A case of eosinophilic fasciitis and generalized morphea overlap

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Abstract

A 60-year old man developed skin hardening and edema on his extremities. Although he had been treated with oral prednisolone at another hospital, skin stiffness relapsed during tapering of prednisolone. At the initial visit to our department, physical examination showed skin hardening of the extremities and also symmetric erythematous macules on the back. Histological examination revealed fasciitis on the forearm and morphea on the back. Eosinophilic fasciitis is occasionally associated with morphea. However, cases of concurrent eosinophilic fasciitis and generalized morphea are rare. In the present case, CD34 was differentially expressed in both lesions, suggesting eosinophilic fasciitis and morphea are separate diseases with different origin of mesenchymal cells.

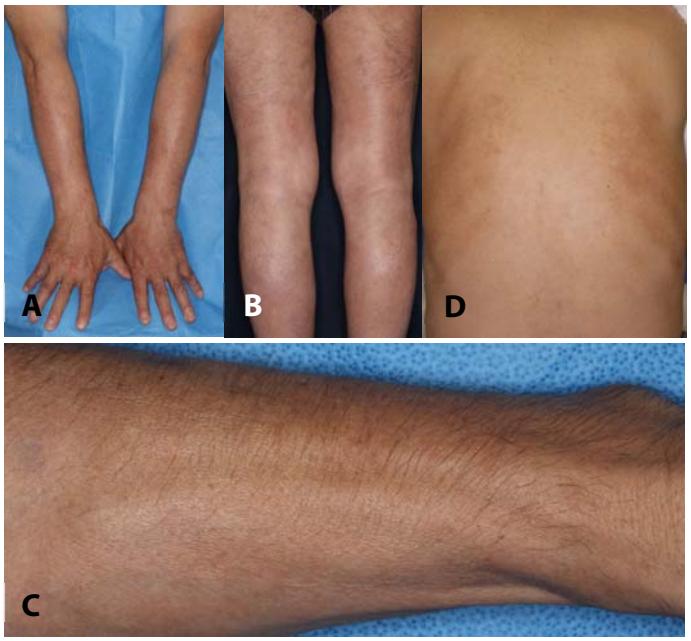
Keywords: eosinophilic fasciitis, generalized morphea, CD34

Introduction

Eosinophilic fasciitis is occasionally associated with morphea. However, cases of concurrent eosinophilic fasciitis and generalized morphea are rare. We herein describe a concurrent case of eosinophilic fasciitis and generalized morphea.

Case Synopsis

A 60-year-old man was referred to our hospital complaining of skin hardening and edema of his extremities. He had pruned plants 10 months prior to presentation. One week following the pruning, he experienced pain in his left shoulder and edema in the extremities. He noted limited range of movement in the joints. At initial presentation in his local hospital, laboratory examination showed an elevated eosinophil subset, and he was diagnosed as having eosinophilic fasciitis. He was treated with oral prednisolone (20mg/day). However, skin hardening and peripheral eosinophilia relapsed when the prednisolone was gradually decreased by a dose of 2.5mg/day. Physical examination showed skin hardening of the upper and lower extremities (**Figure 1A**, **B)**. The groove sign was observed in the



