



Eosinophilic Fasciitis Responds Well to Steroids and Methotrexate

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ABSTRACT

Eosinophilic fasciitis (EF) is a rare systemic inflammatory disease with an unknown etiology. Making a diagnosis in such a case is always a challenge as it is a rare disease and mimics scleroderma and scleroderma-like syndrome but should be kept in mind as it carries a high mortality. Furthermore, it is a treatable disease. Here, we report a 41-year-old woman who presented to the rheumatology clinic at the Royal Hospital, Muscat, Oman, with a one-month history of bilateral swelling of the forearms along with skin tightness and fingers contraction. Her history and physical examination along with histopathological examination and magnetic resonance imaging findings were consistent with EF. She showed an excellent response to steroids and methotrexate which is not a combination therapy that has been tried or mentioned previously.

Eosinophilic fasciitis (EF) is a rare systemic inflammatory disease with unknown etiology characterized by symmetrical swelling and induration of the skin, sparing the distal parts of the arms and/or legs, evolving into a scleroderma-like appearance, accompanied by peripheral blood eosinophilia. The diagnosis is further confirmed by a full-thickness skin biopsy and/or magnetic resonance imaging (MRI). Corticosteroid treatment remains the standard therapy, either alone or with an immunosuppressive drug.¹

CASE REPORT

A 41-year-old woman with asthma (well-controlled on inhalers), hypothyroidism (controlled on thyroxin), and gastroesophageal reflux disease presented to the rheumatology clinic at the Royal Hospital with a one-month history of bilateral swelling of the forearms with skin tightness and fingers contraction. She had no constitutional symptoms or history of Raynaud's phenomena, weight loss, or change in her bowel habits. Physical examination revealed edema and hardening of the subcutaneous tissue of the forearm. The skin of both forearms showed a linear depression along the course of the superficial veins consistent with groove sign.

She was unable to flex or extend her fingers and to make a fist or hold objects well. The skin over her fingers and palms was normal. Her face was unaffected. There were no clinical features suggestive of malignancy or infection. Laboratory tests revealed raised eosinophil count of $1.8 \times 10^9/L$ (normal range $0-0.5 \times 10^9 g/L$). Her level of C-reactive protein was mildly raised; creatine kinase and erythrocyte sedimentation rate (ESR) were normal. Rheumatoid factor, anti-nuclear antibody, and extractable nuclear antigen and lactate dehydrogenase were negative. Full-thickness biopsy of the skin and muscles of the forearms showed inflammatory process involving the interstitial tissue in and around the skeletal muscle along with occasional muscle necrosis and some regenerative fibers with an increased number of eosinophils in the fascia fibroconnective tissue [Figure 1 a-f], which confirmed EF. Contrast MRI revealed extensive bilateral enhancing thickened fascia between the muscles of the forearm [Figure 1 g-i]. She was started on oral prednisolone 0.75 mg/kg for four weeks, which was subsequently slowly tapered. She made a remarkable response with reduced limb swelling and normal mobility. Unfortunately, the disease relapsed on tapering and high dose prednisolone was restarted along with adding oral methotrexate 20 mg per week. Her disease responded well to treatment; however, she

