Eosinophilic fasciitis (Shulman's disease)

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Abstract

Eosinophilic fasciitis is an uncommon connective tissue disorder characterized by symmetrical thickening and hardening of the skin and underlying fascia, mainly involving the extremities. Usually it is not associated with internal organ involvement unlike other fibrosing disorders. It is associated with peripheral eosinophilia, elevated inflammatory markers, and hyper-gammaglobulinaemia. Biopsy findings are typical. The etiology and pathogenesis are poorly understood. Associations with statin therapy, preceding extreme exertion, insect bite and borreliosis are reported.

As this is a very rare condition guidelines for management are currently not available. However corticosteroids remain the mainstay of treatment.

This case report describes a 30 year old female with clinical findings of eosinophilic fasciitis. Diagnosis was proved by histology and MRI findings. Her condition improved considerably with steroid therapy and physiotherapy.

Case report

A 30 year old female presented with indurations and thickening of skin on both arms of five months duration. She initially noticed painful swelling on the left forearm that gradually became pigmented and thickened. Similar involvement both forearms and arms were seen later. Cubital fossae and digits were spared. There was no history of trauma, any significant drug intake or travel abroad.

On examination, she looked well; her pulse rate 80/min and blood pressure was 110/70mmhg. She was not pale or icteric. Skin on both arms and forearms was thickened and indurated with mild pigmentation. Typical venous furrowing, the 'groove sign' was present (Figure 1). Changes were more marked on the left side. The hands and the cubital fossa were spared. Joint movements and muscle power was normal on both upper limbs. Systemic examination was normal.

Investigations revealed normochromic and normocytic anaemia (Hb 10 mg/dl), WBC was 5800 with eosinophil of 14% (1100) with an ESR of 22. Renal function, liver function and serum proteins were normal. Her CPK, serum calcium, uric acid and thyroid function were normal. ANA and anti- Scl 70 were negative.

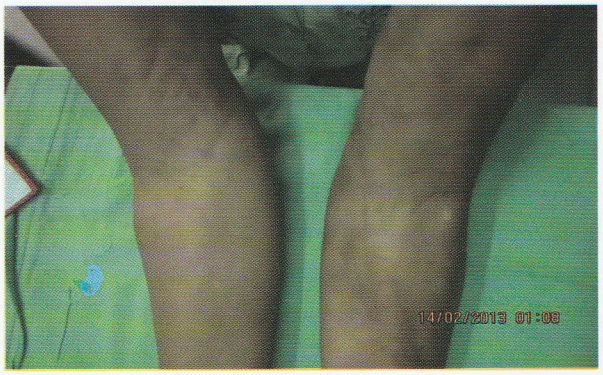

Figure 1a.

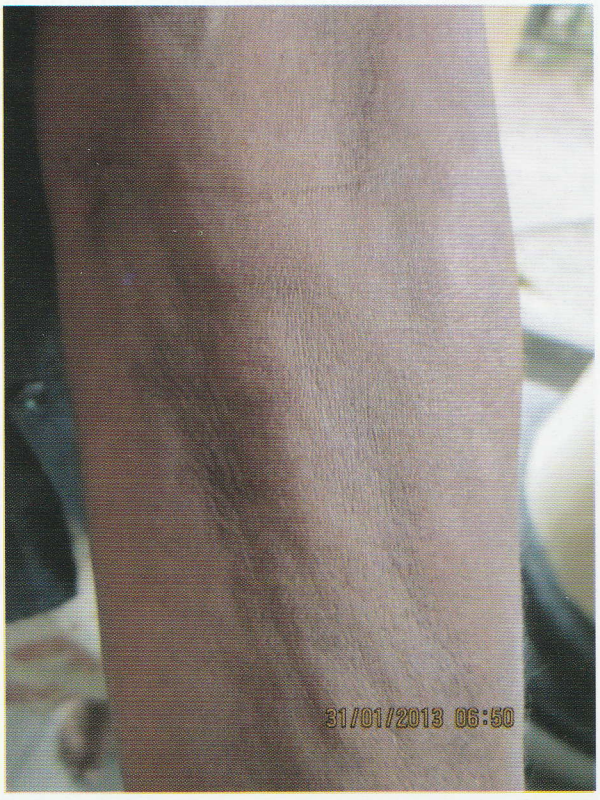

Figure 1b.

