

# Eosinophilic Fasciitis Associated with Overlying Intraepidermal Blister Formation

## - A Case Report -

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Eosinophilic fasciitis is a scleroderma-like disease and it may present with paraneoplastic syndrome or as an isolated form of the disease. We report here on a case of eosinophilic fasciitis in a 20-year-old woman who presented with an abrupt onset of subcutaneous limb swelling and peripheral eosinophilia. Pathologically, the specimen was characterized by acute inflammation and thickening of the collagen bundles in the reticular dermis and superficial muscle fascia in addition to the overlying intraepidermal blisters that contained many eosinophils. Eosinophils, some lymphocytes and plasma cells were infiltrated in the superficial muscle fascia and subcutaneous fat. The diagnosis of eosinophilic fasciitis was confirmed by biopsy. It is intriguing that eosinophilic fasciitis showed the microscopic findings of intraepidermal blister with predominant inflammation, and the patient showed a good response to steroid therapy.

**Key Words** : Eosinophilia; Fasciitis; Panniculitis; Blister

Eosinophilic fasciitis is a scleroderma-like syndrome and this was first described in 1974 by Shulman in patients with diffuse fasciitis and peripheral eosinophilia.<sup>1</sup> It commonly presents as cutaneous swelling, tenderness and stiffness of the extremities and it shows characteristic peau d'orange with hyperpigmentation.<sup>2</sup> The diagnosis of eosinophilic fasciitis may be delayed due to a variety of extracutaneous manifestations or overlapping features of other rheumatologic diseases, and patients with this illness may present with paraneoplastic syndrome.<sup>3</sup> Most cases are idiopathic, and its pathogenesis remains uncertain. Diverse etiologies have been suggested as triggering factors; large amounts of contaminated L-tryptophan, the ingestion of adulterated rapeseed oil and the use of simvastatin.<sup>4</sup> *B. burgdorferi* has also been suggested as one possible cause of eosinophilic fasciitis.<sup>5</sup>

Eosinophilic fasciitis typically presents with a scleroderma-like syndrome, but bullous lesions are rare findings for patients with eosinophilic fasciitis and for patients with scleroderma.<sup>6</sup>

We report here on a case of eosinophilic fasciitis that displayed overlying intraepidermal blister formation and we briefly discuss its differential diagnosis. We also review the relevant med-

ical literature.

## CASE REPORT

A 20-year-old, previously healthy woman presented with a palpable hard mass-like lesion at the right lower leg and she had this lesion for the previous six days. A similar lesion subsequently developed at the contralateral leg. Edema, warmth and red discoloration of both feet were also detected. A complete blood count and comprehensive metabolic profile revealed hypereosinophilia (21,510/ $\mu$ L, 79%) with an increased level of eosinophil cationic protein (200  $\mu$ L/L). She had no habit of eating raw-fish or meat. Anti-nuclear antibody, anti-Smith antigen, anti-MP, anti-double stranded DNA, anti-J0-1, and anti-SCL-70 antibodies were all negative. Elevated serum levels of IgE (845.65 mU/mL) and CRP (2.34 mg/dL) were found. Circulating antibodies of against cysticercus, sparganum, paragonimus, *Borrelia burgdorferi* were not detected. No organism was identified on the blood culture. Three-phase liver CT revealed multiple variable-

sized low density nodules at both lobes of the liver and these were prominent on the portal phase (Fig. 1). Those findings were

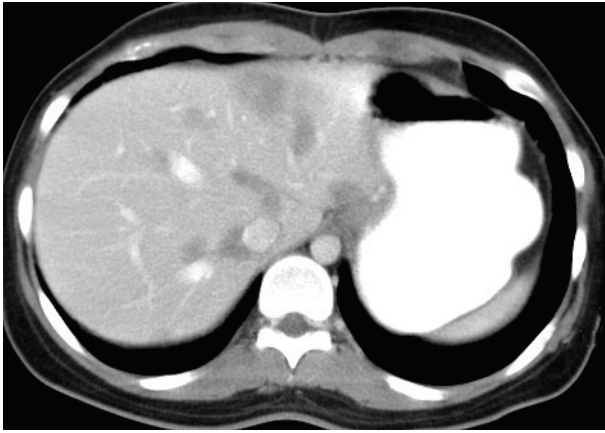


Fig. 1. Three phase liver CT reveals multiple low densities at both lobes that are prominent on the portal phase.

consistent with inflammatory lesion or metastatic nodules. Yet no malignancy was detected on further examination. Two incisional biopsies were taken from the skin of the left ankle, and the fat, fascia and superficial muscle of the gastrocnemius. The second biopsy which was composed of subcutaneous fat and muscle was taken 3 days after the first one because the first biopsy did not contain include muscle. Pathologically, the specimen was characterized by a massive infiltration of many eosinophils and some lymphocytes and plasma cells at the subcutaneous fat and muscular fascia (Fig. 2). Deep dermal fibrosis and sclerosis were found (Fig. 3A). The overlying epidermis showed intraepidermal blisters that contained many eosinophils on the first biopsy (Fig. 3B). We made the diagnosis of idiopathic eosinophilic fasciitis. Eosinophilic liver abscess was also likely based on the clinical and radiologic findings. Biopsy was not taken from the hepatic lesion because of the patient's refusal. The cutaneous lesions improved and the size of the hepatic lesion diminished