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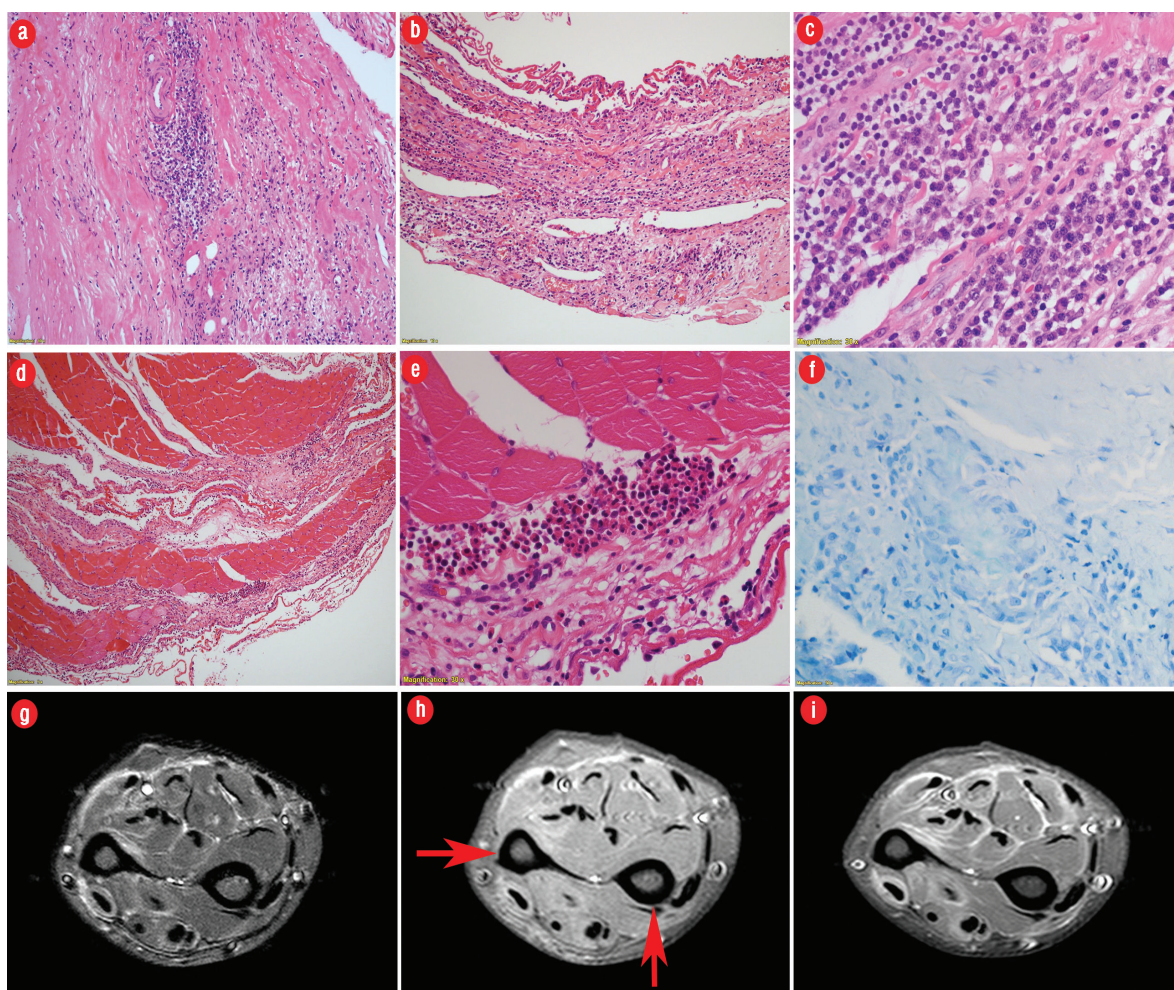


Figure 1: (a) Hematoxylin and eosin (H&E) staining of fascia showing perivascular and interstitial chronic inflammation and fibrosis (magnification = 200 ×). (b) H&E staining showing intense lamellar chronic inflammatory reaction (magnification = 200 ×). (c) H&E staining showing dense chronic inflammation including numerous plasma cells, lymphocytes, and occasional macrophages (magnification = 600 ×). (d) H&E staining showing secondary involvement of skeletal muscle which shows few pale degenerate myofibers and extensive perimysial infiltration by chronic inflammatory cells (magnification = 100 ×). (e) H&E staining of skeletal muscle showing perimysial eosinophilic microabscess formation (magnification = 200 ×). (f) Ziehl–Neelsen staining was negative for acid-fast bacilli in granuloma (magnification = 600 ×). (g) Axial fat-suppressed, T2-weighted fast spin-echo MRI reveals markedly increased signal intensity within superficial and deep fascial layers and mildly increased T2 signal intensity within superficial muscle fibers adjacent to fascia. (h) Axial fat-suppressed T1-weighted spin-echo MRI shows prominent superficial and deep fascial thickening (arrows) with slightly increased signal intensity relative to muscle. (i) Axial enhanced, fat-suppressed, T1-weighted spin-echo MRI revealed intense fascial enhancement corresponding to locations of T2 signal abnormality.

was lost to follow-up and stopped the medication resulting in recurrence of her disease.

