Int J Clin Exp Pathol 2020;13(7):1739-1744
www.ijcep.com /ISSN:1936-2625/IJCEP0112683

Case Report

Vigorous exercise-induced unilateral eosinophilic fasciitis: rare and easily misdiagnosed subtype

Hasan S AL-Ghamdi

Internal Medicine Department, Albaha University, Albaha, Saudi Arabia

Received April 16, 2020; Accepted May 25, 2020; Epub July 1, 2020; Published July 15, 2020

Abstract: The hallmark of eosinophilic fasciitis (EF) is painful symmetric skin stiffness and limb sclerosis with deep fascia inflammation. Two cases of unilateral EF have been reported in the literature but were not related to strenuous physical activity. In this report, a young female presenting with unilateral scleroderma-like skin changes, blood and tissue eosinophilia, and hypergammaglobulinemia proven to be EF after strenuous physical activity is described. This case represents the first case reported in the current literature of unilateral EF after vigorous exercise. A skin to muscle biopsy and magnetic resonance imaging (MRI) study indicated classic EF features. Cases of unilateral eosinophilic fasciitis are under-recognized and have rarely been described in the literature. EF requires a high index of suspicion to be diagnosed accurately and differentiated from another scleroderma variant, especially localized types. Early diagnosis and management of unilateral EF are very crucial because EF management and prognosis are completely different from other scleroderma mimics. EF heals rapidly in response to glucocorticoid or combination therapy. In the current case, corticosteroids alone failed to induce complete disease remission, but with the addition of methotrexate, complete resolution of both skin and systemic features was obtained. She is now in good health with no medication use. The current literature review indicates that this the first reported case of unilateral EF after vigorous exercise.

Keywords: Eosinophilic fasciitis, groove sign, eosinophilia, vigorous exercise

Introduction

Eosinophilic fasciitis (EF) is an uncommon connective tissue disease that clinically presents as scleroderma-like skin changes. Its etiology is unknown, and the pathogenesis is poorly understood [1]. Occasionally, antinuclear antibodies and rheumatoid factor present in EF patients is the reason why some authors have suggested autoimmune patho-mechanisms [2]. Associated hypergammaglobulinemia (usually IgG), peripheral eosinophilia, high erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) have also been found [3].

EF presents clinically with symmetric painful swelling, stiffness, and skin and subcutaneous limb tissue sclerosis. Since there is no associated Raynaud's phenomenon and no involvement of internal body organs, these features usually distinguish this condition from collagen vascular diseases, such as scleroderma. EF can be a paraneoplastic syndrome either preceding or occurring concurrently with internal malignancies, especially hematological types, such as myelomonocytic leukemia, multiple myeloma, Hodgkin's disease, and non-Hodgkin's lymphoma [4, 5].

Universally accepted diagnostic criteria are lacking, but diagnosis can be made via clinical, laboratory, imaging studies, and a deep full-thickness skin-to-muscle biopsy. Corticosteroid are the first line and most effective treatment for EF.

In this report, a very interesting classic case of EF after vigorous physical activity proven by histopathology and magnetic resonance imaging (MRI) is described.

Case report

A 20-year-old female patient was seen in our dermatology clinic with complaints of tightness and restriction of left leg movement. These

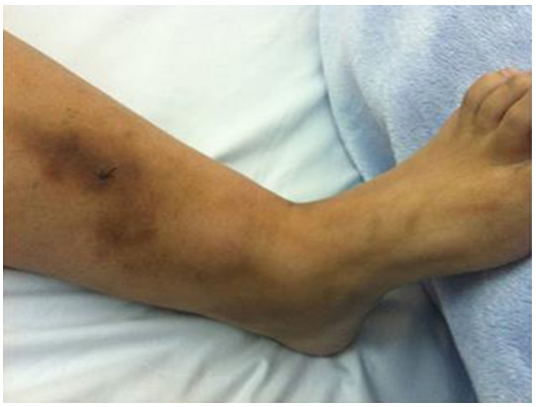

Figure 1. Sclerosis and thickened hyperpigmented skin on the left leg.