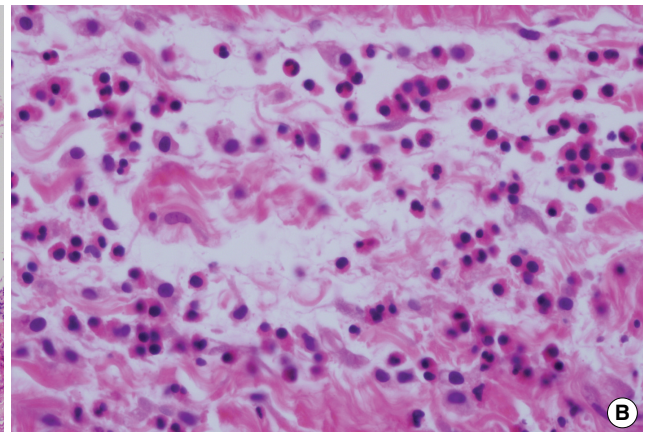
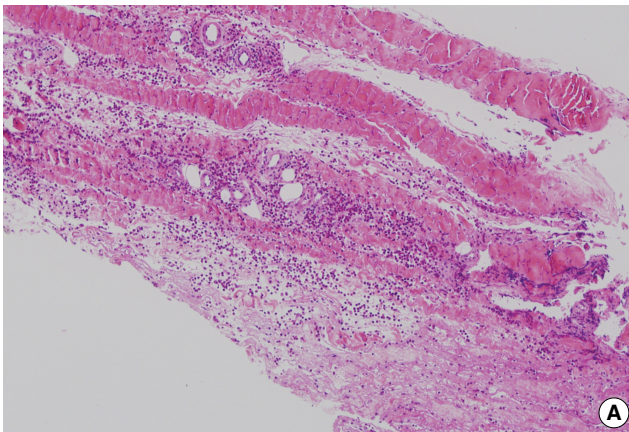


Fig. 2. (A) Infiltration of inflammatory cells is found in the fascia and adipose tissue. (B) Massive infiltration of inflammatory cells is composed of mainly eosinophils and some lymphoplasmic cells.

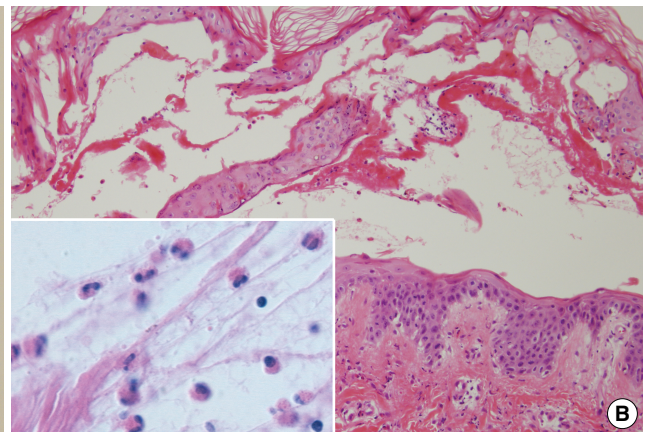
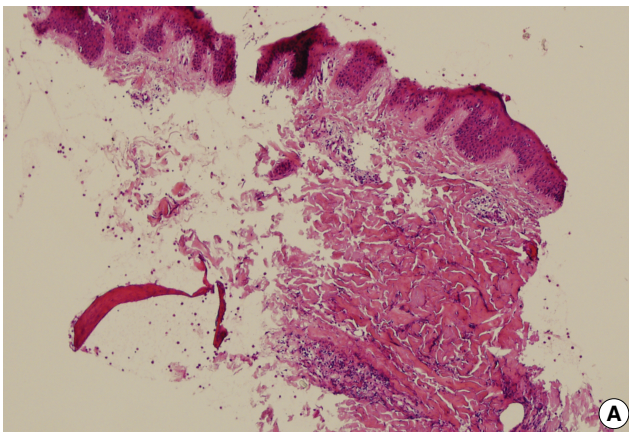


Fig. 3. (A) Marked collagen lay-down is found at the reticular dermis beneath the epidermal blister. (B) Epidermal suprabasal blisters contain many floating eosinophils (inset).

after systemic steroid therapy (oral prednisolone 20 mg/day for 21 days). The percentage of eosinophils dropped to normal. After 50 months of follow-up, further follow up biopsy was not done because the patient was lost to follow up.

