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Dermatomyositis: nailfold capillaroscopy patterns and a general survey

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Abstract

Introduction: Dermatomyositis (DM) is a group of autoimmune idiopathic inflammatory myopathies characterized by typical cutaneous signs and symptoms of muscle involvement. The diseases can be associated with cancer in the paraneoplastic syndrome, calcinosis, interstitial lung disease, other autoimmune connective tissue diseases (in overlap syndrome), and Raynaud's phenomenon.
Methods: Clinical and capillaroscopic data were gathered from 43 patients with DM. The diagnosis was based on the Bohan–Peter and European League against Rheumatism / American College of Rheumatology (EULAR/ACR) classification criteria. In addition, nailfold capillaroscopy was performed in all patients.
Results: In our cohort, eight patients had overlap syndrome, six had paraneoplastic syndrome, eight presented with interstitial lung disease, and nine had calcinosis, two of whom also had a cancerous pathology. Raynaud's phenomenon was reported in 74% of patients. Upon nailfold capillaroscopy, 84% of patients presented giant capillaries, 81% ramified capillaries, and 70% both. The latter, notably giant ramified capillaries, could be considered specific for DM. The detection of prominent subpapillary venous plexuses was associated with pulmonary involvement. In contrast, alterations of the pericapillary spaces were associated with the severity and prognosis of DM.
Conclusions: Our results underline the usefulness of nailfold capillaroscopy in the diagnosis and prognosis of DM. Based on the results and literature data, specific nailfold capillaroscopy features should be included in DM diagnostic criteria.

Keywords: dermatomyositis, nailfold capillaroscopy, giant ramified capillaries, autoantibodies, venous plexuses

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Introduction

Dermatomyositis (DM) and polymyositis (PM) are a group of autoimmune idiopathic inflammatory myopathies (IIM). DM is a rare disease with about five to 10 cases per million per year, affecting more females than males (ratio 2:1). All ethnic groups are involved; however, it is more common in African Americans (1). Cutaneous and muscular manifestations mainly characterize the clinical picture. At the skin level, definite signs are a heliotrope rash (Fig. 1) characterized by purple, lilac-colored, or erythematous patches over the eyelids or in a periorbital distribution, often associated with periorbital edema. Additionally, Gottron's papules (Fig. 2) and Gottron's sign, which are erythematous to violaceous papules, sometimes squamous, over the extensor surfaces of joints. These may occur over the finger joints, elbows (Fig. 3), knees, malleoli, and toes (2). Other cutaneous manifestations are mechanic's hands, characterized by papules and hyperkeratosis on the palms and linear squamous lesions on the fingers, which may extend to the distal toes; cutaneous telangiectasias, which can appear as reddish papular lesions on the fingers and nailfolds (Fig. 4); and shawl erythema. Skin manifestations can precede the onset of muscle symptoms by months or years (3). The primary muscular symptoms are muscle weakness, tenderness, and contractures, and in the advanced stages muscle atrophy can be observed. The proximal musculature of the limbs, shoulder, and pelvic girdles are usually symmetrically affected. Over time, muscle weakness tends to intensify with the possible involvement of other muscle groups. Patients may present dysphonia, dysphagia, and symptoms of aspiration for involvement of dedicated muscles. The progression is usually slow (4). Arthralgias are frequent during periods of active disease; however, they tend to regress over time.

Due to the presence of associated conditions, in addition to the classic form of DM, there are several variants, such as the juvenile DM (5), the amyopathic form (*dermatomyositis sine myositis*) (6), paraneoplastic syndrome (7), DM associated with calcinosis (Fig. 5) (8), and DM associated with interstitial lung disease (ILD) (9). In overlap syndrome, DM can be associated with other autoimmune connective tissue diseases (10), such as scleroderma, lupus erythematosus, rheumatoid arthritis, and Reiter's syndrome (11); all of them can be associated with Raynaud's phenomenon (12).

The pathogenesis of DM is multifactorial, complex, and incompletely understood (1). Genetic predisposition for carriers of the human leukocyte antigen (HLA)-DRB1 alleles and environmental and immune mechanisms are the leading players in DM development. Possible triggers of the immune/autoimmune reaction have also been investigated among various infectious agents, including

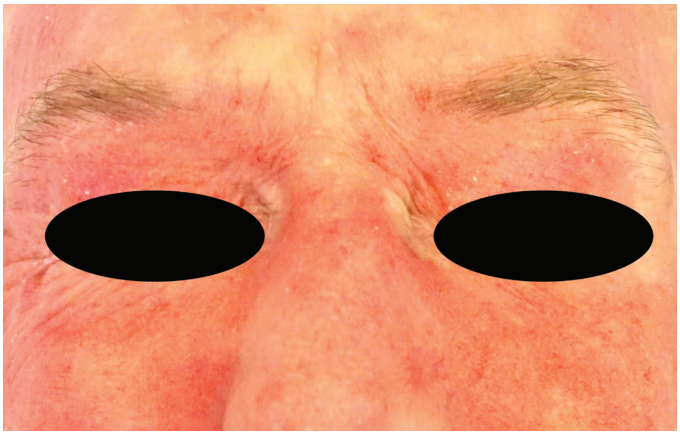

Figure 1 | Heliotrope rash.

