Chapter 6

Idiopathic Inflammatory Myopathies: Immunological Aspects

R. Mantegazza1, P. Bernasconi¹, F. Cornelio²

Muscle inflammation is generally termed “myositis” whether the aetiology is known (viral, bacterial or parasitic) or unknown (idiopathic). The inflammatory myopathies are a heterogeneous group of subacute/chronic muscle disorders sharing a common characteristic muscle degeneration mediated by inflammatory mechanisms [1]. This review will be concerned with the main pathogenetic features of the three major inflammatory myopathies: dermatomyositis (DM), polymyositis (PM) and inclusion body myositis (IBM). The latter includes sporadic (s-IBM) and hereditary inclusion body myopathy (h-IBM), which is an a hereditary progressive muscle disease with muscle pathology similar to the s-IBM, but lacking lymphocytic inflammation [2].

PM and DM are considered to be autoimmune diseases on the basis of the following features: muscle damage at the endomysial level by infiltrating T cells in PM and complement-mediated humoral attack against endothelial cells in DM; frequent association with other autoimmune diseases; serum positivity for autoantibodies and positive responses to immunosuppressive treatment [3-7]. Figure 1 provides a simplified representation of the main pathogenetic mechanisms of PM/IBM and DM. With respect to s-IBM, it is still unclear whether the immune response is a primary or a secondary event [8, 9].

Inflammatory Features

The immunological characteristics of muscle cells in the inflammatory myopathies are summarised in Table 1. The main characteristic of polymyositis and s-IBM is a mononuclear cell infiltrate, mainly composed of CD8+ T cells and macrophages, which surrounds and invades single non-necrotic muscle fibres located in the endomysium [10]. The CD8+ T cells are in the activated state since they are HLA-DR+ [10] and LFA-1+ [11] and have a memory phenotype (CD45RO+) [12]. The antigens that initiate and trigger the immune reaction are
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Cell death mediated by cytotoxic enzymes: perforin, granzyme, TIA-1

Perifascicular atrophy induced by complement-mediated microangiopathy

Fig. 1. The possible mechanisms leading to muscle derangement in inflammatory myopathies are illustrated. Left-hand side of picture refers to PM/IBM degeneration as showed in hematoxilin/eosin stained muscle biopsy. Muscle damage is mainly due to the action of CD8+ T lymphocytes via release of cytotoxic mediators. Right-hand side of picture refers to DM degeneration as showed in NADH-stained muscle biopsy. Perifascicular atrophy may result from the action of immunoglobulins (IgM and IgG) fixing complement secreted by B lymphocytes. The trigger, still unknown, induce activation and recruitment of specific T helper lymphocytes into muscle tissue. NK cell, natural killer cell

MHC Class I and Class II and Co-stimulatory Molecule Expression on Muscle

Major histocompatibility complex (MHC) class I and class II molecules are involved in antigen presentation to immune-competent T cells. MHC class I molecules are constitutively expressed on most cell types but are low or absent on normal muscle fibres, while MHC class II are expressed only on professional antigen-presenting cells (APC) or other cell types after adequate stimulation [16]. In the inflammatory myopathies, MHC class I and II may be variably expressed (Tables 1, 2).