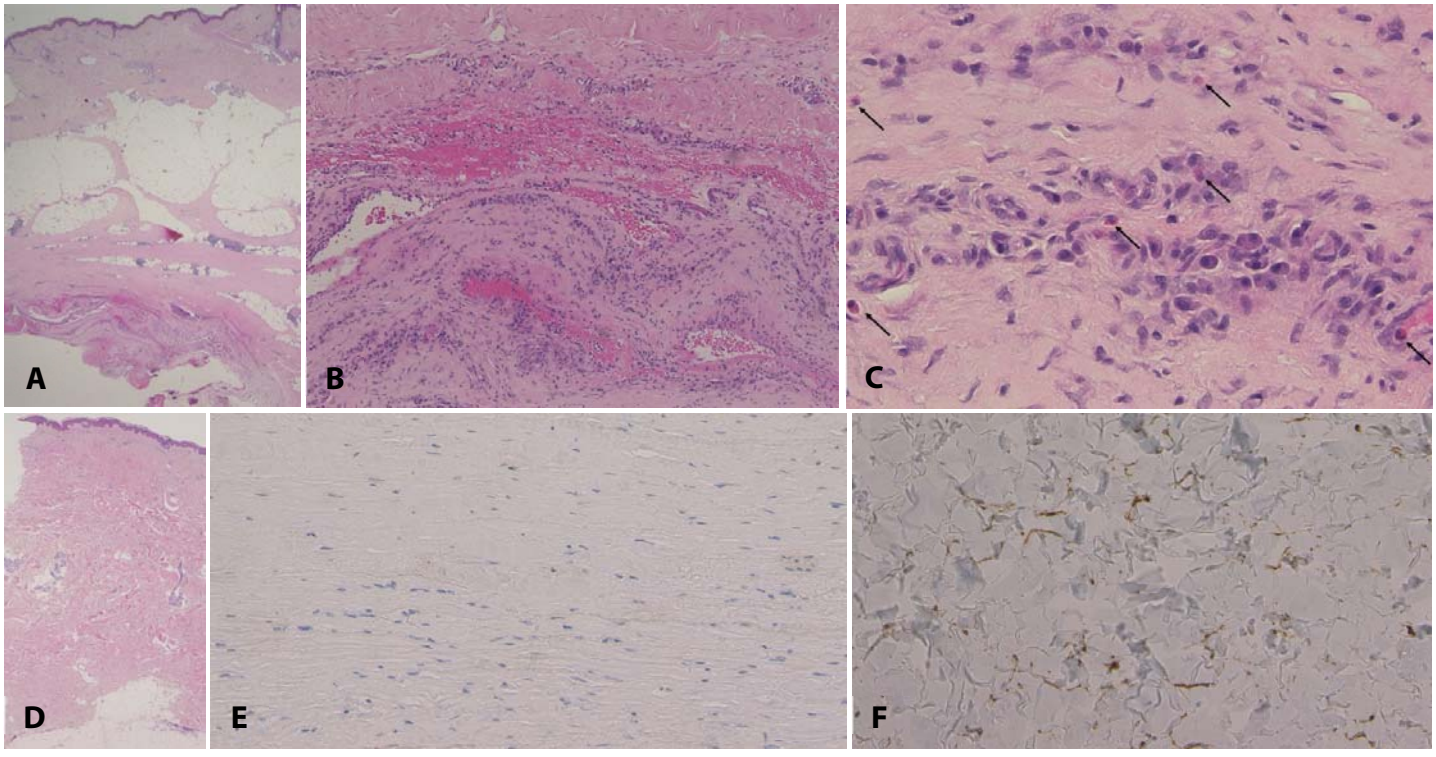
Figures *1. Clinical features showing induration of the skin of the **A)** upper, and **B)** lower limbs. **C)** Groove sign was observed on the forearm. **D)** Brownish erythema was present on the bilateral sides of the back.*

forearm (**Figure 1C)**. Neither sclerodactyly nor Raynaud phenomenon was recognized. Further examination revealed symmetric erythematous macules on the back, but without hardening of the skin (**Figure 1D)**.

Laboratory examination showed a slightly elevated eosinophil subset (7%) and increased C-reactive protein levels (1.14mg/dl). However, antinuclear antibody, anti-dsDNA and creatine kinase levels were normal. A biopsy specimen taken from the left forearm revealed thickened collagen bundles in the dermis and subcutaneous tissues with focal lymphocyte infiltrates in the subcutis and thickened fascia involvement (**Figure 2A)**. There were perivascular and interstitial infiltrates of lymphocytes, plasma cells, and a few eosinophils in the thickened fascia (**Figures 2B, C)**. The underlying skeletal muscle was not involved. Another specimen taken from the patient's back showed that the collagen bundles of the reticular dermis were thickened (**Figure 2D)**. A diagnosis of eosinophilic fasciitis/generalized morphea overlap was made based on the clinical, analytical, and histopathological findings. Immunohistochemistry results showed a focal loss of CD34 expression in the fascia of the area of eosinophilic fasciitis, whereas abundant expression of CD34 was observed in the morphea lesion (**Figure 2E**, **F)**. The dose of prednisolone was escalated up to 40mg/day and thereafter gradually tapered every one or two months. Currently, the patient is controlled with 15mg prednisolone daily, which is still being gradually tapered.