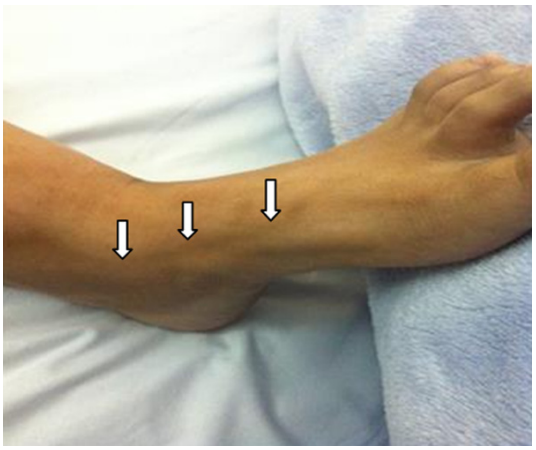

Figure 2. Patient's left leg with groove sign.

complaints started three months prior to presentation and were associated with painful progressive left leg swelling. She otherwise considered herself in good health and took no medications or supplements. She first noticed the sudden onset of swelling in her left leg, which resolved gradually and then showed tight bound down skin. This skin led to marked limitations in her daily activities. The patient reported a history of pain in the shoulder joint but no history of joint stiffness or swelling. She reported a history of heavy physical exercise in the form of weight training in addition to heavy housework. No history of Raynaud's phenomenon, dysphagia, skin rash, hair loss, other joints pain, or stiffness were described. Fever, weight loss, or any other systemic complaints were not reported. She had no known exposure to polyvinylchloride or L-tryptophan. Because of the pain and paresthesia in the left leg, she saw an orthopedic surgeon who prescribed analgesics and antibiotics, but these drugs did not help her. Sometimes, her condition improved with the use of non-steroidal anti-inflammatory drugs (NSAIDs). Her past medical history was unremarkable. The family history was negative for any allergic or rheumatic diseases.

During examination, the patient looked healthy, had stable vital signs, and showed no skin rash. Examination of the musculoskeletal system showed sclerotic, brownish, thickened skin on the left leg (**Figure 1**). Non-pitting edema was confirmed on palpation. A groove sign was obvious on the left foot (**Figure 2**). Shoulder joint movement was slightly restricted because of pain. Neck and other joint movements were normal and painless. No sign of arthritis in the joints were noted, and a neurological examination was normal. She had no lymphadenopathy, telangiectasia, cyanosis, sclerodactyly, microstomia, digital infarcts, or gangrene. The patient had normal cardiovascular, chest, and abdomen examinations.

Gross nailfold examination was unremarkable. Hair, nails, and mucous membrane were normal.

Her laboratory parameters showed a total white blood cell count of 10.9 × 10^9/L (normal 4.0-10.0 × 10^9/L) with eosinophilia of 7% (normal 1%-4%). A peripheral blood smear showed normocytic hypochromic smear with mild absolute eosinophilia.

Erythrocyte sedimentation rate (ESR) was 55 mm/hour (normal 0-20 mm/hour) and C-reactive protein (CRP) level was 31 mg/L (normal 0.1-3.0 mg/L). Rheumatoid factor and the antinuclear antibody (ANA) tests were negative. Hypergammaglobulinemia was found on protein electrophoresis. Thyroid function tests and stool analysis were within normal limits.

Serology was collected for anti-ds DNA, anti-Scl-70, and anti-centromere antibodies and was negative.

Lung X-rays and electromyographic examinations of the upper and lower extremities were done.

