中文題目：嗜伊紅性筋膜炎：病例報告
英文題目：Eosinophilic Fasciitis: A Case Report
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Introduction:

Eosinophilic fasciitis (EF), first described by Shulman in 1974, presents as scleroderma-like skin changes and is frequently associated with peripheral eosinophilia, hypergammaglobulinemia, and elevated ESR [1]. Most reported cases had cutaneous features, initially presenting as pitting edema involving both upper and lower extremities and then gradually evolved into skin induration or *peau d'orange* pattern [2]. It could be distinguished from scleroderma that eosinophilic fasciitis usually lacks digital and facial skin change, Raynaud's phenomenon, and nailfold capillary abnormalities [3].

For decades, systemic glucocorticoids have remained the first-line therapy, and methotrexate (MTX) has been utilized frequently as a steroid-sparing agent. Recently, biologics targeting different pathways showed favorable outcomes in refractory disease status. Here we demonstrate a female patient in her 20s with EF in its early stages.

Case presentation:

A 24-year-old female sought medical consultation due to progressive swelling and itchiness over bilateral medial thighs, dorsal feet, and hands within two weeks. She denied the presence of Raynaud's phenomenon, digital ulcerations, or skin telangiectasia. On examination, non-pitting edema over her dorsal hands and feet was noted. In addition, neither groove sign nor the appearance of *peau d'orange* was observed over her limbs.

Laboratory examinations revealed hypereosinophilia (absolute eosinophil count [AEC]: 4965/μL) and a high eosinophil cationic protein (ECP) concentration (> 200 μg/L). Renal function, hepatic function, serum albumin, lactate dehydrogenase, creatinine phosphokinase, and thyroid-stimulating hormone were within normal limits. Immunologic tests including antinuclear antibody (ANA), anti-centromere antibody, anti-topoisomerase I antibody, rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (anti-CCP), C3, C4, anti-neutrophil cytoplasmic antibodies (ANCA) and lupus anticoagulant, were all negative.

The MR scan of lower limbs showed the edematous change of deep peripheral fascia affecting bilateral lateral thighs, knees, lower legs, and feet, compatible with fasciitis. Full-thickness skin biopsy over her left dorsal foot disclosed unremarkable epidermis and increased infiltration of eosinophils and lymphocytic cells over subcutis and fascia, compatible with histologic findings reported in eosinophilic fasciitis.

We commenced glucocorticoids with a daily prednisolone equivalent dose of 0.7 mg/kg/day with

MTX as a steroid-sparing agent. We tapered corticosteroids gradually as her symptoms improved, along with regression of her hypereosinophilia. In order to facilitate tapering of oral corticosteroids, we added an anti-interleukin (IL)-5 agent, benralizumab, on the background therapy with steroids and MTX. Despite achieving symptom regression, however, multi-dermatomal herpes zoster (T11-L2) developed after the dose of benralizumab. Therefore, we ceased benralizumab, keeping the regimen of low-dose corticosteroids and MTX, and tapered the dose according to her clinical symptoms, AEC and ECP levels. The follow-up MR scan was arranged eight months after the diagnosis and displayed an interval improvement of preexisting edematous changes. Although her AEC and ECP levels increased slightly after steroid tapering, there is no recurrence of limb edema. Since the patient expressed many concerns about the side effects of corticosteroids and planned pregnancy, we stopped all medications ten months after the diagnosis, with cautious monitoring of symptom progression.

Discussion:

Though the pathogenesis of eosinophilic fasciitis has not been fully elucidated, it may be related to an elevated level of IL-5, which impacts the differentiation, migration, activation, and survival of eosinophils [4]. Traditionally, corticosteroids and methotrexate remain the mainstay of treatment of EF, and the effectiveness of biologics for refractory disease status has been studied. Biologic agents targeting IL-5, IL-6, JAK-STAT signaling pathway and CD-20 have been reported for recalcitrant EF, while there is no consensus on utilizing biologics in early disease yet.

Mortezavi et al. reported a case in her 60s with EF, who was refractory to corticosteroids and MTX, achieving symptomatic improvement with reslizumab, an IL-5 antagonist [5]. Currently, there are three FDA-approved monoclonal antibodies targeting IL-5: reslizumab, mepolizumab, and benralizumab. Reslizumab and mepolizumab are IL-5 antagonists (IgG1 kappa) and can suppress the production and survival of eosinophils by blocking the IL-5 signaling pathway. Benralizumab, targeting IL-5Rα, which was chosen in our case, can also be linked to natural killer cells by its Fc portion, leading to the release of granzymes and perforins, thus facilitating the apoptosis process of eosinophils [6]. A new clinical trial will be initiated to investigate the therapeutic response of mepolizumab on EF (NCT04305678).

Conclusion:

The constellation of the extent of eosinophil activation, histologic findings, and radiographic evidence of fasciitis aids in the diagnosis of EF, which remains an important differential diagnosis with systemic sclerosis. Furthermore, novel treatment has shed light on therapeutic response and clinical outcome; more research is needed to examine the effectiveness of eosinophil-targeted biologics on EF.

References:

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