Autoimmune comorbidities and antibody markers associated with eosinophilic fasciitis

To the Editor: Eosinophilic fasciitis (EF) is a rare connective tissue disorder characterized by edema, painful woody induration, and dimpling of the skin.[1] EF has previously been associated with other autoimmune diseases such as Sjögren's disease and systemic lupus erythematosus.[2] The objective of our review was to examine the relationship between EF and reported autoimmune comorbidities and antibody markers.

The databases Embase and Pubmed were searched on January 16, 2022 for "eosinophilic fasciitis" or "Shulman disease". A total of 2196 studies were screened for inclusion, yielding 489 studies with 1703 total patients. The mean age of patients diagnosed with EF was 45.4 years old (range 1-87 years), and 43% were females. Moreover, 74.5% ($n = 444$) of patients had diffuse EF and 25.5% ($n = 152$) had localized EF with symptoms lasting an average of 11.4 months before EF diagnosis. EF was distinguished from deep morphea through confirmation with magnetic resonance imaging and ultrasound.

A total of 90 patients (5.3%, $n = 90/1703$) had reported autoimmune comorbidities. Among the specific autoimmune comorbidities reported (Table I), autoimmune thyroid disease (1.4%, $n = 23/1703$), Raynaud's phenomenon (1.1%, $n = 20/1703$), and rheumatoid arthritis (0.6%, $n = 10/1703$) were the most common. A total of 193 patients had reported positive antibody markers. Among the reported positive antibody markers (Table II), antinuclear antibodies (53%, $n = 103/193$), immunoglobulin G against Borrelia burgdorferi (52%, $n = 101/193$), and immunoglobulin M (IgM) (13% $n = 26/193$) were noted to have the greatest frequency of reports in cases. Of total patients with EF, inflammatory markers such as elevated erythrocyte sedimentation rate (ESR) was 16% ($n = 266$) and C reactive protein 7.3% ($n = 125$). Erythrocyte sedimentation rate and C reactive protein levels were a mean of 207.4 mm/h (SD = 13) and 54.3 mg/L (SD = 11), respectively. The mean eosinophil count was 3780 μL. A total of 142 patients had hypergammaglobinemia.

Mango et al[3] review of 89 patients with EF revealed 5.6% of patients with autoimmune comorbidities, similar to the 5.3% shown in our review. In

Table I. Autoimmune comorbidities associated with eosinophilic fasciitis

Characteristics	Data
Total no. of patients with EF	1703
No. of cases with reported sex	1452
Female, n (% of cases with reported sex)	733 (50)
Male, n (% of cases with reported sex)	719 (42)
Mean age at presentation in y (range)	45.4 (1-87 y)
Autoimmune comorbidities, n (%)	90 (5.3)
Autoimmune thyroid disease	23 (27.4)
Raynaud's phenomenon	20 (23.8)
Rheumatoid arthritis	10 (12)
Vitiligo	7 (8.3)
Psoriasis	5 (6)
Systemic lupus erythematosus	5 (6)
Autoimmune glomerulonephritis	4 (4.8)
Vasculitis	4 (4.8)
Type I Diabetes mellitus	3 (3.6)
Autoimmune hepatitis	3 (3.6)
Sjogren's syndrome	2 (2.4)
Sarcoidosis	2 (2.4)
Ankylosing spondylitis	2 (2.4)
Crohn's disease	2 (2.4)
Dermatomyositis	1 (1.2)
Bullous pemphigoid	1 (1.2)
Celiac disease	1 (1.2)
Pernicious anemia	1 (1.2)
Myasthenia gravis	1 (1.2)

EF, Eosinophilic fasciitis.

Table II. Antibody markers associated with EF

Characteristics	Data
Total no. of patients with EF	1703
Antibody markers reported, n (%)	193 (11.3)
Anti-nuclear antibody (ANA)	103 (42)
Immunoglobulin G (IgG)	101 (41.1)
Immunoglobulin M (IgM)	26 (10.6)
Rheumatoid factor (RF)	17 (7.0)
Immunoglobulin A (IgA)	11 (4.5)
Anti-dsDNA	9 (3.7)
Thyroglobulin	9 (3.7)
Anti-thyroid peroxidase (TPO)	8 (3.3)
Immunoglobulin E (IgE)	4 (1.6)
Anti-ssDNA	3 (1.2)
c-ANCA	3 (1.2)
Circulating immune complexes (CIC)	3 (1.2)
Anti-histone	2 (0.8)

ANA, Anti-nuclear antibody; *anti-ssDNA,* anti-single stranded DNA; *Anti-TPO,* Anti-thyroid peroxidase; *c-ANCA,* anti-neutrophil cytoplasmic antibodies; *CIC,* circulating immune complexes; *EF,* eosinophilic fasciitis; *IgA,* immunoglobulin A; *IgE,* immunoglobulin E; *IgG,* immunoglobulin G; *IgM,* immunoglobulin M; *RF,* rheumatoid factor.

comparison, while Raynaud's phenomenon was significantly reported in patients with EF (23.8%); we found autoimmune thyroid disease to be the most reported associated comorbidity (27.4%). Autoimmune conditions may be associated with EF, in particular our findings suggest autoimmune thyroid disease. The prevalence of autoimmune thyroid disease in 1703 individuals is 1.35% in comparison up to 10% of the population. The high positivity of antinuclear antibodies found in patients with EF, further indicates the possibility of an autoimmune reaction. While some experts have recommended a workup for undiagnosed hematological malignancies in patients with unexplained EF, autoimmune conditions can also be considered.[4]

Limitations include the possibility of missed studies or incomplete reporting of autoimmune comorbidities, associated antibody markers, and the exclusion of non-English language studies. Most notably, we are unable to determine how many patients were tested for autoimmune comorbidities and autoantibodies. This study highlights autoimmune comorbidities in 5.3% of patients with a diagnosis of EF, future large-scale prospective studies should further investigate the prevalence of autoimmune dysfunction associated with EF. Clinicians caring for patients with EF should incorporate these findings during discussions to ensure proper recognition and treatment of underlying autoimmune comorbidities that can often complicate EF.

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Conflicts of interest
None disclosed.

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