

CAPILLARY MICROSCOPY IN EOSINOPHILIC FASCIITIS

A Comparison with Systemic Sclerosis

MICHAEL B. ROZBORIL, HILDEGARD R. MARICQ, GERALD P. RODNAN,
STEPHANIA JABLONSKA, and GILES G. BOLE

Capillary microscopy was performed on 19 patients with eosinophilic fasciitis. These patients were compared with 13 individuals with progressive systemic sclerosis (scleroderma). Capillary patterns were normal in 16 of 19 (84%) eosinophilic fasciitis patients; 3 exhibited either borderline or nonspecific changes, and none showed a definite scleroderma pattern. In contrast, characteristic nailfold capillary changes, consisting of both dilatation and loss of capillaries, were present in 11 of 13 (85%) scleroderma patients; the remaining 2 showed scleroderma-type abnormalities of only 1 finger and were, therefore, classified as borderline. These results suggest that capillary microscopy may help to distinguish these 2 disorders.

Using widefield capillary microscopy, a characteristic pattern of nailfold vascular changes has been found in progressive systemic sclerosis (scleroderma, PSS) (1-7). These changes consist of dilated, often distorted capillary loops, areas of capillary dropout, and loss of the orderly appearance of the capillary bed (8). This pattern has been noted in over 80% of PSS patients (6,9). Similar changes may be seen in several other rheumatic conditions such as dermatomyositis and mixed connective tissue disease (overlap syndromes), especially when a component of PSS is present, but the frequency is much lower than in PSS.

Eosinophilic fasciitis (EF) is a recently recognized scleroderma-like disorder characterized by symmetric, often widespread inflammation and sclerosis of the deep fascia, subcutis, and dermis, chiefly affecting the extremities; on occasion the face and trunk are involved as well. The disorder typically commences with pain and swelling of the forearms, hands, legs, and feet. This is followed by evident inflammation and induration of the skin and subcutaneous tissues of these parts; striking contractures may develop in a period as short as a few weeks (10-16). Abnormal laboratory findings include peripheral blood eosinophilia, hypergammaglobulinemia, and elevated sedimentation rate. A full thickness biopsy from skin to muscle is diagnostic with findings of thickened, sclerotic dermis, subcutis, and fascia and infiltration with mononuclear cells, often with tissue eosinophils (12,13). Sclerodactyly, seen almost without exception in PSS, is often absent in EF; Raynaud's phenomenon and visceral involvement are distinctly unusual (16,17). Prognosis has generally been good with many patients responding to corticosteroids during the early,

From the University of Michigan Medical Center, Ann Arbor; Medical University of South Carolina, Charleston; University of Pittsburgh School of Medicine; and Warsaw Medical School, Warsaw, Poland.

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Michael B. Rozboril, MD: Fellow, Arthritis Division, University of Michigan Medical Center; Hildegard R. Maricq, MD: Professor of Research Medicine, Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina; Gerald P. Rodnan, MD: Professor of Medicine and Chief of the Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine; Stephania Jablonska, MD: Professor of Dermatology, Warsaw Medical School; Giles G. Bole, MD: Professor of Medicine and Chief of the Arthritis Division and Rackham Arthritis Research Unit, University of Michigan Medical Center.

Address reprint requests to Michael B. Rozboril, MD, Box 18, Kresge I, University of Michigan Medical School, Ann Arbor, MI 48109.

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Figure 1. Normal nailfold capillary pattern.

inflammatory stage; with time there is gradual resolution of induration and contractures.

Nailfold capillary changes have not been described in eosinophilic fasciitis. We performed nailfold capillary microscopy on 19 patients with EF to determine what changes, if any, were present in individuals with this disorder. Since at first glance the appearance of EF resembles that of PSS, we hoped to determine whether capillary microscopy could help differentiate these 2 disorders and resolve controversy concerning the relationship, if any, between EF and PSS.

PATIENTS AND METHODS

Patients. Thirty-six patients were examined at the following medical centers: University of Michigan, Ann Arbor, 20 patients; University of Pittsburgh, 8 patients; Medical University of South Carolina, Charleston, 3 patients; and Klinika Dermatologiczna, Warsaw, Poland, 5 patients. They were divided into the following groups: eosinophilic fasciitis: 19, progressive systemic sclerosis: 13, normal controls: 4.

