Unusual presentation of eosinophilic fasciitis: Report of two cases and literature review

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Abstract

Introduction: Eosinophilic fasciitis (EF) is an uncommon disorder with unknown etiology and its pathogenesis is poorly understood.

Case presentation: Herein, we present two cases of EF with unusual presentation and describe theirs clinical characteristics and laboratory findings. The first case was a 29-year-old male admitted with pain, edema and induration of the right upper limb and left lower limb. There was unilateral edema and stiffness with prominent pretibial edema on physical examination, and high eosinophil count on peripheral smear. The second case was a 63-year-old man who had pain, edema, erythema and itching on the upper and lower extremities which developed after strenuous physical activity. He had cervical lymphadenopathy and polyarthritis on his physical examination and rheumatoid factor and antinuclear antibody positivity on laboratory examination.

Conclusion: In conclusion, EF may present with various symptoms. When patients exhibit eosinophilia, arthralgia and myalgia, eosinophilic fasciitis should be also considered among the possible diagnoses.

Keywords: Eosinophilia, fasciitis, eosinophilic fasciitis.
Introduction

Eosinophilic fasciitis (EF) is an uncommon disorder with unknown etiology and its pathogenesis is poorly understood. It has symmetrical involvement and is characterized, in its early phase, by limb or trunk erythema and edema, and later by collagenous thickening of the dermis and subcutaneous fascia. EF is also referred to as diffuse fasciitis with eosinophilia, and eponymously as Shulman syndrome [1-3]. The onset is typically acute and findings include erythema, swelling and induration of the extremities usually accompanied by eosinophilia.

Herein, we present two cases of eosinophilic fasciitis (EF) with unusual presentation and describe theirs clinical characteristics and laboratory findings. The first patient displayed unusual features including a high eosinophilia count and asymmetry. The second patient had cervical lymphadenopathy and polyarthritis with rheumatoid factor (RF) and a positive antinuclear antibody (ANA).

Cases Presentation

Patient-1

A 29-year-old Turkish male admitted to our clinic with disability because of the significant pain, edema and stiffness of his right upper limb and left lower limb. He reported that these same clinical picture firstly appeared 3 years ago and had repeated many times during the last 3 years and improve sometimes spontaneously and sometimes with the use of non-steroidal anti-inflammatory drugs. Unilateral edema and stiffness in the right upper limb (left arm circumference was 28.5 cm and right arm circumference was 30.5 cm) and left lower limb (left thigh circumference was 53 cm and right thigh circumference was 46.4 cm) with prominent non-pitting pretibial edema were detected on his physical examination. White blood cell count (WBC) was 22.8 ×10⁹/L with 26.4% neutrophils, 11.2% lymphocytes and 60% eosinophils, hemoglobin was 14.6 g/dL and erythrocyte sedimentation rate (ESR) was 3mm/h. Stool specimens were examined for
ova and parasites, results of renal, thyroid and liver function tests were negative and electrolytes were normal. Results were also negative for RF, C-reactive protein and ANA. Results of chest radiography, esophagography, abdominal ultrasonography and pulmonary function studies were all within normal limits. Bone marrow aspirate smears showed 60% eosinophils. A full thickness biopsy of the left calf revealed active fasciitis (Figure 1A). Magnetic resonance imaging of the lower limbs revealed that the left limb muscle group was thicker than the right (Figures 2A and B). The diagnose of EF was established with these clinical and laboratory findings. Symptoms disappeared completely after a few days of treatment with 1mg/kg/day oral methyl-prednisolone.

**Patient-2**

A 63-year-old Turkish male admitted to our clinic with edema, erythema, pain and itching on his upper and lower extremities for 10 days, that started after strenuous physical activity when he began working with an axe in the forest. There mobile, palpable lymph nodes were found in the right anterior cervical (2×1cm), left submandibular (3×1cm) and left submental (2×2cm) regions of his body. Both shoulder and elbow joints were warm, their range of movement, the flexion and extension of the wrist were limited, and both knee joints were warm and painful on flexion. WBC count was 12.9 ×10^9/L with neutrophils 5.3 ×10^9/L, eosinophils 4.9 ×10^9/L (37.9%), ESR 98mm/h, ANA was positive and RF was 0.59 IU/L. Peripheral blood smears showed 34% eosinophils. Examination of stool specimens was negative for ova and parasites. The electrolytes, renal, thyroid and liver function values were all within normal limits. Results of chest radiography, abdominal ultrasonography and pulmonary function studies were all within normal limits. Mild hepatomegaly was detected on abdominal ultrasonographic examination (165mm). A full thickness biopsy revealed active fasciitis (Figure 1B). The diagnose of EF was established with these clinical and laboratory findings. His symptoms improved completely after a few days of treatment with 1mg/kg/day oral methyl-prednisolone.
Discussion