## DISCUSSION

Eosinophilic fasciitis is a rare fibrosing disorder that primarily affects the limbs. Erythema and edematous swelling of the limbs or trunk is characteristic in its early phase, and collagenous thickening of the dermis and subcutaneous fascia appears later. Shulman first described this illness as a new clinical syndrome of diffuse fasciitis with hypergammaglobulinemia and eosinophilia, and it was later termed as eosinophilic fasciitis.<sup>1-3</sup> The clinical spectrum has broadened since its first description, which makes its clinical definition challenging. In the revised classification system of morphea (localized scleroderma) proposed by Peterson *et al.*,<sup>7</sup> eosinophilic fasciitis belongs to a subtype of deep morphea. The fascia is the predominant level of involvement. It is characterized by the acute or subacute development of induration of the skin and subcutaneous tissues of the forearms, flank, and upper legs. The hands and face are usually spared. Hypereosinophilia is not necessary to make the diagnosis of eosinophilic fasciitis and it does not correlate with the clinical severity of the disease.<sup>2</sup> Although it clinically resembles morphea, eosinophilic fasciitis bears many unique features and it is now considered by many authors to be a separate disease.<sup>3</sup>

The most important diseases to differentiate when making the diagnoses of eosinophilic fasciitis include polymyositis and systemic sclerosis.<sup>8</sup> The absence of Raynaud's phenomenon and sclerodactyly are useful distinguishing features for scleroderma. Eosinophilic fasciitis arising in pediatric patients rarely mimics a myopathy because eosinophilic fasciitis can display painless joint contractures and muscle weakness with the absence of skin changes.<sup>9</sup> In such circumstances, eosinophilic fasciitis should be included as a differential diagnosis of painless joint contractures in children. The differences of eosinophilic fasciitis from scleroderma are that eosinophilic fasciitis affects, in a primary way, the fascia and the subcutaneous fat tissue instead of the dermis, and it responds to corticoids. Systemic sclerosis usually involves the skin, and polymyositis involves the muscles. According to the recent radiologic literature, delineation of predominant fascial involvement on the magnetic resonance images is a clue to correctly diagnose eosinophilic fasciitis.<sup>10</sup> Yet, the final diagnosis can be made by biopsy. Skin biopsy of eosinophilic fasciitis usually

shows a primary fascial infiltration with lymphocytes, plasma cells, mast cells and eosinophils through eosinophilic-triggered fibroblast activation that is mediated by transforming growth factor B. As the disease process continues, the fascia becomes fibrotic and excessive collagen fibers replace the subcutaneous tissue.<sup>11,12</sup> Patients with early isolated skin involvement may present to a dermatology practice with a suspected rash, and this limits the cases seen in rheumatology clinics to those patients who have extensive skin disease that mimics scleroderma. The common dermatologic manifestations of eosinophilic fasciitis are as followings; 1) hypopigmented plaques that exhibit wrinkling, scaling, and follicular plugging, 2) epidermal atrophy; a subepidermal zone of pale-staining, homogenized collagen and a band-like lymphocytic infiltrate, and especially in a patient with chronic cutaneous graft-versus-host disease or tryptophan ingestion.<sup>4,13,14</sup> Unlike in hypereosinophilic syndrome or eosinophilic cellulitis (Wells syndrome), cutaneous bullae seen in the present case are extremely rare in eosinophilic fasciitis.<sup>6</sup> Therefore, the present case should be differentiated from hypereosinophilic syndrome and Wells syndrome. Wells syndrome is a recurrent granulomatous dermatitis with eosinophilia and the cutaneous manifestations of plaque or bullae. It shows the characteristic histologic features of edema, flame figures, and marked inflammatory infiltrates that are almost always restricted to the epidermis and dermis. Hypereosinophilic syndrome is a disease process that is characterized by a persistently elevated eosinophil count ( $\geq 1,500$  eosinophils/mm<sup>3</sup>) in the blood for at least six months without any recognizable cause after a careful workup, with evidence of systemic involvement of either the heart, nervous system, or bone marrow, and so on. Various imaging tools are utilized to detect organ involvement, while eosinophilic fasciitis does not generally involve the internal organs. However, eosinophilic fasciitis may, on rare occasion, be accompanied with peripheral polyneuropathy.<sup>15</sup> Primary biliary cirrhosis and focal hepatitis have been reported as rare hepatic lesions that accompany eosinophilic fasciitis.<sup>16,17</sup> The coexistence of focal eosinophilic liver abscess and eosinophilic fasciitis has not been previously described in the literature. Focal eosinophilic liver abscess is relatively common and this is associated with parasitic infestations, allergic conditions, drug hypersensitivity, internal malignancies, hypereosinophilic syndrome, and so on.<sup>18</sup> All these lesions appear as multiple, oval or round, ill-defined low attenuation densities on the portal phase of dynamic CT with indistinct margins.<sup>19</sup> Multiple eosinophilic liver abscesses were highly suspected in the present case, but unfortunately, this was not pathologically confirmed.

The clinical course of eosinophilic fasciitis varies. The duration of symptoms is known to be a few months to several years, but a complete remission within a week has been rarely reported.<sup>20</sup> Treatment with immunosuppressant may lead to an excellent response with complete remission regardless of the underlying cause, and even in a patient with paraneoplastic syndrome.<sup>2</sup> High dose corticosteroid treatment lasting longer than a month with or without an immunosuppressive agent is helpful, and systemic corticosteroid is the mainstay of therapy with a better response being seen in those patients who present early and who potentially have more inflammatory rather than fibrotic skin lesion, like the present case.

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