The diagnosis of EF was made in all 19 patients by the presence of characteristic clinical findings in the skin and subcutaneous tissues, peripheral blood eosinophilia, and positive full thickness biopsies. Hypergammaglobulinemia and elevated sedimentation rates were variable and were not used as inclusion criteria. PSS was diagnosed by the presence of typical sclerodermatous skin changes over the fingers (10 of 13) or proximal to the metacarpophalangeal joints (7 of 13), and by Raynaud's phenomenon (13 of 13), digital pitting scars (3 of 13), and interstitial lung disease by radiographic examination or abnormal diffusing capacity of carbon monoxide (9 of 13). Four normal controls (personnel associated with the arthritis center, free of rheumatic disease) were included to provide additional photographs of nailfold capillaries. These were mixed with the patients'

photographs to improve the accuracy of the "blind" analysis of coded photographs. Information on the range of normal variations of the nailfold capillary bed is available from previous studies (18).

Technique. Observations and photography of the nailfold capillaries were performed using capillaroscopic technique as previously described (7,8). In addition to direct evaluation of patients by the authors (MBR, HRM, SJ), photographs of all patients examined at the Universities of Michigan and Pittsburgh (11 EF, 13 PSS, and 4 normal controls) were coded without diagnosis and sent to the second author (HRM) for "blind" evaluation and diagnostic interpretation. Eight digits from each patient were examined; photographs of at least 2 digits from each patient (most often the ring or little fingers) were submitted for analysis. When difficulties in interpretation or borderline abnormalities were seen in isolated photographs, pictures of other digits from the same patient were examined.

Findings were described as normal, definite scleroderma (SD) pattern, borderline SD, or nonspecific. A normal pattern (Figure 1) contains a uniform arcade of thin, hairpin shaped capillary loops along the edge of the nailfold and an even distribution of proximal capillaries (4,8). Enlargement of capillary loops, loss of capillaries, and disruption of the orderly capillary bed characterize the "SD pattern," so called because this group of abnormalities was observed in over 80% of progressive systemic sclerosis patients (8). As defined previously (8), at least 2 definitely enlarged capillaries per nailfold and at least 2 involved digits were necessary to place a patient in the "definitely abnormal" category (Figure 2). The borderline SD pattern included abnormalities confined to a single digit. A nonspecific pattern referred to findings such as increased tortuosity of vessels or increased variation in the caliber of otherwise normally shaped capillary loops (often more apparent in individuals with a prominent subpapillary plexus), changes that are not specific for PSS but represent deviations from a normal pattern (4,18).

Complete photographic data from the 5 Polish pa-



Figure 2. Definite SD pattern with capillary dilatation and avascular areas in a patient with systemic sclerosis.

Table 1. Clinical and laboratory findings in 32 individuals studied

	Eosinophilic fasciitis	Progressive systemic sclerosis
Total number	19	13
Mean age (range)	45 (10–71)	46 (15–66)
Males/females	10/9	1/12
Raynaud's phenomenon	0/19	13/13
Mean duration*		
Symptoms, months (range)	30 (1–132)	22 (1–108)
Raynaud's phenomenon	0	85 (8–108)
Involvement of fingers	7/19	10/13
Eosinophilia (>600/mm ³)	17/19	0/1
Hypergammaglobulinemia (>1.5 gm/dl)	9/19	3/8
Elevated ESR† (>20 mm/hour)	8/15	3/12
Positive ANA‡ (>1:10)	2/19	6/12

* From onset of symptoms to time of capillary microscopy.

† ESR = erythrocyte sedimentation rate.

‡ ANA = antinuclear antibodies.

tients with EF were not readily available; the evaluation of their capillary patterns was based on the reinterpretation of capillary observations reported from Warsaw, to conform with the capillary classification used for the patients in American medical centers. The capillary abnormalities seen in scleroderma and Raynaud's disease have been divided into scleroderma loops and Raynaud's loops (19,20) which roughly correspond to the SD pattern with and without capillary loss described by Maricq (8).