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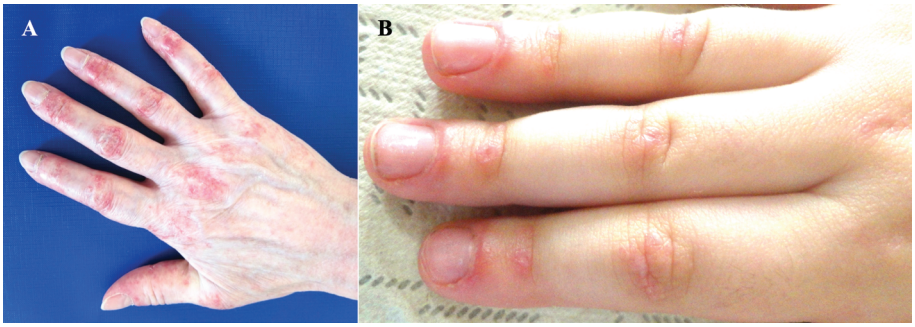

Figure 2 | Gottron's papules, A: in an adult, B: in a child.

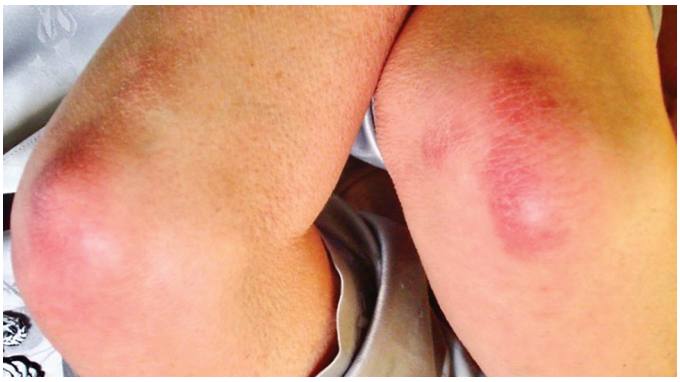

Figure 3 | Gottron's sign: erythematous to violaceous macules over the elbows, which are not palpable.

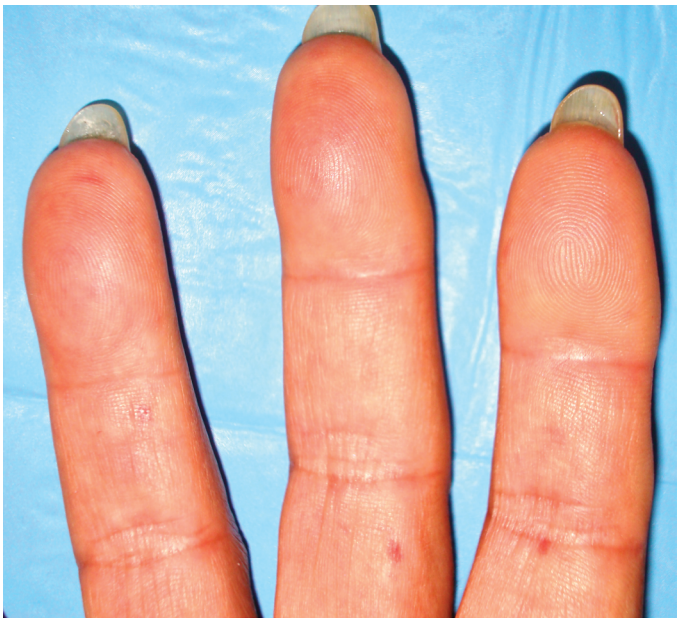

Figure 4 | Finger spider angioma in a patient with paraneoplastic dermatomyositis.

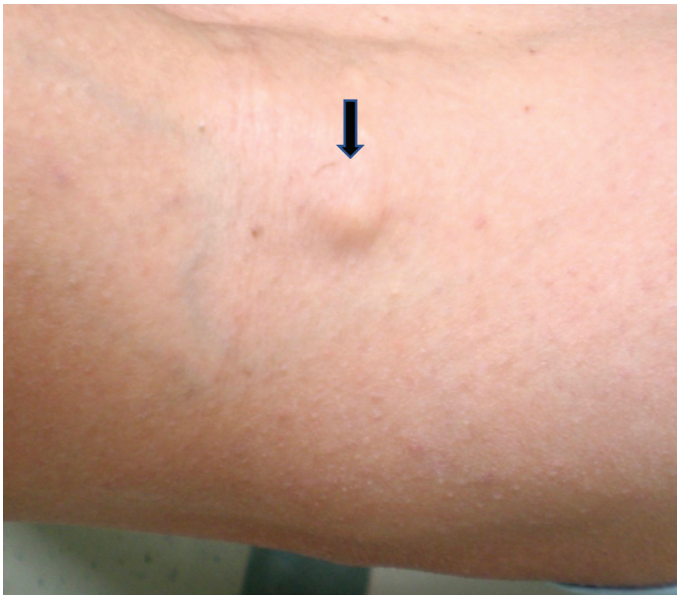

Figure 5 | Skin calcification, indicated by the arrow.