Because of the suspicion of EF, a deep full-thickness biopsy sample that included skin, subcutis, fascia, and muscle was taken from the clinically involved lower left leg. Results

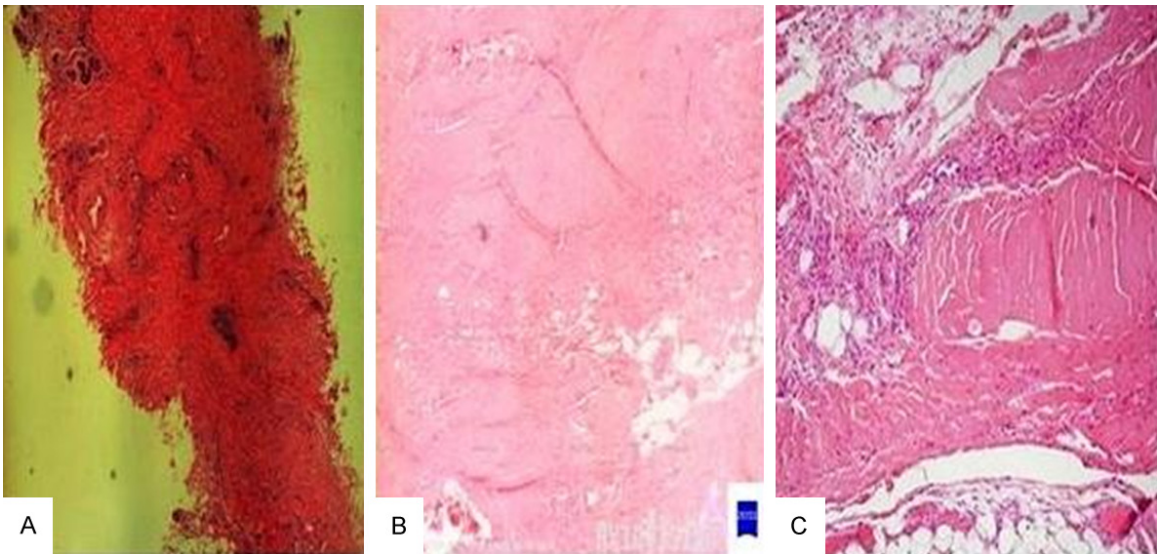

Figure 3. A. Scanning view for a case of eosinophilic fascitis (hematoxylin and eosin [H&E] staining × 40). B and C. Significantly thickened and fibrosed fascia (H&E stain, × 100 and 200).

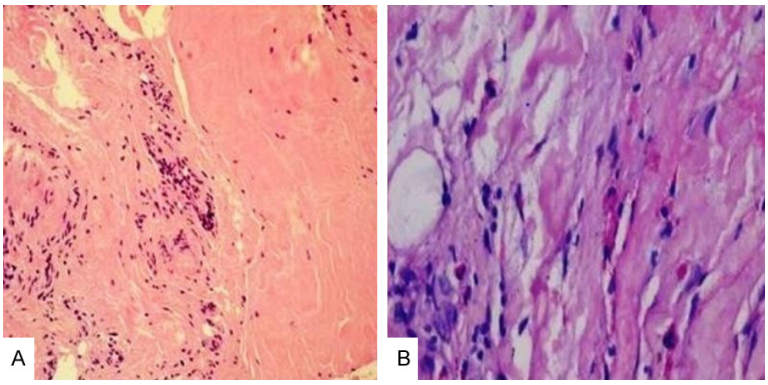

Figure 4. A and B. Marked Inflammatory infiltration with predominance of mononuclear cells (H&E stain, × 100 and 200).

showed a discrete perivascular infiltration composed of lymphocytes, plasma cell, histiocytes, and eosinophils involving mainly the deep dermis and subcutis and deep fascia. Epidermis and upper dermis were inflammation free.

The fascia was extremely thick and fibrosed and was infiltrated by the mononuclear infiltrate, including eosinophils (**Figures 3** and **4**).

