Eosinophilic Fasciitis

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Practice Essentials

Eosinophilic fasciitis (EF), also called Shulman syndrome, is a rare, localized fibrosing disorder of the fascia. [1] The etiology and pathophysiology are unclear.

In 1974, Shulman provided an early description of eosinophilic fasciitis as a disorder characterized by peripheral eosinophilia and fasciitis that could be differentiated from scleroderma by the distinctive pattern of skin involvement that spares the digits, involves fascia rather than dermis, and is not accompanied by Raynaud phenomenon. [2, 3, 4]

Since 1974, over 300 patients with eosinophilic fasciitis have been reported. [5, 6] Despite this, the current understanding of the disease relies on a relatively few large case series and multiple case reports. Therefore, the understanding of key aspects of the disease continues to evolve.

The etiology of eosinophilic fasciitis remains unknown, although many possible triggers and disease associations have been suggested. Some aspects of pathophysiology have been elucidated; however, a more complete understanding has yet to develop.

The available literature has generated a broader clinical image of the condition, but fascial thickening in the setting of eosinophilia, elevated erythrocyte sedimentation rate, and hypergammaglobulinemia remain critical elements of the syndrome. Visceral involvement in eosinophilic fasciitis is generally absent, a finding that helps differentiate eosinophilic fasciitis from systemic sclerosis and other differential considerations. However, an association with several hematologic diseases is recognized and frequently carries a grave prognosis.

The diagnosis of eosinophilic fasciitis is suspected in a patient presenting with characteristic skin changes and consistent laboratory findings. It is confirmed with full-thickness biopsy or characteristic MRI findings. See Presentation and Workup.

Eosinophilic fasciitis is generally corticosteroid-responsive, and initial treatment regimens are based on this therapy. Multiple additional agents have been used in steroid-refractory disease. The evidence for many of these agents is anecdotal, and there is no general consensus regarding the best agent for treatment of steroid-resistant disease or cases refractory to steroid withdrawal. See Treatment and Medication.

See also Dermatologic Manifestations of Eosinophilic Fasciitis.

Pathophysiology

Although the etiology of eosinophilic fasciitis is unknown, studies have shed light on some of the mechanisms involved in its pathogenesis.

In general, the pathophysiology underlying eosinophilic fasciitis is postulated to involve an inflammatory response resulting in an activated inflammatory cell infiltrate of affected tissues and subsequent dysregulation of extracellular matrix production by lesional fibroblasts.

Viallard et al demonstrated that, when stimulated, peripheral blood mononuclear cells of eosinophilic fasciitis patients produce significantly higher amounts of five cytokines, including interleukin (IL)–5 and interferon (IFN)–gamma. [7] IL-5 is known to activate mature eosinophils and to stimulate eosinophil chemotaxis, growth, and differentiation. IFN-gamma activates tissue macrophages and T cells. The findings of Dziadzio et al support increased levels of IL-5 in eosinophilic fasciitis, in addition to increased levels of transforming growth factor (TGF)–beta, another fibrogenic cytokine. [8]

Toquet et al investigated the phenotype of the lesional inflammatory cell infiltrate in patients with eosinophilic fasciitis and demonstrated a predominance of macrophages, $CD8^+$ lymphocytes, and few eosinophils. [9] Pathologic specimens from patients with eosinophilic fasciitis demonstrate increased numbers of eosinophils, especially early in the disease course.

Taken together, the findings of these studies suggest a mechanistic framework marked by a proinflammatory and fibrogenic cytokine response with resultant tissue inflammatory cell infiltration.

In the tissues, the end effector cell of fibrosis is the fibroblast. Fibroblasts from lesional tissue of patients with eosinophilic fasciitis produce excess collagen in vitro and display elevated TGF-beta and type 1 collagen mRNA levels when examined via in situ hybridization with specific cDNA. [10, 11] Therefore, the pathogenesis appears to involve the concomitant increase in the expression of genes for TGF-beta and extracellular matrix proteins in fibroblasts in the affected tissues.

