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Review

Eosinophilic myositis: An updated review ☆

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ABSTRACT

Eosinophilia-associated myopathies are clinically and pathologically heterogeneous conditions characterized by the presence of peripheral and/or muscle eosinophilia. There are at least three distinct subtypes: focal eosinophilic myositis, eosinophilic polymyositis, and eosinophilic perimyositis. Infiltrating eosinophils are not always identified in conventional muscle histologic examination, but the eosinophil major basic protein, whose extracellular diffusion is considered a hallmark of eosinophilic cytotoxicity, is usually detected by immunostaining in muscle biopsy. Whereas focal eosinophilic myositis seems to be a benign and isolated condition, and perimyositis is usually related with the inflammatory infiltrate due to fasciitis, eosinophilic polymyositis can be associated with muscular dystrophy or be a feature of multiorgan hypereosinophilic syndrome. Muscle biopsy remains the cornerstone for the diagnosis. Parasitic infections, connective tissue disorders, hematologic and non-hematologic malignancies, drugs, and toxic substances are the main etiologic agents of eosinophilia-associated myopathy. However, in some cases, no known etiologic factor is identified, and these are considered idiopathic. Glucocorticoids are the mainstay therapy in idiopathic forms. Imatinib and mepolizumab, a humanized anti-interleukin 5 monoclonal antibody, may be useful in patients with eosinophilic myositis as part of a hypereosinophilic syndrome.

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1. Introduction

Eosinophilia-associated myopathies (EAM) comprise a clinically and pathologically heterogeneous group of rare diseases that include three main subtypes: focal eosinophilic myositis, eosinophilic polymyositis, and eosinophilic perimyositis [1–4]. All of them are characterized by high peripheral blood eosinophil counts and/or eosinophilic muscle infiltration detected by means of eosinophil major basic protein antibody staining. No epidemiologic studies on this condition are available to date.

2. Diagnosis, clinical manifestations, and classification of eosinophilia-associated myopathy subsets

2.1. Focal eosinophilic myositis

As its name indicates, focal eosinophilic myositis is the most limited form of eosinophilic myositis and is considered a benign disease [5]. Although patients may present with proximal weakness, muscle

Abbreviations: EMG, Electromyography; EAM, Eosinophilic-associated myopathies; HES, Hypereosinophilic syndrome; LGMD, Limb girdle muscular dystrophy; MRI, Magnetic resonance imaging; MBP, Major basic protein.

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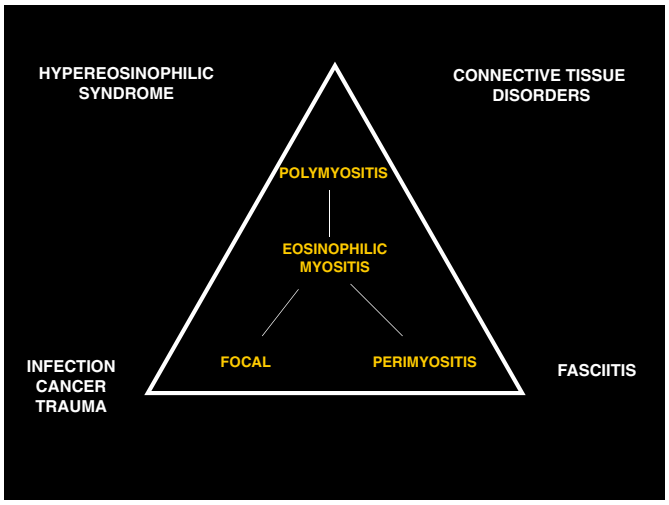

Fig. 1. Eosinophilia-associated myopathy subtypes and their relationships. (Adapted from Hall et al. [1]).

involvement is usually focal and circumscribed to the lower legs. Patients are well otherwise, with no organ involvement or systemic manifestations. Lower limb pain, soft-tissue tenderness, and calf swelling are characteristic features of this condition. This typical clinical presentation can mimic deep vein thrombosis of lower legs or a localized nodular pseudotumor [6,7]. Ultrasonography and sometimes MRI are needed to establish the diagnosis in these cases. Evidence of peripheral blood eosinophilia ($>0.5 \times 10^9$ eosinophils/l, or >5%) is a typical finding in this disease. Muscle pathology features include perimysial and endomysial mononuclear cell infiltration with or without eosinophils, and muscle fiber necrosis and regeneration. Symptoms usually resolve spontaneously, but relapses can occur even some years after the initial episode. In some cases, glucocorticoid administration or non-steroidal anti-inflammatory agents lead to resolution of the symptoms and laboratory abnormalities.