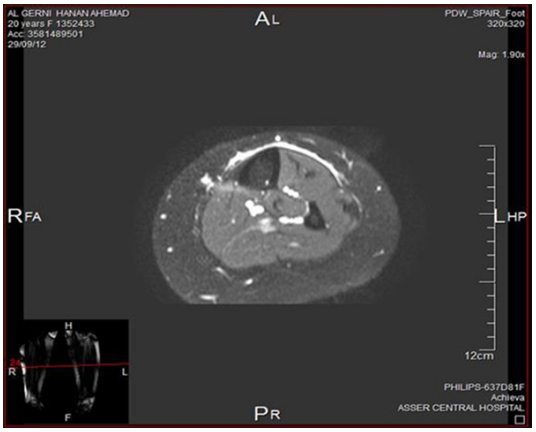

Figure 5. T2-weighted magnetic resonance imaging (MRI) scan (axial view) showing intense fascial enhancement.

Superficial spread of the infiltration into the muscle tissue was observed as was fibrous septa. These findings were reported as in agreement with a diagnosis of EF.

Radiological imaging via MRI was done. The results showed intense superficial fascial enhancement (**Figure 5**), soft tissue-swelling and edema associated with periosteal reaction, and cortical thickening mainly of the middle and lower parts of the left tibia (**Figure 6**).

She was started on prednisolone 40 mg daily for two months but showed no clinical improvement. Therefore, methotrexate (0.3 mg/kg/week) as a test dose was added to the prednisolone treatment after basic investigations.

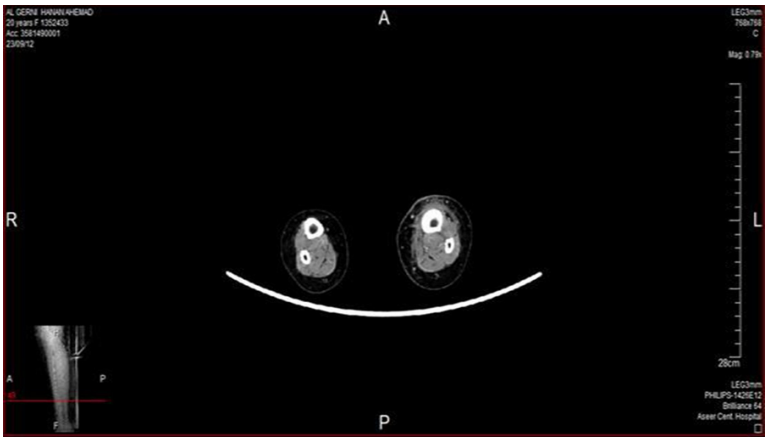

Figure 6. T1-weighted MRI Axial view: soft tissue-swelling and edema associated with periosteal reaction and cortical thickening mainly of the middle and lower part of the left tibia.

She was followed in our clinic weekly after combination therapy. After two months, swelling, stiffness, and edema had almost disappeared. ESR and CRP levels returned to normal values, and there was no peripheral eosinophilia after three months of combination therapy. Physical therapy was done for the left lower limb joint to prevent restriction and regain her full range-of-motion.

Discussion

EF is a rare fibrosing inflammatory disease first described by Shulman in 1974 [6]. EF is characterized by scleroderma-like skin changes associated with blood and tissue eosinophilia, hypergammaglobulinemia, and elevated ESR and CRP levels. Males and females are affected equally by the disease. A comprehensive literature review showed that the cutaneous changes of EF typically involve the limbs in a symmetric manner. Two cases were reported as unilateral EF. The first one described a 39-year-old woman with unilateral EF involving her left upper and lower limbs [7]. The second one described a 23-year-old female with unilateral presentation involving her left upper extremity [8]. Our case represents the first case of unilateral EF after vigorous exercise reported in the current literature.