Mori et al suggested that an autocrine stimulatory loop involving major basic protein, a product of eosinophil degranulation, IL-6, which enhances collagen production and is induced my major basic protein, and TGF-beta could account for the progressive fibrosis seen in several eosinophil prominent disorders. [12]

Other studies showed elevated levels of serum manganese superoxide dismutase and tissue metalloproteinase 1 (TIMP-1) in eosinophilic fasciitis, suggesting a role in pathogenesis and providing a possible marker of disease activity. [13]

Fasciitis may be a common manifestation of various pathophysiologic processes associated with eosinophilia. The existence of primary and secondary forms of fasciitis has recently been suggested.

Understanding the mechanisms involved in the development of fascial inflammation and fibrosis in these conditions may yield insights into the pathogenesis of other fibrotic skin diseases.

Epidemiology

Frequency

United States

Eosinophilic fasciitis is very rare.

Mortality/Morbidity

No data are available on morbidity or mortality rates associated with eosinophilic fasciitis. Morbidity may result from joint contractures or carpal tunnel syndrome associated with fascial fibrosis. Rarely, a fatal aplastic anemia may develop.

Race-, sex-, and age-related demographics

Eosinophilic fasciitis affects whites more often than it affects other races. It has been reported in African Americans, Africans, and Asians. [14, 15, 16, 17, 18]

In adults, eosinophilic fasciitis affects women more often than men. [19, 20, 21]

The age range in eosinophilic fasciitis is 1-88 years, although most patients present during the third to sixth decades of life. [20] The average age of onset in two case series was 54.4 and 49.8 years. [20, 21]

Eosinophilic Fasciitis Clinical Presentation

History

Classically, patients with eosinophilic fasciitis (EF) present with symmetric swelling of the skin associated with an aching of the affected extremities, which may develop acutely over a period of days to weeks. Eosinophilic fasciitis may also manifest subacutely. In addition, if patients present later in their disease course, they are more likely to have symptoms of induration or fibrosis of the affected areas.

The onset of illness is not accompanied by fever or other systemic symptoms. In up to half of all patients, disease onset follows an episode of strenuous physical exercise or activity. [19]

Neither Raynaud phenomenon nor symptoms of respiratory, gastrointestinal, or cardiac involvement are typically present.

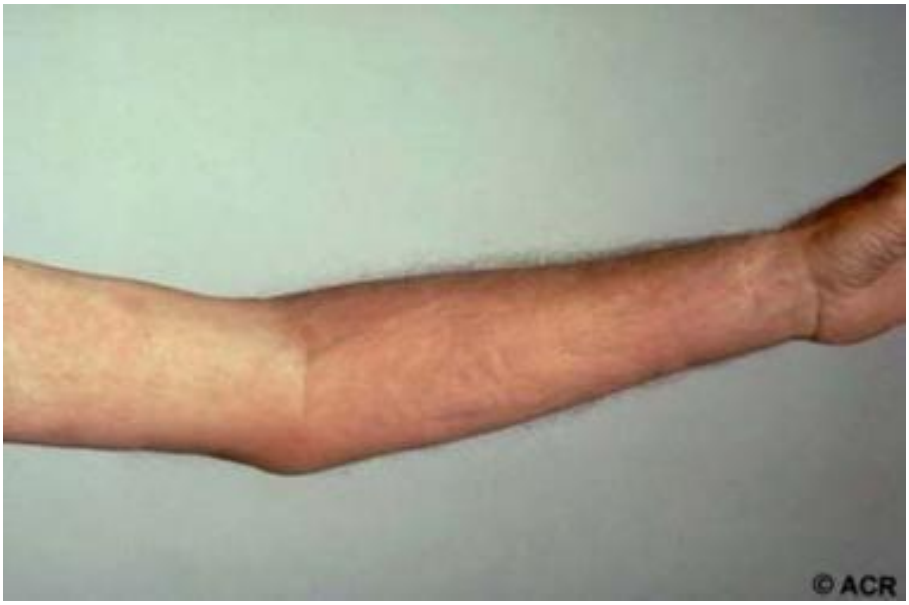
Inflammatory arthritis has been reported and manifests as joint pain, swelling, and morning stiffness. [19, 21]

With progressive fibrosis, patients may endorse limited range of motion due to joint contractures and paresthesias in a distribution pattern consistent with carpal tunnel syndrome.

