Clinicopathologic and immunophenotypic features of eosinophilic fasciitis and morphea profunda: A comparative study of 27 cases

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Background: Eosinophilic fasciitis (EF) and morphea profunda (MP) are inflammatory and sclerosing disorders of the subcutis that can exhibit clinical and pathologic presentations that overlap.

Objective: To identify clinicopathologic features that can be used to distinguish EF from MP.

Methods: We performed a retrospective review of 16 patients with EF and 11 patients with MP. Hematoxylin-eosin, CD123, CD34, and Verhoeff-Van Gieson stains were evaluated on skin biopsies that included the fascia.

Results: EF patients were more likely than MP patients to be men ($P = .047$), have forearm involvement ($P = .003$), and have peripheral eosinophilia ($P < .01$). Compared with MP patients, patients with EF were more likely to have fascia that contained eosinophils ($P = .003$), although eosinophils were absent in 3 (19%) patients with EF. Focal absence of CD34 staining was more prominent in the fascia of EF patients ($P = .04$). The extent of Verhoeff-Van Gieson staining did not differ between the 2 groups. Dermal sclerosis was not detected in many cases of EF and MP (56% and 36%, respectively).

Limitations: This was a retrospective study at a single institution.

Conclusion: Although EF and MP share clinical and pathologic features, our results indicate that the presence of eosinophils in the blood and fascia and focal loss of CD34 staining might be more suggestive of EF than MP. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2017.06.148.)

Key words: dermatopathology; eosinophilic fasciitis; eosinophils; histopathology; immunohistochemistry; morphea profunda; sclerosing disorder.

Eosinophilic fasciitis (EF) and morphea profunda (MP) are inflammatory and sclerotic disorders of the subcutis that exhibit overlapping clinical and pathologic presentations. There is controversy as to whether EF and MP are distinct disorders or whether they fall within a spectrum.

Abbreviations used:

EF:	eosinophilic fasciitis
IL:	interleukin
MP:	morphea profunda
TGF:	tumor growth factor

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Funding sources: Supported by the Department of Dermatology, Mayo Clinic, Rochester, Minnesota.
Conflicts of interest: None declared.
Previously presented: Data was presented as a poster at the American Society of Dermatopathology 53rd annual meeting in Chicago, Illinois, October 26-29, 2016.

Accepted for publication June 22, 2017.
Reprints not available from the authors.
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Published online August 30, 2017.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2017.06.148

EF is a rare disorder involving sclerosis first described by Shulman in 1974.[1] It is classically characterized by acute onset of cutaneous edema and induration, often following vibrational or other repetitive trauma.[1,2] Laboratory evaluation often reveals peripheral eosinophilia, hypergammaglobulinemia, and an elevated erythrocyte sedimentation rate. The typical histopathologic finding for EF is lymphoplasmacytic inflammation involving subcutaneous fat septa, fascia, and sometimes muscle. Eosinophils might be a component of the inflammatory infiltrate but are not necessary for diagnosis of EF. The dermis often appears spared[3-6]; however, morphea-like plaques have also been described in patients with EF.[2,7-9]

MP is a type of morphea that primarily affects the deep dermis and subcutaneous fat but can extend into the fascia and muscle. During the inflammatory stage, perivascular, interstitial dermal, and subcutaneous septal spaces exhibit lymphocytes, plasma cells, and sometimes eosinophils. During the sclerotic stage, there might be minimal inflammation.[10-13]

We sought to describe the clinicopathologic features that distinguished cases of EF from those of MP. The features evaluated included the $CD123^{+}$ plasmacytoid dendritic cell population, expression of CD34, and elastic fiber patterns.

CAPSULE SUMMARY

- Distinguishing between eosinophilic fasciitis and morphea profunda can be difficult due to their similar clinical and histopathologic features.
- Our results indicate that the presence of eosinophils in the blood and fascia and focal loss of CD34 staining might be more suggestive of eosinophilic fasciitis.
- Accurate diagnosis of these diseases is needed because they might exhibit differing clinical courses, prognoses, and responses to treatment.

MATERIALS AND METHODS

Study design

With the approval of our institutional review board, we retrospectively reviewed the electronic medical records of patients clinically diagnosed with EF and MP from January 1992 through November 2015. We searched our electronic pathology (CoPath) database for the terms "eosinophilic fasciitis," "deep morphea," "morphea profunda," and "scleroderma" and found 235 cases. We reviewed the clinical charts of the 235 cases without reviewing the pathology, and identified 16 patients with EF and 11 with MP who had clinical features that fit well with classical descriptions of these diseases recorded in the electronic medical records. To avoid circular reasoning, we did not consider the histopathologic diagnosis when selecting the cases for this study.

The clinical criteria used to select EF cases included acute onset, erythema, edema, induration, peripheral blood eosinophilia, elevated inflammatory markers, polyclonal hypergammaglobulinemia, and associated vibrational or strenuous exercise. The clinical criteria used to select MP cases included indolent onset of skin tightening and lack of clinical evidence of systemic sclerosis, sclerodermoid graft-versus-host disease, or EF.

We excluded patients with scleroderma and cases with ambiguous or overlapping clinical features. A board-certified dermatopathologist reviewed all available hematoxylin-eosin stained slides and excluded cases in which the biopsy specimen did not include the fascia.

Data collection

We collected data on patient demographics, clinical presentation, and laboratory data including peripheral blood eosinophilic count, erythrocyte sedimentation rate, serum protein electrophoresis, and antinuclear antibodies whenever available.

Histopathologic, histochemical, and immunophenotypic data

Hematoxylin-eosin stained sections were examined for the degree, nature, and distribution of inflammation; presence of eosinophils, plasma cells, and edema in the fascia; sclerosis; and eccrine trapping. Newly cut sections obtained from the formalin-fixed, paraffin-embedded tissue blocks were stained with CD34, CD123, and Verhoeff-Van Gieson. The slides were reviewed by a board-certified dermatopathologist (Dr Lehman) who was blinded to the clinical diagnoses.

Statistical analysis

Features of EF and MP were compared by using *P* values obtained from 2-sample t, Wilcoxon rank sum, chi-square, or Fisher's exact tests. Statistical analyses were performed with statistical analysis software (SAS) package version 9.4 (SAS Institute Inc, Cary, NC). All tests were 2-sided and *P* values $<.05$ were considered statistically significant.

RESULTS

Patient demographics and clinical presentations

Twenty-seven patients were included in the study: 16 with EF and 11 with MP (Table I). The