EF has been considered as a part of the spectrum of scleroderma/systemic sclerosis. However, many features associated with systemic scleroderma, such as Raynaud's phenomenon, telangiectasias, dermal and epidermal involvement, extracutaneous manifestations, and a lack of serological features characteristic for systemic scleroderma, are not present in EF [9, 10]. The most accepted pathogenesis nowadays is an immuno-allergic reaction, a theory that has gained support by the presence of hypergammaglobulinemia in the blood and IgG and C3 deposition in fascia of some patients [10]. EF's cause is unknown, but many associations with other conditions have been proposed. The most well-known association reported in the literature is vigorous exercise in up to 66% [10, 11]. In the above case, she relates the onset of the disease to strenuous exercise (weight training and heavy housework). Antigenicity of the fascia and subcutis may be triggered by vigorous exercise [12]. Other associations include trauma [10, 11, 13], simvastatin [11] and phenytoin [13], arthropod bites [14, 15], Borrelia infection [11, 13, 16], hematological malignancies [11-14], and thyroid disease [11].

None of these causes were obvious in our case except strenuous exercise, which appeared to be the triggering factor.

EF diagnosis may be diffcult but can be done using clinical pictures, histological findings, and MRI imaging studies.

Histo-pathologically, in EF, the perivascular mononuclear infiltrate, including eosinophils, is predominantly involved deep skin and fascia layers. In scleroderma, signs of inflammation mainly occur in the superficial dermis [17].

MRI is very helpful for confirming an EF diagnosis, especially in its acute phase, which is defined as <6 months from the onset of disease.

Classical findings include facial thickening on T1-weighted images and intense facial enhancement after gadolinium contrast on T2-weighted images [18]. Our patient's MRI also showed these specific findings. Interestingly, MRI is useful for confirming the diagnosis, guiding the

choice of a biopsy site, and monitoring and assessing therapeutic responses [19].

Our case had the characteristic findings of EF that led to severe skin tightness and eventually impaired her joint motility. A groove sign was evident on the left leg. Tissue and blood eosinophilia and elevated ESR were present.

Corticosteroids are effective and generally considered the first line of treatment. When full disease remission is not obtained with corticosteroid alone, other immunosuppressive agents are added, such as methotrexate as in our case [20]. This combination leads to full resolution of the disease.

The prognosis of EF is very difficult to predict, and some patients show dramatic improvements while others may develop systemic sclerosis or overlapping disorders [21]. Some authors have stated that spontaneous remission occurs in 10%-20% of patients after two to five years of the disease [22].

Conclusion

As mentioned previously, the typical EF presentation is symmetrical distribution of its scleroderma-like skin changes. Unilateral presentation is very uncommon, and this case is the first reported one of unilateral EF after vigorous exercise that has been reported in the current literature. Diagnosis is confirmed by biopsy and MRI findings. The patient responded fully to a combination of corticosteroid and methotrexate. Unilateral EF should be kept in mind when EF is suspected, especially after occurrence of the well-known triggering factors. EF is underrecognized and can be easily misdiagnosed by dermatologists and rheumatologists. Since its response to treatment and prognosis is good, recognition of this subtype is of high importance for differentiation from other scleroderma variants.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hasan S Al-Ghamdi, Internal Medicine Department, Albaha University, Albaha, Saudi Arabia. Tel: 00966533013355; E-mail: Hasanalghamdi8@gmail.com; H.saeed@bu.edu.sa

References

[1] Danis R, Akbulut S, Altintas A, Ozmen S and Ozmen CA. Unusual presentation of eosinophilic fasciitis: two case reports and a review of the literature. J Med Case Rep 2010; 4: 46.

[2] Bukiej A, Dropiński J, Dyduch G and Szczeklik A. Eosinophilic fasciitis successfully treated with cyclosporine. Clin Rheumatol 2005; 24: 634-636.

[3] Chun JH, Lee KH, Sung MS and Park CJ. Two cases of eosinophilic fasciitis. Ann Dermatol 2011; 23: 81-84.

[4] Minciullo PL, Morabito F, Mandaglio R, Iacopino P and Gangemi S. Eosinophilic fasciitis associated with autoimmune phenomena after bone marrow transplantation: report of two cases. Clin Rheumatol 2006; 25: 80-82.