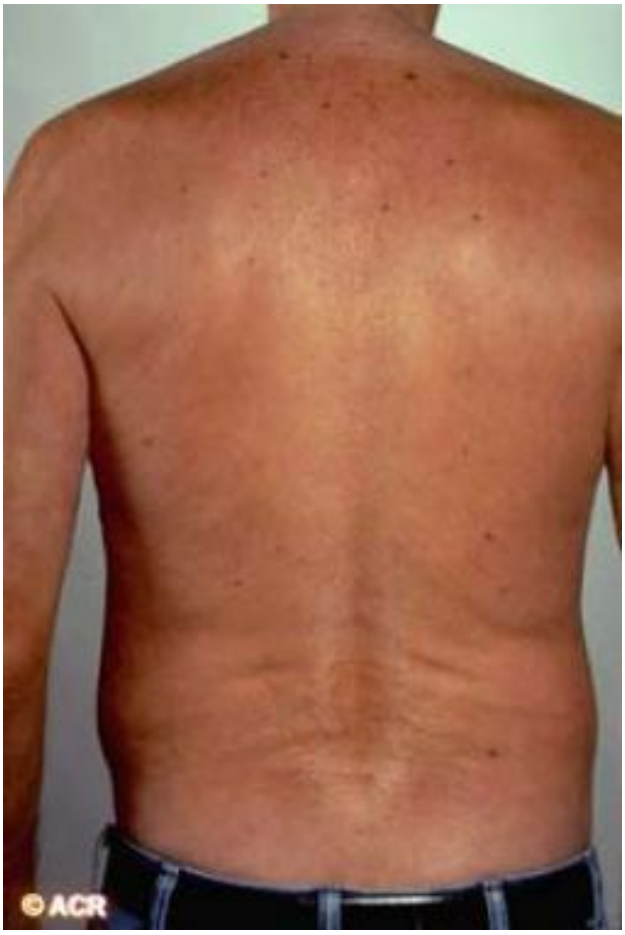
Physical

Cutaneous manifestations include the following [19, 21] :

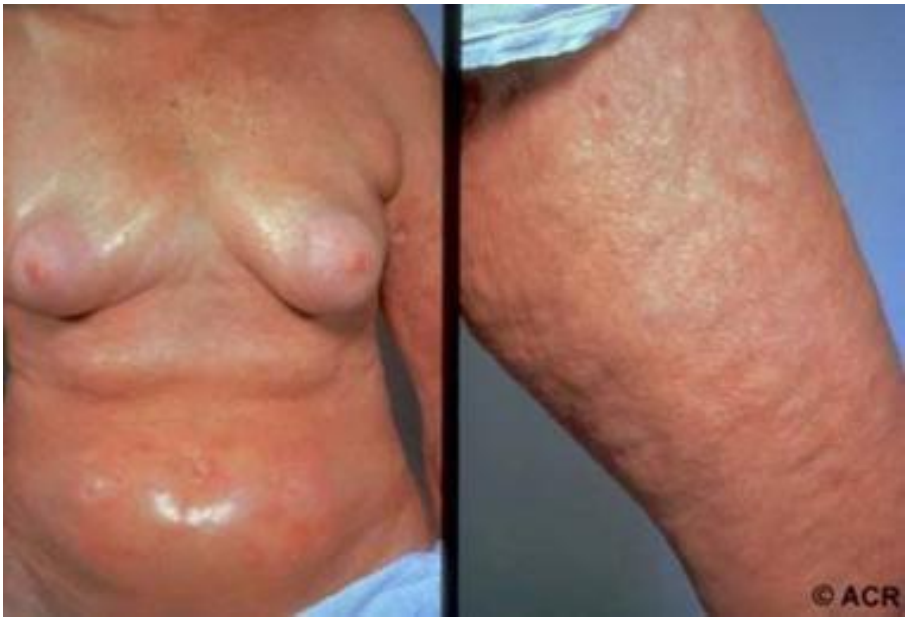
- The cutaneous manifestations of eosinophilic fasciitis evolve as the disease progresses. In the acute inflammatory stage, cutaneous changes include erythematous swelling and nonpitting edema. These findings are later replaced by skin induration, and, eventually, fibrosis predominates. The affected skin is taut and firmly adherent to underlying tissues. Dimpling, *peau d'orange*, and venous furrowing, or the "groove sign," can be seen. See the images below.