parvovirus B19, coxsackievirus, polyomavirus, Epstein–Barr virus (EBV), hepatitis, influenza, the human immunodeficiency virus (HIV) (13), *Borrelia burgdorferi* sensu lato (14, 15), and *Toxoplasma gondii* (16).

Indices of inflammation (erythrocyte sedimentation rate, C-reactive protein, alpha-2-globulin, etc.) and serum muscle enzymes, particularly creatine kinase (CK), are usually increased in patients with DM. However, CK can be normal in about 30% of patients at DM onset and rarely even in the acute phase, especially in amyopathic DM (17) or when DM is associated with systemic connective tissue diseases or neoplasms. Aldolase is a less sensitive indicator of active myositis but is sometimes elevated when CK is normal. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) can also be increased, and their ratio has recently been associated with prognosis in DM (18). Several types of autoantibodies can be detected in patients with DM. Antinuclear antibodies (ANAs) are present in 50% to 80% of patients with DM/PM. Myositis-associated autoantibodies (MAA), such as Ku and Ro52, are found in the serum of patients affected by myositis with a frequency ranging from 20% to 50%, especially in connective tissue overlap myositis, but they are not specific to DM/PM because they can also be positive in other connective tissue diseases. However, myositis-specific autoantibodies (MSA) are almost exclusively associated with IIMs and are detected in 30% to 40% of patients with DM (19). Anti-melanoma differentiation-associated protein 5 (MDA5), anti-nuclear matrix protein 2 (NXP2), transcription intermediary factor 1 (TIF-1), and anti–small ubiquitin-like modifier-activating enzyme (SAE) antibodies are specific for DM; anti-Mi-2α and Mi-2β are antinuclear antibodies found in 10% to 20% of patients and are associated with typical cutaneous manifestations of DM, such as Gottron's sign or papules and/or heliotrope rash (20). The anti-Mi-2 antibody has also been found to predict DM with benign evolution (21) with a good response to steroid therapy. It also seems to rule out paraneoplastic myositis: in particular, 97% of patients with anti-Mi-2β have been reported to heal within 44 months (1, 21).

Microvascular changes are present in DM and involve capillary loops (giant and ramified capillaries) and pericapillary interspaces (22–24). Recently, nailfold capillary density has been proposed as a dynamic marker of global disease activity in adult DM (25).

This study evaluates the impact of nailfold capillaroscopy on the diagnosis, severity, and evolution of DM. The relationships

between DM and ILD, cancer, calcinosis, and autoantibody profiles with nailfold capillaroscopy were also investigated.

Methods

In this study, 43 patients (33 women and 10 men) were enrolled with a diagnosis of DM based on data reported in Supplementary Table 1. In all selected patients, the diagnosis met both the Bohan–Peter criteria (26, 27) and the European League against Rheumatism / American College of Rheumatology (EULAR/ACR) classification criteria summarized in Table 1 (28).

The EUROLINE Autoimmune Inflammatory Myopathies Profile (catalog number 1530-1601-4 G) was used to investigate autoantibodies in plasma or serum, detecting 16 antigens. Specifically, the test identified the following autoantibodies: Ku, polymyositis-scleroderma 100 (PM-Scl100), polymyositis-scleroderma 75 (PM-Scl75), and Ro-52 for MAA; Mi-2α, Mi-2β, TIF-1γ, MDA5, NXP2, small ubiquitin-like modifier activating enzyme 1 (SAE1), and signal recognition particle (SRP) for MSA; and histidyl-transfer RNA synthetase (Jo-1), threonyl-transfer RNA synthetase (PL-7), alanyl-transfer RNA synthetase (PL-12), glycyl-transfer RNA synthetase (EJ), and isoleucyl-transfer RNA synthetase (OJ) for anti-transfer RNA (tRNA)-synthetase antibodies.

Muscle biopsy

Muscle biopsy was carried out in seven patients to confirm the diagnosis. Sampling was performed with a Bergström needle under local anesthesia on the clinically more involved muscle (usually the biceps or quadriceps). Staining with hematoxylin and eosin, and immunophenotyping with CD4 and CD8 markers were performed.

