ASSOCIATION OF EOSINOPHILIC FASCIITIS WITH MORPHEA

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ABSTRACT

Eosinophilic fasciitis is a rare inflammatory disease of unknown etiology, described for the first time by Shulman in 1974. The disease presents with induration of the skin, connective tissue and the underlying muscle fascia, sometimes accompanied by myalgia, most commonly in the lower extremities. Unlike scleroderma, it presents with absence of visceral organ involvement and Raynaud’s phenomenon. Hypergammaglobulinemia and eosinophilia have been reported. Eosinophilic fasciitis is often associated with hematological disorders – there are reports of combinations with other autoimmune diseases such as systemic sclerosis, systemic lupus erythematosus, Hashimoto thyroiditis, Sjogren syndrome, vitiligo, etc. Occurrence of morphea, in the course of eosinophil fasciitis is considered a rarity. We have observed such a case with the simultaneous presence of both types of lesions. A 20-year-old female patient is reported, wherein the clinical picture developed for 6 months. The initial erythematous edema and subsequently the livedo-like painful plaques in both lower legs gradually swell, thicken and hyperpigment. Almost simultaneously with these complaints small brown livid body plaques emerged. The patient was diagnosed based on history, clinical picture, peripheral eosinophilia and histological findings from the affected areas. There was no systemic involvement and accompanying hematologic or other disease. Therapeutic management and significant clinical improvement were achieved using systemic corticosteroid therapy combined with methotrexate.

Keywords: eosinophilic fasciitis, morphea, corticosteroids, methotrexate

CASE REPORT

ASSOCIATION OF EOSINOФILЬНОГО ФАСЦИИТА С MORPHEA

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РЕЗЮМЕ

Эозинофильный фасциит представляет собой редкое воспалительное заболевание неизвестной этиологии, описанное впервые в 1974 г. Shulman-om LE. Заболевание проявляется индурацией кожи, соединительной ткани и подлежащей мышечной фасции. Иногда заболевание сопровождается миалгиями, чаще всего в области нижних конечностей. В отличие от склеродермии отсутствуют поражения внутренних органов и Рейно феномен. Устанавливаются гипергаммаглобулинемия и эозинофилия. Эозинофильный фасциит часто ассоциируют с гематологическими заболеваниями. Описаны и сочетания с другими аутоиммунными заболеваниями как системная склеродермия, системный lupus erythematosus, тиреоидит Hashimoto, синдром Sogren, витилиго и др. Появление morphea в ходе эозинофильного фасциита считается редкостью. Авторы наблюдали подобный случай с наличием одновременно двух типов повреждений. Описывается случай 20-летней пациентки, у которой клиническая картина развивается в течение 6 мес. Начальный отек, а впоследствии и щеноподобность, сопровожденные болевыми бляшками в области двух голеней, постепенно переходят в утолщение, уплотнение и гиперpigментацию. Почти одновременно с этими жалобами появляются и мелкие коричнево-синюшные бляшки по телу. Диагноз поставлен на базе анамнеза, клинической картины, периферической эозинофилии и гистологической находки с пораженных участков. У пациентки отсутствует системное поражение и сопровождающееся гематологическое или другое заболевание. Терапевтическое овладение и значительное клиническое улучшение достигнуты благодаря применению кортикостероидной терапии, сочетанной с мототрексатом.

Ключевые слова: эозинофильный фасциит, склеродермия, morphea, corticosteroids

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INTRODUCTION

Eosinophilic fasciitis is a rare inflammatory disease of unknown etiology, described for the first time in 1974 by Shulman.¹

The etiology and pathogenesis of the disease are unknown. The onset of the disease in most of the patients begins after exertional physical activity, less frequently it is caused by chemical agents or drugs.²,³

It is assumed that next comes tissue injury with antigenic alteration of the dermis, hypodermis, fascia, and muscle. Eosinophils are attracted to affected tissues, which promotes fibrosis. This is accounted for by the inclusion of lymphokines and by complement activation. Elevated levels of interleukin-5 and interferon-gamma have been found.² Fibroblasts from eosinophilic fasciitis affected tissues of patients produce excessive collagen in vitro and display elevated levels of type I TGF-beta and tRNA.²

The hypothesis of autoimmune genesis of eosinophilic fasciitis, despite the fact that immune disorders are rarely found (anti-nuclear autoantibodies, anticytoplasm autoantibodies, increased levels of Ig of different classes) is supported by the frequent association of this condition with other autoimmune disorders.⁴

The clinical picture of eosinophilic fasciitis develops gradually. The disease presents with pain, the initial edema and erythema are later on replaced by skin induration and involvement of the fascia, most commonly in the areas of the lower limbs. The affected skin is tight and hard; it may become orange in colour; residual hyperpigmentation develops as a consequence.¹⁻³ Progressive muscle weakness is often observed. Unlike scleroderma there are no visceral structures affected and Raynaud’s phenomenon.²,³

Hypergammaglobulinemia and eosinophilia are found in 61% - 83% of cases.¹⁻³

Eosinophilic fasciitis affects women more frequently than men. The age range of the disease is from 1-88 years.²,³

Eosinophilic fasciitis is often associated with hematological disorders such as aplastic anemia, thrombocytopenia, myeloproliferative disorders, lymphoma, and leukemia.²,³ Combinations with other autoimmune diseases such as systemic sclerosis, systemic lupus erythematosus, Hashimoto thyroiditis, Sjogren syndrome, vitiligo, etc have been reported.²,³ The condition has been described also as a paraneoplastic syndrome.²

A combination of eosinophilic fasciitis with morphea is considered extremely rare.⁴,⁵