The arm of this patient demonstrates the puckered, so-called orange-peel or cobblestone skin that may occur in eosinophilic fasciitis.



The skin of the patient's back appears shiny due to the stretched dermis overlying an inflamed fascia. Mild diffuse hyperpigmentation is present, along with a U-shaped area of hypopigmentation extending approximately from T10 to L4.



The skin of the abdomen and breasts is shiny and taut. The thigh reveals puckering or cobblestoning of the overlying dermis due to scattered retraction from scarred fascia.

- Other cutaneous changes reported include urticaria, bullae, alopecia, lichen sclerosus et atrophicus, vitiligo, and hyperpigmentation.
- Cutaneous manifestations are generally bilateral and symmetric. The upper extremity, proximal and distal to the elbow, and the lower extremity, proximal and distal to the knee, are most commonly involved. The trunk and neck can also be involved. Face and hand involvement are rare.
- A concurrent localized lesion of morphea may be seen in 25% of patients.

Extracutaneous manifestations include the following:

- Joint contractures represent the most common extracutaneous manifestation of eosinophilic fasciitis, occurring in 50%-75% of patients, and can affect elbows, wrists, ankles, knees, and shoulders. [19, 21] Extensive truncal fibrosis may limit chest expansion. A clawlike deformity of the hand has been described.
- Inflammatory arthritis was reported in roughly 40% of patients in two series. [19, 21] The knees, wrists, hands, and feet appear to be most commonly involved.
- Carpal tunnel syndrome is seen in 16%-23% of patients. [19, 21, 22]
- Clinically significant visceral involvement is rare, limited to case reports. If present, significant visceral involvement should prompt investigation of an alternative diagnosis. When pursued, specific testing with pulmonary function testing, esophagogastroduodenoscopy (EGD), and electromyelography (EMG) may demonstrate subtle or nonspecific abnormalities. [23]

Causes

The etiology of eosinophilic fasciitis is unknown. The clinical manifestations of eosinophilic fasciitis are the result of an inflammatory response in the affected tissues. As explained above, our current understanding of eosinophilic fasciitis relies on a relatively few case series and case reports. As such, many etiologic factors have been suggested with varying degrees of

supporting evidence. It may be possible that any of these factors, alone or in combination, could initiate this inflammatory response.

Several possible triggers have been reported with some consistency. A preceding history of vigorous exercise or trauma has been reported in 30%-50% of patients. [19, 21] Multiple drugs have also been implicated, including simvastatin, atorvastatin, and phenytoin. [24, 25, 26]

Several cases have demonstrated positive *Borrelia* serologies. The significance of this finding continues to be debated. Spirochetes were visualized by silver stain in 4 patients in one study. [27] These findings have not been repeated. It has been suggested that positive serology for *Borrelia* represents an epiphenomenon among cases from *Borrelia* -endemic areas and is insufficient evidence of infection and therefore does not support a causal association. [28]

Eosinophilic fasciitis shares clinical similarities, as well as key differences, with eosinophilia-myalgia syndrome. Some studies have suggested an association between l-tryptophan ingestion and eosinophilic fasciitis. [29, 30] Despite this, there is no consistent association between l-tryptophan or other dietary exposure and eosinophilic fasciitis. As evidence, l-tryptophan use was significantly associated with dyspnea, an uncommon finding in eosinophilic fasciitis cases. In another instance, a patient with eosinophilic fasciitis had used l-tryptophan for several years but had started a formal exercise program 2 weeks prior to disease onset.

Multiple additional etiologic triggers have been suggested by single or infrequent case reports.

As with etiology, eosinophilic fasciitis has been associated with several diseases. [31]

Hematologic diseases have been consistently reported and are supported by large case series and case reports. [19, 21, 32] The spectrum of associated hematologic disease is broad and includes aplastic and hemolytic anemia, thrombocytopenia, myeloproliferative disorders, myelodysplastic disorders, lymphoma, leukemia, monoclonal gammopathy of undetermined significance (MGUS), and multiple myeloma. [32, 33, 34]

An association with thyroid disease has been reported in several cases. [35] Eosinophilic fasciitis has rarely been linked to solid-organ tumors and primary biliary cirrhosis, in addition to several other diseases. These disease associations may suggest a shared pathophysiology of cellular dysregulation and/or autoimmunity.