[5] Khanna D, Verity A and Grossman JM. Eosinophilic fasciitis with multiple myeloma: a new haematological association. Ann Rheum Dis 2002; 61: 1111-1112.

[6] Arlettaz L, Abdou M, Pardon F and Dayer E. Eosinophllic fasciitis (Shulman disease). Rev Med Suisse 2012; 8: 854-858.

[7] Daniel RS and Brown AN. Case report of unilateral eosinophilic fasciitis in a Vietnamese woman. Am J Med Sci 2009; 337: 153-154.

[8] Daniel RS, Lavery S, Maize JC Jr, Brown AN and Bolster MB. Unilateral eosinophilic fasciitis: an under-recognized subtype? J Clin Rheumatol 2009; 15: 247-249.

[9] Schiener R, Behrens-Williams SC, Gottlöber P, Pillekamp H, Peter RU and Kerscher M. Eosinophilic fasciitis treated with psoralen-ultraviolet A bath photochemotherapy. Br J Dermatol 2000; 142: 804-807.

[10] Haddad H, Sundaram S, Magro C and Gergis U. Eosinophilic fasciitis as a paraneoplastic syndrome, a case report and review of the literature. Hematol Oncol Stem Cell Ther 2014; 7: 90-92.

[11] Pinal-Fernandez I, Selva-O' Callaghan A and Grau JM. Diagnosis and classification of eosinophilic fasciitis. Autoimmun Rev 2014; 13: 379-382.

[12] Antic M, Lautenschlager S and Itin PH. Eosinophilic fasciitis 30 years after-what do we really know? Report of 11 patients and review of the literature. Dermatology 2006; 213: 93-101.

[13] Blaser KU, Steiger U, Würsch A and Speck B. Eosinophilic fasciitis with aplastic anemia and Hashimoto's thyroiditis. Review of the literature and report of a typical example. Schweiz Med Wochenschr 1989; 119: 1899-1906.

[14] Belot V, Mulleman D, Perrinaud A, Abdallah-Lotf M, Machet MC and Machet L. Eosinophilic fasciitis associated with Borrelia burgdorferi

infection. Ann Dermatol Venereol 2007; 134: 673-637.
[15] Carneiro S, Brotas A, Lamy F, Lisboa F, Lago E, Azulay D, Cuzzi T and Ramos-e-Silva M. Eosinophilic fasciitis (Shulman syndrome). Cutis 2005; 75: 228-232.
[16] Lamloum M, Sioud DA, Ben Ghorbel I, Smiti KM, Haouet S, Khedher I and Houman MH. Shulman syndrome. A report of 4 cases and review of the literature. Tunis Med 2006; 84: 189-194.
[17] Chang CW and Lau MS. Atypical presentation of eosinophilic fasciitis with pitting edema. Hawaii J Med Public Health 2015; 74 Suppl 2: 36-38.
[18] Lese AB and Dodds SD. Eosinophilic fasciitis: case report. J Hand Surg Am 2013; 38: 2204-2207.
[19] Baumann F, Brühlmann P, Andreisek G, Michel BA, Marincek B and Weishaupt D. MRI for diagnosis and monitoring of patients with eosinophilic fasciitis. AJR Am J Roentgenol 2005; 184: 169-174.
[20] Mendoza FA, Bai R, Kebede AG and Jimenez SA. Severe eosinophilic fasciitis: comparison of treatment with D-penicillamine plus corticosteroids vs. corticosteroids alone. Scand J Rheumatol 2016; 45: 129-134.
[21] Mosconi S, Streit M, Brönimann M and Braathen LR. Eosinophilic fasciitis (Shulman syndrome). Dermatology 2002; 205: 204-206.
[22] Lamback EB, Resende FS and Lenzi TC. Eosinophilic fasciitis. An Bras Dermatol 2016; 91 Suppl 1: 57-59.