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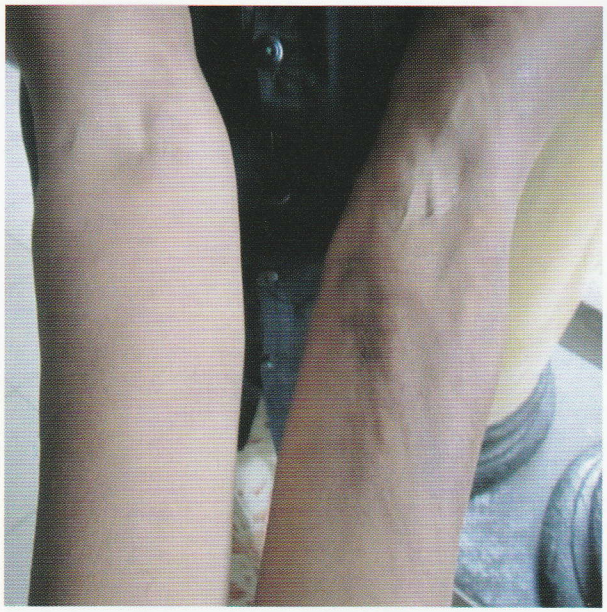

Figure 1c.

Fig. 1a, b and c: *Eosinophilic fasciitis with typical groove sign.*

Deep incisional skin biopsy from the arm showed thickened collagen bundles and eosinophils in the upper dermis with chronic inflammatory cell infiltrate between the collagen and in the fascia and between the muscles (figure 2a and b).

MRI scan of the arm showed mild thickening of superficial and deep fascia on T1 and increased signal intensities with variable enhancement on T2 suggestive of fasciitis.

After treatment with methylprednisolone eosinophil count reduced to 500.

Further investigations were done to exclude any associated conditions. Urine Bence Jones proteins was negative and serum protein electrophoresis did not reveal any monoclonal bands. 2D Echo and lung function test were normal.

Diagnosis of eosinophilic fasciitis was made and she was started on prednisolone 20mg and azathioprine 50mg daily. However she developed reaction to azathioprine and it had to be stopped. Following this she was started on dexamethasone intravenous monthly pulses. In between pulses daily prednisolone and hydroxychloroquine were given. Physiotherapy also was started. After two pulses, the disease progression has halted and she felt better.

However she defaulted after 9 pulses and was readmitted with exacerbation of symptoms over upper limbs and was restarted on monthly steroid pulses and weekly methotrexate. Currently her disease is continuing to improve.