Eosinophilic Fasciitis Differential Diagnoses

Diagnostic Considerations

Differential considerations include the following:

- The localized forms of scleroderma, morphea, and linear forms of scleroderma
- Limited and diffuse cutaneous systemic sclerosis
- Other localized cutaneous fibrosing disorders, eg, nephrogenic systemic fibrosis, scleromyxedema, and scleredema

In general, these alternative etiologies can be excluded by the absence of peripheral eosinophilia. However, cases of diffuse morphea with features that overlap with eosinophilic fasciitis have been reported. [36, 37] The absences of Raynaud phenomenon, abnormal capillaroscopy findings, and visceral involvement are key findings that differentiate eosinophilic fasciitis (EF) from systemic sclerosis.

Eosinophilia-myalgia syndrome and toxic oil syndrome are two disorders that share common clinical and histopathological features with eosinophilic fasciitis, including peripheral eosinophilia. In contrast to eosinophilic fasciitis, these two conditions present in epidemic form and, after epidemiological analysis, appear to be almost universally toxin-associated. [38, 39]

In 1989, an epidemic of a connective-tissue disease with peripheral eosinophilia and prominent myalgias was recognized in the United States and was therefore termed eosinophilic myalgia syndrome. Subsequent epidemiologic studies indicated that most individuals who developed eosinophilic myalgia syndrome had consumed l-tryptophan from a single source. Diffuse induration of the integument affecting the extremities and occasionally the torso, but sparing the face, hands, and feet, developed in a large number of patients with eosinophilic myalgia syndrome. In contrast to eosinophilic fasciitis, patients with eosinophilic myalgia syndrome typically presented with prominent systemic symptoms, including fever, myalgia, and rash.

Similarly, in 1980 in Spain, an epidemic of connective-tissue disease with peripheral eosinophilia was recognized. The epidemic was eventually traced to rapeseed oil that had been denatured with aniline and sold in bulk as olive oil for cooking. As many as 20,000 Spaniards were affected. Acute symptoms were similar to those of eosinophilic myalgia syndrome, with prominent systemic symptoms in addition to cutaneous changes. In contrast to eosinophilic myalgia syndrome, acute symptoms included more prominent pulmonary manifestations. In chronic disease, patients with toxic oil syndrome were more likely to demonstrate systemic (pulmonary, neurologic) symptoms. [12, 40, 41]

Differential Diagnoses

- Eosinophilia
- Eosinophilia-Myalgia Syndrome
- Localized Fibrosing Disorders - Linear Scleroderma, Morphea, and Regional Fibrosis
- Scleroderma
- Systemic Sclerosis
- Toxic Oil Syndrome

Eosinophilic Fasciitis Workup

Laboratory Studies

Characteristic laboratory findings of eosinophilic fasciitis (EF) include the following:

- Peripheral blood eosinophilia is present in 61%-83% of patients. The degree of eosinophilia is variable over time, even in the absence of specific therapy. [19, 42, 43]
- Hypergammaglobulinemia is characteristic, although this finding varies widely by case series, occurring in 18%-67% of patients. It is most often due to a polyclonal increase in immunoglobulin G. [20, 21, 42]
- An increase in the erythrocyte sedimentation rate (ESR) is found in 29%-70% of cases. [20]

Additional laboratory findings of eosinophilic fasciitis include the following: [19, 21, 42]

- Serum creatine kinase and aldolase levels are generally normal.
- Rheumatoid factor (RF) and antinuclear antibodies are occasionally positive.
- Hematologic abnormalities and disease are associated with eosinophilic fasciitis. Aplastic anemia, although rare, is the most frequent common associated hematological complication, but cases have been described with thrombocytopenia, hemolytic anemia, pernicious anemia, lymphoma, and leukemia. [44, 45]
- *Borrelia* serology or polymerase chain reaction (PCR) findings are occasionally positive and may suggest a treatable etiology. However, as discussed above, the exact correlation between eosinophilic fasciitis and *Borrelia* remains unclear. [27, 28]
- Metalloproteinase 1 (TIMP-1) may be a new serological marker of disease activity. [13]