DISCUSSION

The etiology of EF is unknown. It has been reported after localized trauma, intense exercise, autoimmune disease (such as thyroid disease), and infection with *Borrelia burgdorferi*.^{2–4} EF may be associated with

hematological disorders like aplastic anemia.^{5–9} It has also been reported in association with solid organ tumor, and post-allogeneic bone marrow transplant.¹⁰ Bronchial and allergic asthma has been reported in the literature with EF.¹¹

EF affects the limbs and spares the face and hands, it usually begins with painful swelling, and tightening of the limbs, which within weeks to months progresses to fibrosis leading to flexion

contractures and limited mobility.¹ Groove sign (a depression along the course of the superficial veins seen best when elevating the affected limb) is typically found in EF, and its presence distinguishes EF from scleroderma in the absence of Raynaud's phenomenon.¹²

Peripheral blood eosinophilia is seen in the majority of patients with EF, though not necessary for making the diagnosis. Around half of patients have elevated ESR and hypergammaglobulinemia. Serum anti-nuclear antibodies are not present.

A full-thickness biopsy (including skin, fascia, and muscle) is the gold-standard test for diagnosing EF.^{13,14} Involvement of the deep dermis and fascia is typical of the disease and is useful in excluding disease mimickers such as scleroderma and scleroderma-like syndromes. In the early stages of the disease edema of the deep subcutaneous tissue and fascia along with lymphocytic, plasma cell, histiocytic and eosinophilic infiltrates is usually seen. Later, collagen thickening and sclerosis of the deep dermis and fascia occurs with disappearance of the inflammatory cell infiltrates. Thickening and inflammation can also be seen in the adjacent muscle.

According to a recent study, EF may be histopathologically distinguished from localized scleroderma (morphea) based on helper T-cell (Th) subtype polarization where Th1/Th2 and the presence of Th17+ cells were significantly higher in EF compared to morphea, while the CD4/CD8+ T-cell ratio was significantly greater in morphea.¹⁵ If the biopsy is not possible to obtain or inconclusive, then MRI of the affected area may be used to confirm fascial inflammation.¹⁶

Due to the rarity of the disease, there is limited evidence in the therapeutic efficacy in treating this disease. The treatment is mainly dependent on expert opinion, case reports and case series. Steroids at a high dose (1–1.5 mg/kg) remain the first-line treatment.¹⁷ The issue with steroid is its complications on the short- and long-term period of treatments. Hence, there is a need to introduce other immunosuppressive medications such as steroid-sparing agents. Methotrexate was highly used in some case series and as intuitive because of its known safety profile in rheumatic disease.¹⁸

Other treatment possibilities that have been used in the treatment of EF are mycophenolate mofetil, hydroxychloroquine, sulfasalazine, and azathioprine.¹⁹ Biological agents like infliximab and

rituximab have also been used in few cases refractory to the usual treatment with good response.^{20,21} Surgical intervention is sometimes needed in cases where the response to steroid is inadequate or treatment delays for release of joints contractors.²²

In our case, there was a clear response to the high dose steroid, which was working well as induction for the therapy and the methotrexate was used to maintain the disease remission. However, the disease relapsed upon treatment discontinuation by the patient. This emphasizes the need for long-term follow-up of these patients by rheumatologist and treatment tapering and cessation should be done carefully.

CONCLUSION

EF is a rare systemic inflammatory disease with unknown etiology. Clinical examination is necessary for the diagnosis of EF in the presence of peripheral eosinophilia. It is further confirmed by histopathological examination. Systemic glucocorticoids are the first-line treatment. In relapsing or resistant cases, immunosuppressive drugs can be used.

Disclosure

The authors declared no conflicts of interest.

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