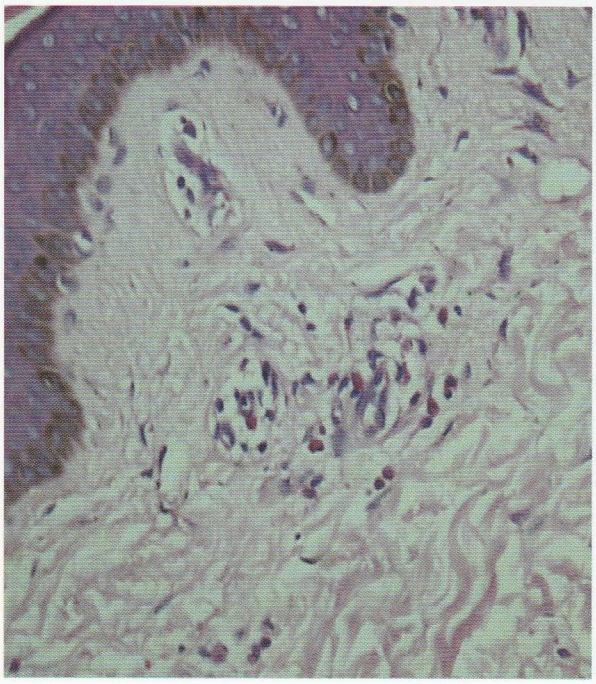

Figure 2a: *Thickened collagen bundles and eosinophils in the upper dermis.*

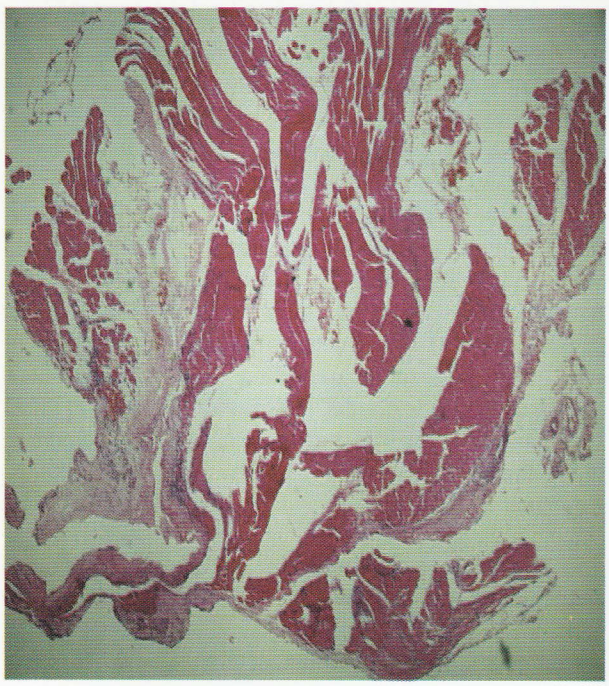

Figure 2b: *Chronic inflammatory cell infiltrate between the collagen and in the fascia and between the muscles.*

Discussion

Eosinophilic fasciitis (Shulman's syndrome) is a rare disease of unknown etiology, characterized by symmetrical swelling and skin induration of limbs, accompanied by peripheral blood eosinophilia. The skin changes typically evolve through stages. It starts symmetrically with an edematous diffuse phase, which is followed by a distinct *peau d'orange* appearance of the skin, resulting in induration and characteristic venous furrowing, 'groove sign' along the superficial veins[5,6]. It typically involves the extremities but spares the fingers, toes and the face. In contrast to scleroderma, it has distinctive pattern of skin involvement that spares the digits, involves the fascia rather than dermis and is not accompanied by Raynaud's phenomenon[7]. Other differential diagnosis is scleredema of Buschke and eosinophilia myalgia syndrome associated with L-Tryptophan ingestion and morphoea.

Haematological abnormalities include peripheral eosinophilia, high ESR and hypergammaglobulinaemia. However the changes are transient (as in our patient) and do not correlate with disease activity[8].

Investigation of choice is full thickness skin biopsy that includes skin, fascia and superficial muscle. The histological hallmark is fascial fibrosis. Early in the course of the disease the deep fascia and lower subcutis are oedematous and infiltrated with lymphocytes, plasma cells, histiocytes and eosinophils. In a later stage the dermis and the subcutis become thickened, collagenised and sclerotic[9].

MRI is an alternative method of diagnosing eosinophilic fasciitis in addition it is also a marker of disease activity and can be used to monitor treatment response. The findings are those of abnormal fascial signal intensity and enhancement, both of which are directly proportional to the disease activity.

Carpel tunnel syndrome, flexion contractures and impaired mobility are common complication. Low-grade myositis with normal creatinine kinase and arthritis may develop. Systemic involvement is rare, with isolated case reports of esophageal, pulmonary, neural and cardiac involvement. Association with hematological disease is well described with aplastic anaemia being commonly reported. Eosinophilic fasciitis is also reported in associated with thrombocytopenic purpura, myelodysplastic syndrome, myeloproliferative disorders, leukemia and lymphoma[11, 12].