RESULTS

Selected clinical and laboratory findings are listed in Table 1. Mean age at time of capillary microscopy was similar in both groups. The frequency of Raynaud's phenomenon was 0 in EF patients and 100% in PSS patients. The time from disease onset to date of examination ranged from 1 month to 132 months in patients with EF. At the time of capillary microscopy exam, 17 of 19 patients had clinically active disease, 1 had minimal cutaneous activity, and 1 was in complete remission (the patient seen at 132 months). Involvement of the skin of the fingers was



Figure 3. Normal capillary pattern in a patient with eosinophilic fasciitis.

seen in 7 of 19 (37%) patients with EF and in 10 of 13 (77%) PSS patients. Three of 13 PSS patients had proximal sclerodermatous skin changes only at the time of evaluation. Hypereosinophilia (as defined by maximum counts >600/mm³) was seen in 17 of 19 patients with EF; 15 had counts >1,000/mm³, and peak values reached 4,200/mm³. The 2 other EF patients had counts of 494 and 598/mm³ respectively. Only 1 PSS patient had an eosinophil count measured, and this was normal. At the time of examination, 7 EF patients were taking corticosteroids, ranging from 7.5 mg–40 mg/day; the other 12 were receiving no therapy.

Results of capillary microscopy are presented in Table 2. Sixteen of the 19 patients with EF had normal capillary patterns (Figure 3). Two patients were classified as borderline: 1 had engorged capillary loops that were thicker than normal with no decrease in the density of loops (Figure 4), the other, a patient in Poland, was reported to have Raynaud's loops alone. Although he clearly had abnormal capillaries, there was not sufficient information available to classify him

Table 2. Nailfold capillary microscopic observations*

	Normal	SD pattern	Abnormal†	
			Borderline SD pattern	Nonspecific
Eosinophilic fasciitis (19)	16 (84%)	–	2 (11%)	1 (5%)
Progressive systemic sclerosis (13)	–	11 (85%)	2 (15%)	–
Normal controls (4)	4 (100%)	–	–	–

* Number of patients (% of total). $\chi^2 = 18.66$ ($P < 0.001$) (with Yates correction).

† See text for explanation.

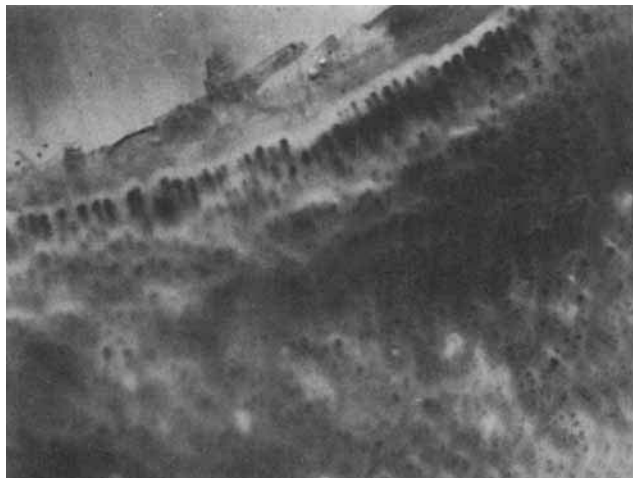


Figure 4. Borderline SD pattern with engorged capillaries but a normal density of loops.

as having a definite SD pattern. It was therefore considered best to include him in the borderline group. The former patient was a manual laborer susceptible to digital trauma. Injury to the nailfold can lead to changes in the capillary bed that can be difficult to distinguish from the SD pattern when only a black and white photograph is examined; there may be focal engorgement of capillaries with associated microvascular hemorrhage that may further increase the apparent size of the capillary loops when the extravasation of red blood cells is confined within the pericapillary space. Direct observation of the fingers and nailfolds permits more accurate distinction between this injury pattern and the SD pattern. On "blind" evaluation of the photographs from this EF patient, the question of injury was raised, although by design of our blind evaluation system the final interpretation led to place-

ment of the capillaries in the borderline SD pattern group. Both patients with borderline abnormalities were in the clinically active group, and neither was receiving therapy at time of examination.