Nailfold capillaroscopy

In all patients, nailfold capillaroscopy was performed on eight fingers with the exclusion of the thumbs (29) using a Videocap capillaroscope (DS Medica, Milano, Italy) for image recording. A 200× objective with immersion in cedar oil was used for measuring capillary loops. The parameters described below were gathered from each patient (29) (Fig. 6).

Capillary density anomalies were assessed as follows. Mean capillary density was calculated by averaging three measurements of the number of loops/mm. Normal values range from eight to 14 loops (the number of loops/mm in children is lower than in adults). Fewer than eight loops/mm indicates microangiopathy; the desert area is characterized by fewer than two capillaries/mm.

Qualitative anomalies of the capillaries included the following:

- Minor dystrophies: crisscross capillaries with at least two crossings (type 5), tortuous (type 6), notched (type 7), ramified capillaries (type 8), characteristic of DM;
- Capillaries with a range between 30 µm and 50 µm;
- Major dystrophies: giant capillaries (diameter > 50 µm) and capillaries in regression;
- Filiform loops: in which the erythrocyte column is reduced or absent (Raynaud's phenomenon, anemia, arterial hypotension);
- Elongated handles: length > 700 µm;
- Neoangiogenesis: a thin newly formed capillary.

Abnormalities in the pericapillary spaces included the following:

- Edema: this prevents the focus of the capillary loop and can sometimes be found in manual workers or is linked to trauma without a pathological significance. If pathological, it indicates a developmental microangiopathy but is not specific;
- Exudate: it consists of edema associated with hemorrhages, is related to organic microangiopathy, indicates a severe form, and is predictive of a poor prognosis;
- Hemorrhages: these form in the pericapillary spaces, and they progressively move away from the capillary (30). Sometimes they are of micro-traumatic origin, and they often appear during an organic microangiopathy.

Subpapillary venous plexuses are usually not visible in normal subjects; a prominent venous plexus is observed and is considered physiological up to 12 years of age. It can be observed in acrocyanosis, connective tissue disorders, and—often dilated with aspects of venous engorgement—in venous hypertension (31).

Raynaud's phenomenon

Raynaud's phenomenon was investigated by clinical manifes-

Table 1 | Dermatomyositis score (points) according to the European League against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria.

Variable	Points, muscle biopsy	
	–	+
Age of onset of first related symptoms		
18–40	1.3	1.5
› 40	2.1	2.2
Muscle weakness		
Objective symmetric weakness progressive, proximal upper extremities	0.8	0.7
Objective symmetric weakness progressive, proximal lower extremities	1.9	1.6
In the legs, proximal muscles relatively weaker than distal muscles	0.9	1.2
Skin manifestations		
Heliotrope rash	3.1	3.2
Gottron's papules	2.1	2.7
Gottron's sign	3.3	3.7
Other clinical manifestations		
Dysphagia or esophageal dysmotility	0.7	0.6
Laboratory measurements		
Anti-tRNA synthetase	3.9	3.8
Elevated serum levels of creatine kinase	1.3	1.4
Muscle biopsy features		
Endomysial infiltration of mononuclear cells surrounding, but not invading, myofibers	—	1.7
Perifascicular atrophy	—	1.9

tRNA = transfer RNA.