Diagnosis is based on several criteria - deep subcutaneous induration, eosinophilia in blood and bone marrow, elevated ESR and gammaglobulin, histological changes mainly of the fascia, myalgia, arthralgia, absence of visceral involvement and Raynaud syndrome, beginning after unusual physical exertion, response to corticosteroid treatment.²,³,⁶

Eosinophilic fasciitis is usually a benign disease. There may be occasional complications such as limited range of motion, joint contractures (50% - 75%) and carpal tunnel syndrome associated with fascial fibrosis.²,³,⁶

Figure 1. Eosinophilic fasciitis combined with morphea (before treatment).
Early, effective treatment is essential because of the risk of complications. Systemic corticosteroids are the mainstay of therapy. Long courses of treatment with gradual dose reduction and prolonged maintenance therapy are recommended. Immunosuppressants and extracorporeal photopheresis are also considered. D-penicillamine, chloroquine, hydroxychloroquine are taken into account as alternative therapies. UVB and PUVA result in significant improvement.\textsuperscript{3,6}

**CASE REPORT**

**MEDICAL HISTORY**

We report a 20-year-old female patient with a gradually developing clinical picture over 6 months (since June 2012). The initial swelling and livedo-like plaques, accompanied by pain in the area of the two lower legs, were gradually replaced by significant skin thickening and induration. The skin became first orange in colour, then brown hyperpigmentation developed. Hyperpigment patches appeared on the body after 1-2 months (Fig. 1).

**GENERAL STATUS – NORMAL**

The dermatological examination found brownish hyperpigmentation on both lower legs, with a considerable skin thickening. On the truncus we found brownish plaques of irregular shapes, sizes up to 5 cm, slightly thickened. No skin lesions in other places was found.

**TESTS**

*Paraclinical tests* revealed elevated ESR (26 mm) and peripheral eosinophilia (Eo 7.5); creatinine kinase was normal. Other tests were within the norm. Tests for Borrelia burgdorferi - Ig G (-) negative, IgM (-) negative.

*Immunological tests:* Immunoglobulins - normal, ANA + 1 with titre 1:40, anti ds DNA < 25 (-) negative, anti Sm < 25 (-) negative, anti SCL 70 – 0.193 (-) negative, anti-histone – 62.76 (+) positive.

The chest X-ray, abdominal ultrasound scan, capillaroscopy of the nail fold and electromyography found no abnormalities. The consultation with a hematologist associated the eosinophilia with the underlying disease. Lung function tests were normal.

*Histopathological examination of plaque on the right lower leg:* In the hypodermis we found perivascular infiltration of eosinophils and single horizontally oriented homogeneous, thickened collagen with few fibroblasts, confluent with the fascia. The fascia was thickened, homogeneous, with the presence of chronic inflammatory infiltrates with single eosinophils (Fig. 2).

*Histopathological examination of plaque from the chest:* The reticular dermis displayed thickened collagen bundles, mainly moderate lymphocytic infiltrates around vessels and inter-collagen bundles (Fig. 3).

**DIAGNOSIS**

Diagnosis was made based on history - acute onset, rapid development for 6 months, symmetrical involvement of the lower extremities, accompanied by pain, peripheral eosinophilia, absence of systemic involvement and the histological findings.

**THERAPY**

The disease was managed with corticosteroids: methylprednisolone (40 mg i.m. as a starting dose), with gradual tapering down of the dose and the maintenance therapy for 15 months; methotrexate - 15 mg/week for 1 month, 10 mg/week for 1 month, 5 mg/week for 1 month; physiotherapy; tacrolimus (Protopic ing. 0.1%) - b.i.d. for 2 weeks, q.d. for 2 weeks and once a week for a month.

**Figure 2.** Histopathological examination of plaque on the lower leg. HE staining, x200.

**Figure 3.** Histopathological examination of plaque from the chest. HE staining, x100.
**DISEASE COURSE AND FOLLOW UP**

The treatment resulted in a significant clinical improvement: pain was resolved and the plaques softened but the residual pigmentation persisted (Fig. 4). The patient was followed up for 16 months; the follow-up will continue to be done.

**DISCUSSION**

The present case is reported because of the extreme rarity of eosinophilic fasciitis. The combination with morphea makes it even more interesting.

There are a lot of diseases which present clinically with thickened skin that can be confused with systemic scleroderma. Most patients with eosinophilic fasciitis have been initially diagnosed as having scleroderma because of the skin induration and fibrotic changes in the tissues. Scleroderma presents similarly - it begins with erythema and edema and ends with sclerosis. It is a slowly progressing disease, presenting with sclerodactyly, Raynaud’s syndrome and visceral involvement. The histology study and capillaroscopy can differentiate these two diseases.²,³

Eosinophilia-myalgia syndrome occurs with scleroderma-like induration, but lung, heart, gastrointestinal and neurological symptoms are more severe and intense.²,³,⁶-⁸

Muscle weakness in eosinophilia fasciitis can be confused with myalgias and myopathies. The differential diagnosis should also include the hypereosinophilic syndrome.³,⁶-⁸ The clinical manifestations of eosinophilic fasciitis can mimic many other diseases, which might delay the diagnosis of the condition. Accurate diagnosis of this disease is important, given the large differences in its prognosis and treatment compared with scleroderma and other diseases.

Thorough knowledge of the clinical features of eosinophilic fasciitis and early treatment can slow disease progression.⁷,⁸ As combinations of eosinophilic fasciitis with other autoimmune diseases such as systemic scleroderma and systemic lupus erythematosus are possible and because eosinophilic fasciitis is combined here with morphea, the reported patient will receive a long-term follow-up.

The clinical case we report here is of a patient with the rare disease of eosinophilic fasciitis combined with morphea who was successfully treated with corticosteroids and methotrexate.

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