Imaging Studies

Magnetic resonance imaging (MRI) is the imaging modality of choice. MRI of the involved areas shows characteristic findings of fascial thickening, abnormal signal intensity, and contrast enhancement. Additionally, MRI aids in making the diagnosis, locating the biopsy site, and monitoring the response to treatment. [46, 47, 48, 49]

Although it has not been used frequently or studied extensively in eosinophilic fasciitis, one case report has shown that ultrasonography can aid in early diagnosis. [50] According to a study by Kissin et al that included 12 patients with eosinophilic fasciitis, a 12-MHz, B-mode ultrasound may be used to measure subcutaneous compressibility and thereby serve as an adjunctive tool to distinguish eosinophilic fasciitis from diffuse systemic sclerosis, especially when tissue sampling is less feasible or when the result of tissue sampling is equivocal. [51]

Other Tests

While eosinophilic fasciitis is generally not associated with myositis or myopathy, electromyography has occasionally been performed, and findings may be abnormal in the presence of normal serum muscle enzymes. [21]

Pulmonary function testing may show a restrictive pattern in patients with severe truncal involvement. [21]

Procedures

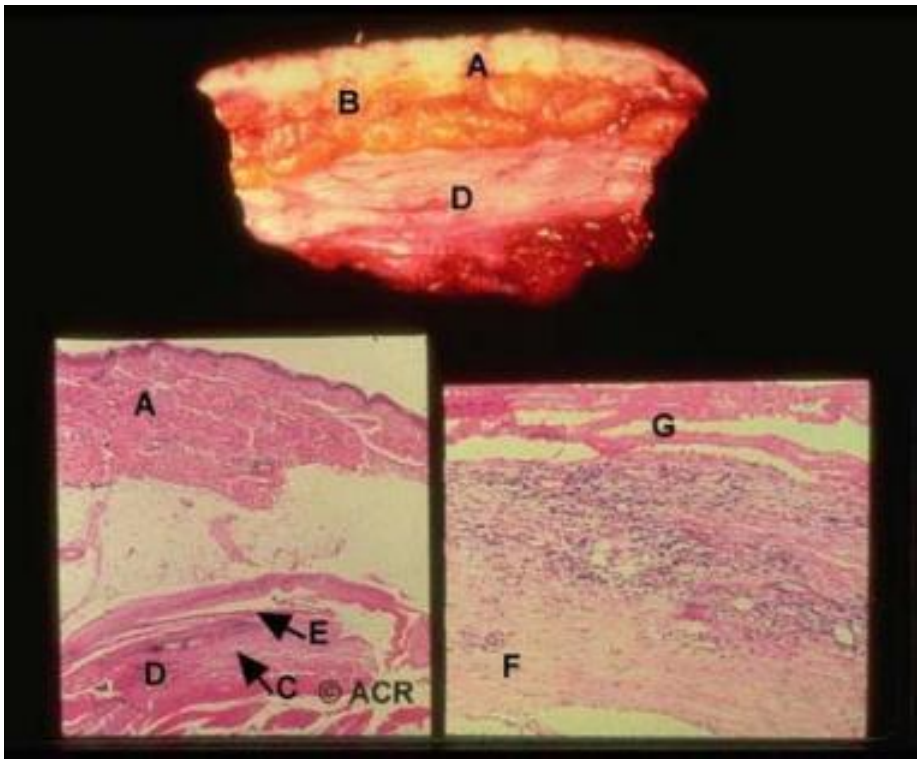
Definitive diagnosis relies on a full-thickness incisional skin biopsy. The specimen should include the skin, fat, fascia, and superficial muscle in continuity. Biopsy is especially important in an atypical presentation. [52, 53, 54]

Histologic Findings

Inflammation, edema, thickening, and sclerosis of the fascia are hallmarks of eosinophilic fasciitis. Acute findings include infiltration of deep fascia and an adjacent subcutis layer with lymphocytes, plasma cells, histiocytes, and eosinophils. Distribution of the eosinophils in the

fascia may be focal, and a close relationship appears to exist between blood and tissue eosinophilia. In the deeper portions of the panniculus, a similar infiltrate is found in the fibrous septa and at the periphery of the fat lobules. Deep in the fascia, the inflammatory infiltrate can extend into the epimysium, perimysium, and endomysium. In addition, vascular cuffing with lymphocytes and plasma cells is often seen. [11, 15, 55]

As the disease progresses, inflammatory changes are replaced by generalized sclerosis and thickening of the fascia and adjacent tissue layers. The sclerosis can be dense with hyalinized collagen bands running parallel to the fascia and small foci of fat cells trapped between them. [42, 56] See the image below.