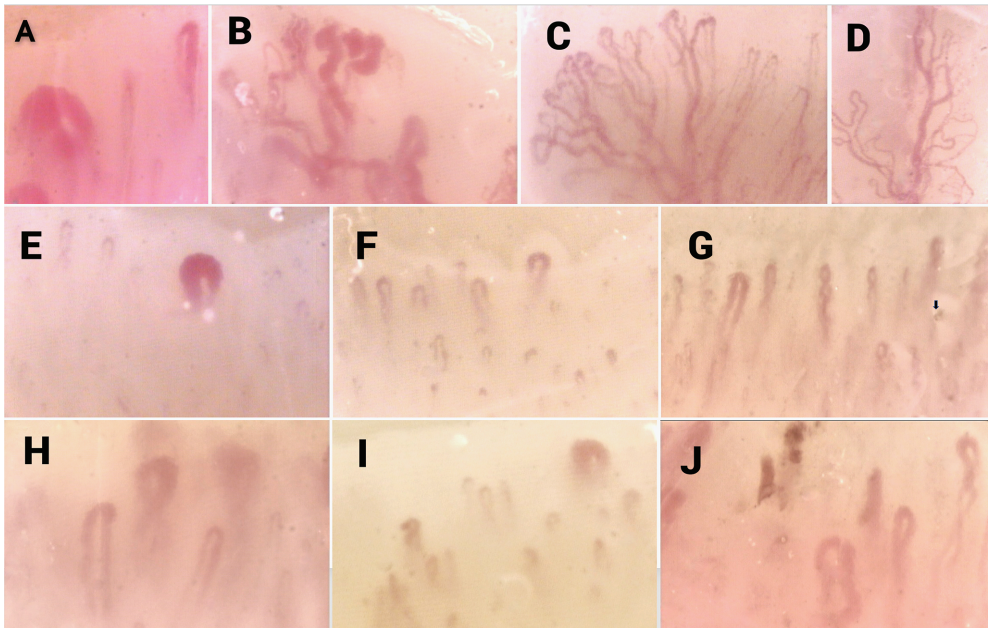

Figure 6 | A: giant capillary and blood sludge, B: giant elongated capillary in a patient with a reduction in the number of loops/mm and two capillaries with dilatation of the intermedium tract with a maximum diameter of 50 µm (borderline giant capillary), C and D: ramified capillaries. The simultaneous presence of giant and ramified capillaries is highly significant for a diagnosis of dermatomyositis. E: Cold pressure test: the phenomenon of extinction of the capillaries is observed, F: pericapillary edema, G: pericapillary edema and small calcification (indicated by the arrow) in a case of DM with calcinosis, H: diffuse edema, with apparent blurring, I: dilated capillaries with minor dystrophies and two hemorrhages near the capillaries, J: numerous hemorrhages, indicative of an associated vasculitic component (52-year-old female patient with the presence of a high titer of anti-cardiolipin antibodies).

tation and nailfold capillaroscopy. Clinically, the finger color change of Raynaud's phenomenon was evaluated in three stages, as follows: 1) white or pale (ischemic phase), 2) bluish or cyanotic (deoxygenation phase), and 3) erythematous (reperfusion phase). Anamnestically, patients were asked if their fingers had been excessively susceptible to cold, if they had changed color when exposed to low temperatures, becoming white or blue, or if they had shown both colors, as previously described (32). Accordingly, the diagnosis of Raynaud's phenomenon was likely if the answers to these three questions were positive.

Nailfold capillaroscopy (33) was performed in association with the cold pressure test (CPT) extinction phenomenon. This test is carried out by immersing the hands in a basin of water at 12 °C for 3 minutes. Primary Raynaud's phenomenon is caused by excessive physiological vasospasm due to cold and sympathetic stimuli; in the secondary form, linked to autoimmune diseases such as DM, we observe a form of Raynaud's phenomenon mainly related to damage to the connective tissue surrounding the loops. We should therefore instead speak of a reaction to the cold evocative of Raynaud's phenomenon.

CPT is positive in less than 10% of normal subjects and in 70% of patients with Raynaud's or Raynaud's-like phenomenon (predictive value 95%).

Results

Of the 43 patients, 33 (77%) were females and 10 (23%) were males, with a female:male ratio of 3.3:1. The mean age at diagnosis was 53 years, with no differences between sexes (p = 0.9), as shown in Table 2. All patients reported muscle weakness, and three of them also presented with dysphagia. Skin manifestations related to the cohort of patients are summarized in Table 3. DM diagnosis was confirmed by electromyography in 27 patients and muscle biopsy in four patients.

As shown in Table 2, eight (19%) patients presented with interstitial lung disease (Fig. 7), nine (21%) with calcinosis (Fig. 8), and six (14%) with tumors (right breast cancer, melanoma, myeloid leukemia, right breast ductal carcinoma with right iliac crest metastasis associated with calcinosis, lower lip carcinoma, and liver carcinoma). In two cases, both cancer and calcinosis were present. Eight patients in our cohort had overlap syndrome; specifically, five patients had associated scleroderma, one presented with lupus erythematosus, and two had rheumatoid arthritis.

Levels of CK were elevated in 39 out of 43 patients (91%), with a mean value of 946 U/l, ranging from 225 to 5,096 U/l. ANAs were detected in 21 (49%) patients with no significant difference between sexes (p = 0.1). MAAs were positive in 12 (28%) patients, and MSAs were positive in 24 (56%) patients, 18 (42%) of whom were positive to tRNA-synthetase autoantibodies, as summarized in Table 4.

In the eight cases submitted for muscle biopsy, the histological picture showed perivascular inflammatory infiltrates, mainly CD4 T-cells, in the interfascicular septa or in the peri-fascicular area, with reduction of capillary density and necrosis of muscle fibers. Raynaud's and Raynaud's-like phenomena were detected

Table 2 | **Clinical and anamnestic data of patients.**

Variable	*n* (%)
Female/male	33/10 (77/23)
Age, years (mean)	53
Overlap syndrome	8 (19)
Paraneoplastic DM*	6 (14)
Interstitial lung disease	8 (19)
Calcinosis*	9 (21)
Raynaud's and Raynaud's-like phenomenon	34 (81)
ANA	20 (47)
MAA	12 (28)
MSA includes anti-tRNA synthetase	24 (56)
Anti-tRNA synthetase	18 (42)

*Two patients had both paraneoplastic DM and calcinosis.
DM = dermatomyositis, ANA = antinuclear antibodies, MAA = myositis-associated autoantibodies, MSA = myositis-specific autoantibodies, tRNA = transfer RNA.

in 34 patients (79%), with similar distributions in all sub-groups of patients (ILD, calcinosis, and cancer). The results of nailfold capillaroscopy are summarized in Table 5 and reported in detail in Supplementary Table 2.

