]. Conversely, cTnI has the highest specificity to detect myocardial involvement and is the most reliable serum marker to detect myocardial damage in myositis [19]. Finally, the dosage of the brain natriuretic peptide (BNP) or the pro-brain natriuretic peptide (pro-BNP) can be useful to assess heart disease in patients with IIM.

4.1.2. Electrocardiography

Electrocardiographic alterations constitute the most frequent findings. They are usually detected in about 30%–80% of patients, which is significantly more frequent compared to general population [15]. ECG and Holter abnormalities observed in PM/DM include: atrial or ventricular premature beats, atrial tachycardia, ventricular tachycardia, atrial fibrillation, atrioventricular conduction block, bundle branch blocks, abnormal Q-waves, as well as nonspecific ST-T wave changes. The most frequent alterations are left anterior hemiblock and right bundle branch block, occurring in 13% and 9% of cases, respectively [15]. Two recent studies reported a longer QRS and QTc intervals compared to controls [20] and a higher prevalence of left ventricle hypertrophy and rhythm and conduction disturbances in patients with PM compared to DM [21]. Rhythm disorders are usually not clinically relevant, however some conditions are potentially severe, and could lead to pacemaker implantation and to fatal arrhythmias [15,22].

4.1.3. Echocardiography

In the current literature, echocardiographic abnormalities are reported in up 14%–62% of the cases [23]. At present, the most important modalities to assess systolic and diastolic myocardial dysfunctions are the ejection fraction calculation and the tissue doppler imaging (TDI) for the systolic function, and the mitral inflow signal for the diastolic function. Left ventricular diastolic dysfunction is the most frequent echocardiographic alteration, and it was described in 12%–42% of patients with an increased frequency in patients with PM or DM compared to health controls, as reported in two recent studies [20,24]. According to this data the presence of diastolic dysfunction correlates with disease duration [20,24]. Conversely, Peter and colleagues reported the development of isolated diastolic impairment, not observed at diagnosis, in early stages of the diseases in 30 patients with PM/DM, in the absence of alterations of the systolic function assessed with TDI [25].

Other echocardiographic abnormalities include mitral valve insufficiency and mitral valve prolapse (7%–23%) [5,12,22,23], left chambers enlargement (8%–12%), left ventricle hypertrophy (8%–15%), septal hypertrophy (8%) [9], segmental or global hypokinetics [28], pericardial disorders (8%–67%) [9,11,21,26], and pulmonary hypertension (63%–75%) [27,29]. An ongoing case–control study on patients with IIM is evaluating the correlation between myositis course and heart involvement assessed by the means of the global longitudinal strain (GLS). Preliminary data show a worse GLS in patients with IIM compared to control[11].

4.1.4. Cardiac magnetic resonance

Cardiac magnetic resonance (CMR) is currently the best technique for diagnosing cardiac fibrosis and is used to detect myocarditis, sarcoidosis, and ischemic myocardial infarction. CMR differentiates between myocardial infarction and inflammatory tissue, because in the last case the subendocardial layer is not affected in enhanced delayed sequences. In a study of Mavrogeni *et al.* [30], 16 patients with PM/DM without cardiac manifestations were studied using CMR to assess the possibility

Please cite this article as: Danieli MG, et al, Cardiac involvement in polymyositis and dermatomyositis, Autoimmun Rev (2016), http://dx.doi.org/10.1016/j.autrev.2016.01.015