The etiology of eosinophilic fasciitis remains unknown, however there are reports of causal relationship with preceding heavy exertion, ingestion of L-tryptophan, statins[13] and *borrelia burgdorferi*[14] infection.

The mainstay of treatment is high dose corticosteroid therapy. Treatment with steroids lead to a rapid fall in peripheral eosinophilia. However steroid refractory cases have been reported. Other immunosuppressive drugs such as cyclosporin, azathioprine, methotrexate and hydroxychloroquine and dapsone[15-16] are used either as a second line drug or steroid sparring agent with variable results. Recently antitumor necrosis factor alpha inhibitor, infliximab has been used for refractory cases[17].

A case of eosinophilic fasciitis, without any systemic involvement and managed with monthly dexamethasone pulse, hydroxychloroquine and methotrexate is being reported. Currently patient is showing favorable response.

References

1. Shulman LE. Diffuse fasciitis with hypergammaglobulinemia and eosinophilia: a new syndrome? *J Rheumatol* 1974; **11**: 569-70.
2. Lebeaux, David, and Damien Sène. Eosinophilic fasciitis (Shulman disease). *Best Practice & Research Clinical Rheumatology* 2012; **26**: 449-58.
3. Falanga V, Medsger TA Jr. Frequency, levels, and significance of blood eosinophilia in systemic sclerosis, localized scleroderma, and eosinophilic fasciitis. *J Am Acad Dermatol* 1987; **17**: 648-56.
4. Bischoff L and Derk CT. Eosinophilic fasciitis: demographics, disease pattern and response to treatment: report of 12 cases and review of the literature. *International Journal of Dermatology* 2008; **47**: 29-35.
5. Tsoi, Ka Lai, *et al.* Eosinophilic fasciitis. *BMJ case reports* 2012 (2012): bcr20126158.
6. Pinal-Fernandez, Iago, *et al.* Groove sign in eosinophilic fasciitis. *Lancet* (2014).
7. Rodnan GP, DiBartolomeo A, Medsger TA, Jr. Proceedings: eosinophilic fasciitis. Report of six cases of a newly recognized scleroderma-like syndrome. *Arthritis Rheum* 1975; **18**: 525.
8. Carneiro, Sueli, *et al.* Eosinophilic fasciitis (Shulman syndrome). *Cutis* 2005; **75**(4): 228-32.
9. Barnes, Leon, *et al.* Eosinophilic fasciitis. A pathologic study of twenty cases. *The American Journal of Pathology* 1979; **96**: 493.

10. Moulton, Stacy J, *et al.* Eosinophilic fasciitis: spectrum of MRI findings. *American Journal of Roentgenology* 2005; **184**(3): 975-78.

11. Adele de Masson, MD, *et al.* Severe Aplastic Anemia Associated With Eosinophilic Fasciitis. *Medicine* 2013; **92**.

12. Haddad, Housam, *et al.* Eosinophilic fasciitis as a paraneoplastic syndrome, a case report and review of the literature. Hematology/oncology and stem cell therapy (2014).

13. Choquet-Kastylevsky, Genevieve, *et al.* Eosinophilic fasciitis and simvastatin. *Archives of internal medicine* 2001; **161**(11): 1456.

14. Hashimoto Y, *et al.* Polymerase chain reaction of Borrelia burgdorferi flagellin gene in Shulman syndrome. *Dermatology* 2009; **192**(2): 136-9.

15. Lebeaux, David, *et al.* Eosinophilic fasciitis (Shulman disease): new insights into the therapeutic management from a series of 34 patients. *Rheumatology* 2012; **51**(3): 557-61.

16. Valencia IC, Chang A, Kirsner RS, Kerdel, Francisco A. Eosinophilic fasciitis responsive to treatment with pulsed steroids and cyclosporine. *International Journal of Dermatology* 1997; **38**: 367-72.

17. Smith, Lynsey C, and Neil H. Cox. Dapsone treatment for eosinophilic fasciitis. *Archives of Dermatology* 2008; **144**(7): 845-7.