Case Discussion

Eosinophilic fasciitis is occasionally induced by vigorous exercise as well as trauma, leading to the hardening of the skin and limited range of movement in the joints. Eosinophilic fasciitis is often regarded to belong to the severe end of the morphea spectrum [1] and an association with morphea has been reported in 19-41% of eosinophilic fasciitis



Figures *2. A)* *A biopsy specimen from the forearm shows fibrosis of deep dermis and subcutis, and thickened muscle fascia with inflammatory cell infiltrates. H&E, 40×.* ***B, C)*** *Higher magnification shows that cellular infiltrates in the thickened fascia are composed of lymphocytes, plasma cells, and eosinophils (arrow). H&E, 200×. 400×.* ***D)*** *A second biopsy from the back shows thickened collagen bundle with deposition of homogeneous materials in the whole dermis. H&E, 40×.* ***E)*** *CD34 expression is absent in the fascia of eosinophilic fasciitis (forearm), 200×.* ***F)*** *whereas it is abundant in the morphea (back). 400×.*

Table 1. *Seven cases of concurrent eosinophilic fasciitis and generalized morphea.*

Case	Age Sex	Involved site of eosinophilic fascilitis	Involved site of generalized morphea	Preceding onset	Duration*	Therapy
1 [5]	25M	Extremities, trunk, scalp	Left thigh	Unknown	—	Prednisolone
2 [6]	50F	Chest, abdomen, breast, proximal portions of the arm and legs	Upper extremities	Generalized morphea	12Mo	Prednisolone, etanercept methotrexate
3 [7]	44F	Forearms, legs	Back, chest, abdomen, proximal extremities	Eosinophilic fasciitis	12Mo	Prednisolone
4 [8]	66M	Upper limbs, chest	Tibialis anterior	Unknown	—	Prednisolone
5 [9]	61M	extremities	Abdomen, trunk	Unknown	—	Prednisolone
6 [10]	24M	Arms, legs, trunk	Chest, upper back	Eosinophilic fasciitis	6Yr	Prednisolone, azathioprine, mycophenolate mofetil, cyclophosphamide, cyclosporine, rituximab
Present case	60M	Extremities	Back	Unknown	—	Prednisolone

** Mo-months; Yr-years.*

patients [2-4]. In contrast, generalized morphea is rarely seen, and to our knowledge only seven cases of concurrent eosinophilic fasciitis and generalized morphea have been reported in the English literature [5-10]. The patient characteristics of these reported cases are shown in **Table 1**. The average age at occurrence was 47.1 years old and men were predominant (5:2 male to female ratio). In all cases, extremities, a common site of eosinophilic fasciitis, were involved. Generalized morphea occurred in the trunk in four cases. Eosinophilic fasciitis was diagnosed prior to generalized morphea in two cases. The onset period was between twelve months and six years. In all cases, treatment was started with prednisolone from small to moderate amounts. Two cases underwent additional treatment with immunosuppressive drugs.

Although generalized morphea and eosinophilic fasciitis are believed to be different diseases, they are similar in presentation and are sometimes difficult to differentiate from each other. Previous studies showed that CD34 expression decreased or disappeared in the lesional skin of scleroderma, including morphea [11], which is inversely related with the extent of morphea [12]. CD34 is a marker of dermal dendritic cells and expression of CD34 and type I collagen suggest fibrocytes in the peripheral circulation. Fibrocytes are induced by transforming growth factor-β to express α-smooth muscle actin, a myofibroblastic property. A recent paper demonstrated a further decreased CD34 expression in the fascia of eosinophilic fasciitis, compared with morphea profunda [13], suggesting that the two diseases have different etiologies. We compared the local CD34 expression of biopsied tissue samples from different sites, which revealed that CD34 expression disappeared in the fascia of eosinophilic fasciitis, whereas it was observed in the morphea lesion, consistent with previous reports.

Conclusion

Our case showed different expression of CD34 between eosinophilic fasciitis and morphea lesions, suggests that both disorders possess separate phenotypes with different origin of mesenchymal cells. Alternatively, the possibility that CD 34 expression simply reflects the intensity of skin fibrosis cannot be excluded. Further studies are needed to clarify the causative mechanisms of eosinophilic fasciitis and deep morphea.

Potential conflicts of interest

The authors declare no conflicts of interests.

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