Capillary density was fewer than nine loops/mm in 28 patients, and reduced capillary density was observed in 65% of cases. Giant capillaries were detected in 84% (36/43) of DM patients. Although not statistically significant, in DM with ILD, giant capillaries were detected in eight out of eight patients (100%) versus 80% without ILD (35 patients).

The capillaroscopic picture in patients with ILD (8/43) versus patients without ILD (35/43) showed the presence of micro-hemorrhages in 62% (vs. 37%) and prominent venous plexuses in 100% (vs. 31%). Anti-tRNA synthetase positivity was significantly asso-

Table 3 | **Results of cutaneous manifestations in all cases of dermatomyositis (DM), in DM with and without interstitial lung disease (ILD).**

	All DM (43)	Overlap (8)	DM with ILD (8)	DM without overlap (35)	DM without ILD (35)
Score criteria					
Heliotrope rash	32 (74%)	5 (62%)	5 (62%)	27 (77%)	27 (77%)
Gottron's papules	36 (84%)	6 (75%)	5 (100%)	30 (86%)	31 (89%)
Gottron's sign	4 (9%)	0	0	4 (11%)	4 (11%)
No score criteria					
Shawl rash	5 (12%)	0	1 (12%)	5 (14%)	4 (11%)
Mechanic's hands	7 (16%)	3 (37%)	2 (25%)	4 (11%)	5 (14%)
Nailfold erythema	6 (14%)	2 (25%)	1 (12%)	4 (11%)	5 (14%)

DM = dermatomyositis, ILD = interstitial lung disease.

Table 4 | **Results of nailfold capillaroscopy in all cases of dermatomyositis (DM), in DM with and without interstitial lung disease (ILD)..**

	Overlap (8)	All DM (43)	DM with ILD (8)	DM without ILD (35)
NFC loops				
Capillary density ‹ 8 loops/mm	5 (62%)	28 (65%)	5 (62%)	23 (66%)
Giant capillaries	6 (75%)	36 (84%)	8 (100%)	28 (80%)
Ramified capillaries	0	34 (79%)	7 (87%)	28 (80%)
Giant and ramified capillaries	0	30 (70%)	7 (87%)	23 (66%)
NFC in pericapillary spaces				
Diffuse edema	3	37 (86%)	8 (100%)	29 (83%)
Micro-hemorrhages	2	18 (41%)	5 (62%)	13 (37%)
Exudates	0	1 (2%)	1 (12%)	0
Venous plexuses	—	19 (44%)	8 (100%)	11 (31%)
Anti-tRNA synthetase	—	18 (42%)	6 (75%)	12 (34%)

DM = dermatomyositis, ILD = interstitial lung disease, NFC = nailfold capillaroscopy, tRNA = transfer RNA.

Table 5 | **Results of autoantibody detection.**

Groups	*n*	ANA	MAA	MSA with anti-tRNA synthetase	Anti-tRNA synthetase
All DM	43	21(49%)	12 (28%)	33 (77%)	18 (42%)
Paraneoplastic syndrome	6	3 (50%)	4 (67%)	5 (83%)	2 (33%)
Calcinosis	9	4 (44%)	1 (11%)	6 (67%)	1 (11%)
Interstitial lung disease	8	4 (50%)	3 (37%)	6 (75%)	6 (75%)
DM w/o ILD	35	17 (49%)	9 (26%)	27 (77%)	12 (34%)

ANA = Antinuclear antibodies, MAA = myositis-associated autoantibodies, MSA = myositis-specific autoantibodies, DM = dermatomyositis, ILD = interstitial lung disease, tRNA = transfer RNA, w/o = without.