EF is an uncommon disease and only a few hundred cases was reported in the literature. The disease is characterized by acute or subacute symmetric swelling of the skin and subcutaneous tissues. The forearms, flanks and upper legs are commonly affected, whereas the hands and face are usually spared [4]. However, our first case had asymmetric edema and pain of his right limb, shoulder and face, which differed from other cases reported in the literature. The etiology of EF is unknown. Possible causes suggested include strenuous exercise, initiation of hemodialysis and infection with Borrelia Burgdorferi [1, 5, 6]. In addition, some drug exposures have been implicated. Cutaneous side effects following simvastatin treatment including the development of EF have been well documented [7]. There was no obvious cause for the first presented case but strenuous exercise appeared to be the triggering factor for the second patient. There was no suspicion of relevant environmental or toxic exposure in either of the patients. Paraneoplastic disease, progressive systemic sclerosis and infection with B. burgdorferi were excluded.

The majority of patients with EF have a peripheral blood eosinophilia during the acute phase of the disease. In one series, 33 out of 52 patients had eosinophilia. Elevated ESR (29%) and polyclonal hypergammaglobulinemia (35%) may also be found [8]. ANA positivity have not been reported previously in EF with any consistency [3]. RF is almost always negative. Both our cases had hypereosinophilia and the second case had a increased RF (0.59 IU/l) and positive ANA test. Definitive diagnosis requires histopathological examination from a full-thickness (epidermis to muscle) biopsy [9]. The biopsy results of both our cases were consistent for EF on histopathological examination. Spontaneous remission rate was 10 to 20% in cases of EF at the time of presentation or relapse after discontinuing corticosteroid therapy [10]. There was a history of spontaneous remission in our first case.

In one serie, hematologic disorders other than eosinophilia were present in five out of 52 patients (10%) [8]. Hematologic abnormalities that have been described in association with EF include aplastic anemia, acquired amegakaryocytic thrombocytopenia,
myeloproliferative disorders, myelodysplastic syndromes, lymphoma, leukemia and multiple myeloma [8]. There was no hematologic abnormality in our cases of EF. The presence of lymphadenopathy is unusual. Ten reported cases of EF with enlarged lymph nodes were identified previously. Six of these patients had lymphoma and four had reactive lymphadenopathy [11]. The second presented case had cervical, submandibular and submental mobile lymphadenopathies with an enlarged liver and with no haematologic disease.

Two cases of EF with rheumatoid arthritis (RA) have been reported, but diagnosis of RA had established in these patients before the diagnosis of EF [12, 13]. The second presented patient’s symptoms at first aforementioned to RA. However, since the symptoms began shortly after strenuous exercise which is not typical for RA, eosinophilia and histopathological evaluation revealed the accurate diagnose. Furthermore, the symptoms did not meet RA criteria. Most EF patients with arthritis complaint from morning stiffness and exhibit changes on joint radiographs similar with RA [8]. This condition may lead to a misdiagnosis.

In conclusion, EF may present with various symptoms. When patients exhibit eosinophilia, arthralgia and myalgia, EF should be considered among the possible diagnoses. It is notable that the first patient described in this case report also displayed unusual features including a high eosinophil count and asymmetrical presentation.
Abbreviations
EF: Eosinophilic fasciitis
RA: Rheumatoid arthritis
ANA: Antinuclear antibody
ESR: Erythrocyte sedimentation rate

Consent
Written informed consent was obtained from the patient for publication of this case report and accompanying image. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no competing interests.

Author’s contribution
RD, SP, SA, DA, SAZ and SO contributed writing the article and review of the literature as well as undertaking a comprehensive literature search; SA, SP, AA contributed design and manuscript preparation. CAO and IK provided the radiological information.
References


**Figure legend**

**Figure 1**: A mixed type infiltration of eosinophils and other inflammatory cells in muscle and fat tissue (A) Patient 1 and (B) Patient 2. Hematoxylin and eosin stain, magnification ×200.

**Figure 2**: Coronal and axial magnetic resonance images of patient 1. The left extremity is thicker than the right extremity as shown on (A) the coronal and (B) the axial magnetic resonance images.