Eosinophilic fasciitis. Top: In this gross specimen, the dermis (A), subcutaneous adipose tissue (B), and skeletal muscle do not appear unusual. However, the fascia (D) is markedly thickened. Bottom left: The gross findings are recapitulated in this low-power photomicrograph. The epidermis, dermis (A), and subcutaneous adipose tissue are not remarkable in this case. The fascia (D) is markedly thickened and focally infiltrated by inflammatory cells (E). The small amount of skeletal muscle (C) appears normal (hematoxylin and eosin stain at low power). Bottom right: A close-up photograph of a portion of the fascia showing mostly edematous cellular connective tissue (F). It is focally infiltrated by inflammatory cells, including lymphocytes, plasma cells, and histiocytes. The more intensely stained hypocellular pink bands across the top of the field (G) are part of an interstitial exudate of fibrin (hematoxylin and eosin stain at medium power).

Eosinophilic Fasciitis Treatment & Management

Approach Considerations

First-line therapy for eosinophilic fasciitis is with systemic corticosteroids. [6] Although patients may require prolonged therapy, it should be noted that up to one third of eosinophilic fasciitis cases may spontaneously resolve. [57]

Case reports describe the use of a number of agents for second-line therapy. No consensus exists on which agent is best for that purpose.

Physical therapy should be initiated to improve joint mobility and to decrease contractures.Surgical release has been used in some cases to manage significant joint contractures. [58]

Dermatologists, rheumatologists, and surgeons (for the skin-muscle biopsy) are consulted most often for management of these cases.

Medical Care

Initial therapy

There is wide consensus that systemic corticosteroids are the initial therapeutic agent of choice. Typically, prednisone or prednisolone is used, in doses ranging from 20-100 mg/day. Response is considered satisfactory with reduction in edema, improvement in skin thickening, resolution of carpal tunnel syndrome, and gradual decrease in joint contracture. Eosinophilia and inflammatory markers frequently resolve promptly after initiation of prednisone therapy. [19, 20, 21, 42, 53, 59, 6]

Additional therapeutic agents and adjunctive therapies

Multiple additional therapeutic agents have been used as disease-modifying or steroid-sparing agents in persistent or steroid-resistant cases of eosinophilic fasciitis. It should be noted that there is no general consensus with regard to the best agent for this type of disease. Treatment numbers are generally small, and controlled trials are lacking. [20, 60, 61, 62, 63]

Case reports detail the use of multiple additional agents, including antihistamines, cimetidine, hydroxychloroquine, chloroquine, azathioprine, cyclosporine, dapsone, infliximab, tacrolimus, methotrexate, D-penicillamine, griseofulvin, ketotifen, and alpha-interferon, with varying rates of response. Some data suggest that other anti–tumor necrosis factor (TNF)–alpha agents may also be beneficial. [57]

One study reviewed the treatment modalities used in 32 adult patients with biopsy-proven eosinophilic fasciitis. All patients received corticosteroids as a first-line therapy. Fifteen patients (47%) received methylprednisolone pulses at treatment initiation, and 14 patients (44%) received an immunosuppressive agent, usually methotrexate (86%), as a second-line therapy. There was complete remission in 69% of patients; remission with disability in 19%; and failure in 12%. A poor outcome was associated with a delay in diagnosis greater than 6 months and lack of methylprednisolone pulses. [64]

In a review of 63 patients with eosinophilic fasciitis, Wright and colleagues reported a higher rate of complete response in patients treated with the combination of corticosteroids and methotrexate (21 of 33 patients), compared with other treatment combinations, corticosteroids only, or treatment without corticosteroids. [6]

Eosinophilic Fasciitis Medication

Medication Summary

The goals of pharmacotherapy are to reduce morbidity and to prevent complications.