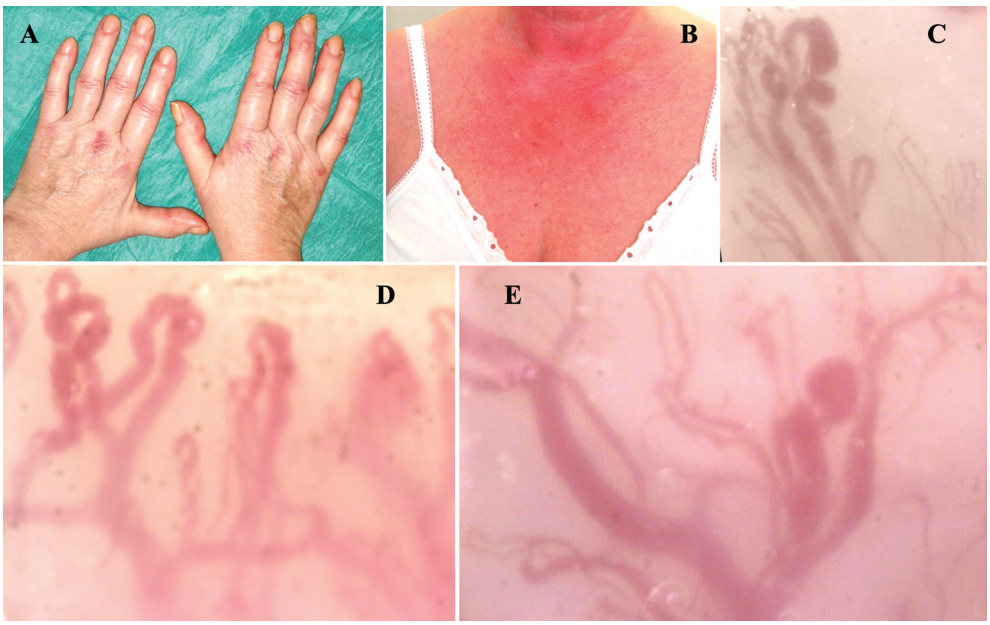

Figure 7 | Dermatomyositis (DM) with interstitial lung disease (ILD) in a 57-year-old woman (ANA = 1:320, negative myositis-specific autoantibodies, autoimmune hepatitis, regressed with prednisone). A: Gottron's papules, B: Shawl erythema, C: giant twisted capillaries and close ramified capillary, D: giant ramified capillaries and visibility of the venous plexuses, E: dilated loops, with visibility of the venous plexuses.

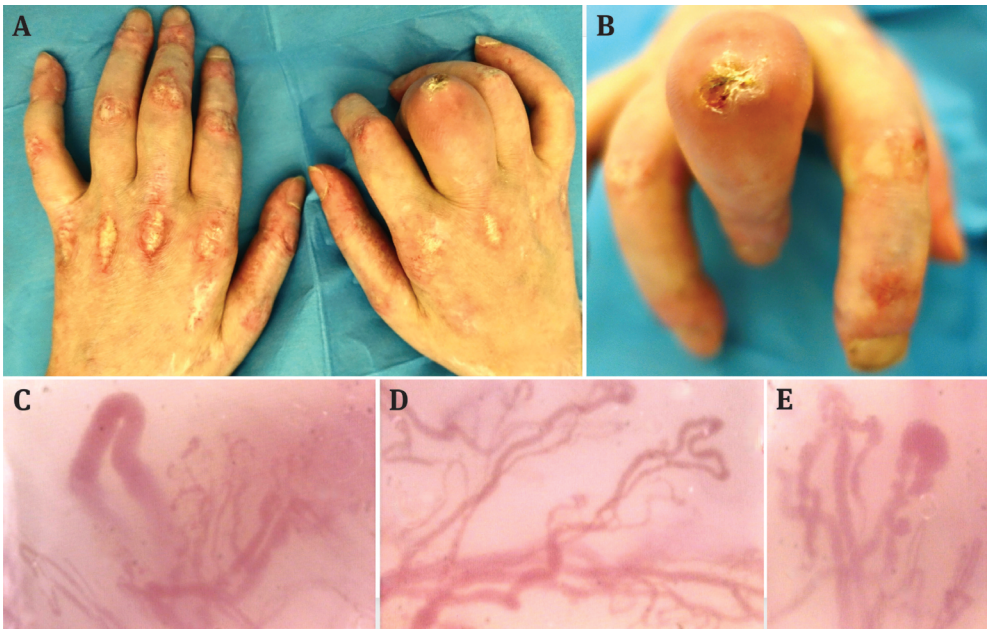

Figure 8 | A: Gottron's papules, B: calcification of the third right finger, C: giant capillary elongated, D: ramified capillaries (neoangiogenesis), E: giant capillary in the initial stage of regression.

ciated with patients with ILD, being detected in 75% of patients with ILD in comparison to 34% of patients without ($p = 0.04$).

Discussion

The cases presented in this study were diagnosed according to both the Bohan–Peter and EULAR/ACR criteria (see appendices), which do not include capillaroscopic aspects. Nailfold capillaroscopy examination has been proven to be helpful in the diagnosis of dermatomyositis (25). Specifically, the simultaneous occurrence of giant and ramified capillaries could be included in the Bohan–Peter and EULAR/ACR diagnostic criteria (34). Overall, a reduction of loops per mm is indicative of microangiopathies (35). In our series, the reduction of capillary density was observed in 28 (65%) cases, in agreement with other studies (36). Giant capillaries were detected in 84% of patients and in 100% of ILD patients. At the same time, ramified capillaries are less frequent in overlap forms, indicating that their presence constitutes a very significant capillaroscopic picture for diagnosing DM. Giant ramified capillaries were almost exclusive of DM, and, based on these elements, we agree with distinguishing between "scleroderma" and "dermatomyositis" patterns (34). Giant capillaries in DM, compared to those in scleroderma, in our experience, are usually less numerous, rounded in shape, and have a more prominent wall diameter, up to 289 µm in our series.