One EF patient had a nonspecific abnormal pattern in which only 1 of her digits contained long, slightly enlarged capillaries with a prominent subcapillary venous plexus; the other digits were normal. This finding has been observed in a variety of diseases as well as in some normal individuals, and is not considered specific (8). Of the 2 EF patients with borderline SD patterns, 1 had cutaneous involvement of the fingers and the other did not. Six other EF patients with changes in the fingers had normal capillaries.

In contrast to the normal pattern seen in 16 of the 19 (84%) patients with EF, none of the 13 PSS patients had a normal capillary pattern. Eleven (85%) had a typical SD pattern while 2 others had a borderline SD pattern. These latter 2 patients each had capillary abnormalities involving only 1 digit; the other digits were normal. A chi-square analysis between normal and abnormal capillary microscopy findings in EF and PSS yielded a χ^2 (with Yates correction) of 18.66 ($P < 0.001$).

Results of the "blind" evaluation correlated well with our direct observations (Table 3). Nineteen of 22 digits from 11 EF patients were read as normal, 2 as borderline SD (both from the same patient), and 1 as nonspecific. Twenty-one digits from 13 PSS patients were definitely abnormal (SD pattern), 3 were borderline SD pattern, and only 2 digits were normal. One PSS patient had 1 borderline and 1 definitely abnormal digit; 2 others each had 1 borderline and 1 normal digit. In all the other PSS patients, both digits examined were abnormal. No abnormalities were found in 8 digits from the 4 normal controls.

Table 3. Results of the "blind" evaluation of nailfold capillary patterns in 56 digits from 28 individuals studied*

	Total no. of digits examined	Normal	Abnormal		
			SD pattern	Borderline SD pattern	Non-specific
Eosinophilic fasciitis (11)	22	19	—	2	1
Progressive systemic sclerosis (13)	26	2	21	3	—
Normal controls (4)	8	8	—	—	—

* Two digits from each individual were evaluated.

DISCUSSION

This study demonstrates that nailfold capillaries are normal in the great majority of individuals with eosinophilic fasciitis. Minor abnormalities were seen in only 3 of 19 patients, with 2 of the 3 having a borderline SD pattern. This is in marked contrast to progressive systemic sclerosis, in which characteristic abnormalities generally occur.

Sclerodactyly per se does not account for the nailfold capillary abnormalities seen in systemic sclerosis. Two of our PSS patients without sclerodactyly (who had proximal sclerodermatous skin changes) had a definite SD pattern. An abnormal pattern has been seen in PSS patients with visceral disease only and no cutaneous changes (9). Six of our EF patients with involvement of the skin and subcutaneous tissue of their fingers had normal capillary patterns.

Nor does the absence of Raynaud's phenomenon account for the normal capillary findings in EF. Patients with Raynaud's phenomenon alone have been shown to have normal capillaries, as have those with systemic lupus erythematosus with Raynaud's phenomenon (6,7). In fact, the presence of capillary changes in individuals with Raynaud's phenomenon is a strong predictor of progressive systemic sclerosis (6, 21). Conversely, PSS patients and dermatomyositis patients without Raynaud's phenomenon have exhibited the typical SD pattern (although dermatomyositis may also manifest a "bushy" pattern that is more frequently seen in dermatomyositis than in PSS, but is not invariably present) (7,22).

Some authors have suggested that EF is a variant in the clinical spectrum of progressive systemic sclerosis, rather than a distinct disease entity (23-27). Although the etiology of both EF and PSS is unknown, microcirculation is a key factor in the pathologic changes that develop in PSS (28). A strong positive correlation has been found between multisystem involvement in PSS and the severity of the capillary pattern abnormality (9). Electron microscopic studies of scleroderma muscle capillaries have revealed thickening of the basement membrane, a decrease in the number of capillaries, and the predominance of large capillaries with increased mean blood vessel diameter (29). Other vascular abnormalities, such as Raynaud's phenomenon and nailfold capillary changes, are an integral feature of PSS. These abnormalities are strikingly lacking in EF, and suggest different underlying processes.

The results of this study suggest that capillary microscopy may be helpful in differentiating eosinophilic fasciitis from progressive systemic sclerosis, and support the theory that eosinophilic fasciitis is a separate disease entity and not a "forme fruste" or subset of systemic sclerosis.

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