2.2. Eosinophilic polymyositis

Eosinophilic myositis is recognized as a specific entity within the spectrum of myopathies [1–3]. The clinical presentation can be indistinguishable from that of idiopathic polymyositis, and consequently, eosinophilic myositis remains a diagnosis of exclusion. Proximal weakness with involvement of the neck flexors and usually an absence of skin manifestations are characteristic of this disease. Creatine kinase and aldolase levels are generally high (>10-fold normal). Systemic organ involvement is not rare, with the lung, gut, and particularly the heart being the most frequently affected organs [4]. In such cases, the possibility that a idiopathic hypereosinophilic syndrome (HES) affects the patient has to be taken into account [4,8]. Myonecrosis and a deep inflammatory infiltrate of eosinophils, sometimes massive and mainly affecting the endomysium, are the pathologic hallmarks of eosinophilic polymyositis. Although most patients reported to date seem to respond in varying degrees to glucocorticoids, the prognosis of some cases is poor, and the condition can even lead to death (Fig. 1).

Eosinophilic polymyositis has a broad differential diagnosis and it is of paramount importance to rule out infectious diseases, since administration of glucocorticoids or immunosuppressive drugs to patients with an infectious process could result in a dramatically bad outcome [9]. Another patient group with features resembling eosinophilic myositis are the systemic autoimmune disorders, including various types of vasculitis such as polyarteritis nodosa or eosinophilic granulomatosis with polyangiitis (formerly Churg–Straus syndrome), and even some cases of idiopathic inflammatory myopathy in its polymyositis or dermatomyositis forms [10,11]. Histopathological assessment is the best way to achieve the correct diagnosis in these cases.

A third group of muscle diseases has recently been associated with eosinophilia: the muscular dystrophies [12–17]. Calpainopathy, caused by mutations of the gene encoding calpain-3 (*CAPN3*), the most prevalent form of autosomal-recessive limb girdle muscular dystrophy (LGMD2A), and γ-sarcoglycanopathy, caused by γ-sarcoglycan mutations (LGMD2C), are reported to be genetic causes of idiopathic eosinophilic myositis. This suggests that eosinophilia, perhaps in relation to T-cell lymphocytes and macrophages, which are usually found near injured muscle cells, plays an important role in the muscle damage

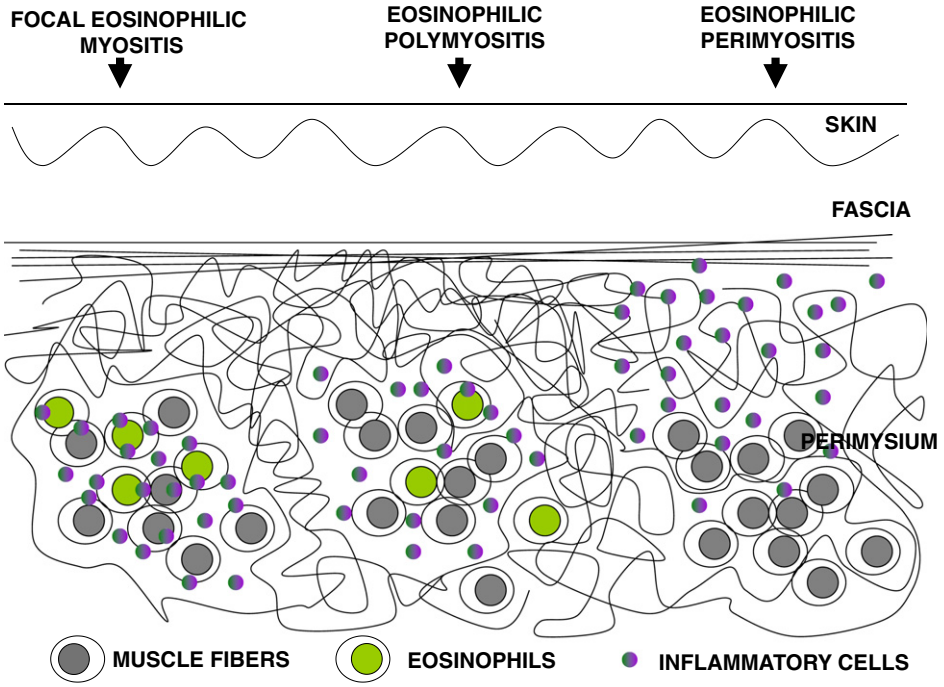

Fig. 2. Differential histologic localization of eosinophilic and mononuclear cell infiltrates in eosinophilia-associated myopathies. (Adapted from Hall et al. [1]).