Corticosteroids

Class Summary

These agents have anti-inflammatory properties and cause profound and varied metabolic effects. Corticosteroids modify the body's immune response to diverse stimuli.

Prednisone (Sterapred)

View full drug information

Useful in the treatment of inflammatory conditions by reversing increased capillary permeability and suppressing neutrophil activity.

Eosinophilic Fasciitis Follow-up

Further Outpatient Care

Patients with eosinophilic fasciitis (EF) should continue to be treated with corticosteroid therapy in the outpatient setting.

Prognosis

A retrospective review found that clinical factors associated with persistent fibrosis included presence of morphealike skin lesions, younger age at onset, truncal involvement, and presence of dermal fibrosclerosis on histopathologic specimen. [5]

Loss of edema is usually the first clinical sign of improvement and can occur within 4 weeks of commencing treatment. Concurrently, the skin becomes softer, but 3-6 months may elapse before maximal reduction in induration and contractures is achieved. [19, 21]

While total resolution of the clinical signs can occur, some degree of induration remaining even after many months of corticosteroid therapy is not unusual.

A direct correlation does not always exist between clinical disease activity and laboratory findings. The eosinophilia and ESR usually return to reference ranges within 6-8 weeks, although the ESR and hypergammaglobulinemia may remain abnormal for up to 12 months. [19, 21]

Eventually, corticosteroid therapy can be withdrawn in many of the patients, without relapse occurring.

The development of aplastic anemia is a rare but grave complication. [44] One study reported on 4 patients with eosinophilic fasciitis and severe aplastic anemia. In 3 cases, the aplastic anemia was refractory to conventional immunosuppressive therapy with antithymocyte globulin and cyclosporine. However, in 1 patient, rituximab displayed significant efficacy for both the skin and hematologic symptoms. In an additional 19 cases of eosinophilic fasciitis and aplastic anemia, corticosteroid regimens improved skin symptoms in 5 of 12 cases but were

ineffective in the treatment of aplastic anemia in all but 1 case. Aplastic anemia was profound in 13 cases and was the cause of death in 8 cases. Only 5 patients achieved long-term remission. [65]

Eosinophilic Fasciitis Questions & Answers

Overview

What is eosinophilic fasciitis (EF)?
What is the pathophysiology of eosinophilic fasciitis (EF)?
What is the prevalence of eosinophilic fasciitis (EF) in the US?
What is the mortality and morbidity associated with eosinophilic fasciitis (EF)?
Which patient groups have the highest prevalence of eosinophilic fasciitis (EF)?

Presentation

Which clinical history findings are characteristic of eosinophilic fasciitis (EF)?
What are cutaneous manifestations of eosinophilic fasciitis (EF)?
What are extracutaneous manifestations of eosinophilic fasciitis (EF)?
What causes eosinophilic fasciitis (EF)?

DDX

How is eosinophilic fasciitis (EF) differentiated from other cutaneous disorders?
How is eosinophilic fasciitis (EF) differentiated from eosinophilia-myalgia syndrome?
How is eosinophilic fasciitis (EF) differentiated from connective-tissue diseases with peripheral eosinophilia?
What are the differential diagnoses for Eosinophilic Fasciitis?

Workup

What is the role of lab testing in the workup of eosinophilic fasciitis (EF)?
What is the role of imaging studies in the workup of eosinophilic fasciitis (EF)?
What is the role of electromyography in the workup of eosinophilic fasciitis (EF)?
What is the role of pulmonary function testing in the workup of eosinophilic fasciitis (EF)?
What is the role of biopsy in the workup of eosinophilic fasciitis (EF)?
Which histologic findings are characteristic of eosinophilic fasciitis (EF)?

Treatment

How is eosinophilic fasciitis (EF) treated?
What is the initial therapy for eosinophilic fasciitis (EF)?
Which medications are used in the treatment of eosinophilic fasciitis (EF)?

Medications

What is the goal of drug treatment for eosinophilic fasciitis (EF)?
Which medications in the drug class Corticosteroids are used in the treatment of Eosinophilic Fasciitis?

Follow-up

What is included in long-term management of eosinophilic fasciitis (EF)?
What is the prognosis of eosinophilic fasciitis (EF)?

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