Considering a prevalence ratio of capillaroscopic "abnormalities" of 14% in idiopathic pulmonary fibrosis (IPF) and of 80% in connective tissue disease–associated interstitial lung disease (CTD-ILD), nailfold capillaroscopy can increase the diagnostic accuracy of ILD (37).

The venous subpapillary plexuses became less easily visible after 10 to 12 years (38) and are better seen when there is lung involvement. In some cases, these plexuses can also appear congested. In our series, these subpapillary plexuses were visible in 31% of patients with DM without ILD, whereas they were present in all eight cases of DM with ILD.

The detection of engorged sub-papillary venous plexuses was clearly associated with pulmonary involvement, as shown in all patients with ILD in our cohort, which can be associated with DM in some cases, in particular when there is also positivity to tRNA-synthetase (39). Capillaroscopic examination in ILD, regardless of a DM diagnosis or connective tissue disease, shows 23% of alterations of the capillary loops, referable to connectivitis/DM (40). In our series of DM with ILD, giant ramified capillaries were detected in all eight patients.

In our cohort, the presence of anti-tRNA synthetase antibody was also most frequent in cases of DMs with ILD (6/8; 75%), and, in our opinion, their positivity must be integrated with the capillaroscopic examination.

The analysis of intercapillary spaces is important from a prognostic point of view rather than a diagnostic point of view. Pericapillary hemorrhages are equally detected in subgroups of DM, including overlap forms, and the presence of diffuse edema (which is evident because it does not allow focus on the capillaries) or exudates (edema with a hemorrhagic component) in the extracapillary spaces is an indicator of DM severity.

Raynaud's-like phenomenon (a positive pressure test) was present in our series in 79% of cases. This percentage is higher in comparison to the literature data (41). This is probably linked to the fact that we carried out the cold pressure test, which also reveals situations in which patients hardly feel Raynaud's phenomenon.

Nailfold capillaroscopy can also provide further information: in paraneoplastic DM, capillaroscopic examination shows giant capillaries, elongated capillaries, decreased mean capillary density with avascular areas, severe disarrangement, single hemorrhages, and clear evidence of neoangiogenesis. These capillaroscopic features, characteristic of the "scleroderma-like" pattern, are indistinguishable from those in idiopathic dermatomyositis, as in the second case (42).

In the case of small calcium deposits, a careful investigation of calcinosis should be performed. The typical skin manifestations of DM are more frequent in pure DM (heliotropic rash 68%, Gottron 62%), regardless of the subgroup, than in overlap forms (heliotropic rash 46%, Gottron 46%). Periungual telangiectasias and subcutaneous calcinoses were more frequent in paraneoplastic DMs (43).

Autoantibodies to Mi-2α and β usually indicate benignity of DM.

These autoantibodies were present in 10/43 of our patients: two had ILD and one had calcinosis, in disagreement with the literature (44). Anti-MSA antibodies, in line with literature data, were detected in 2/7 patients with paraneoplastic DM (TIF-1y) (45) and with ILD (tRNA synthetase) (46). NXP-2 was positive in six of our series (14%), and five patients had calcinosis. NXP-2 autoantibodies were positive in 56% (5/9) of patients with DM associated with calcinosis and in 3% (1/34) of patients with DM without calcinosis (47). DM with calcinosis (48) has a higher risk of being associated with cancer (49). In our series, 2/6 patients with cancer also had calcinosis (33%), and four out of 37 (11%) did not. The forms of DM overlap (39) were more often associated in our cohort (in 30% of cases) with forms of DM without tumors, calcinosis, and ILD.

Conclusions

In cases of suspected myositis, it is advisable to carry out tests to verify muscle pain (CK, aldolase, and AST/ALT), non-specific autoantibodies (ANA, anti-double-stranded DNA antibodies), MAA and MSA with tRNA synthetase, and nail capillaroscopy evaluating the following parameters (30):

- The simultaneous presence of giant capillaries and ramified capillaries.
- The presence of giant ramified capillaries is very useful for the diagnosis. These capillaroscopic manifestations should be included in the diagnostic criteria of DM. In contrast, currently they are not present in the Bohan–Peter criteria or in the EULAR/ACR criteria.
- Easy visibility of venous plexuses is indicative of a possible associated ILD.
- Alterations of the intercapillary spaces (edema, exudates, or hemorrhages) are useful for evaluating severity and for prognosis.

In conclusion, capillaroscopy helps define the different clinical possibilities of this pathology and correlates them with the autoantibody response (in addition to the ANA) occasionally associated.

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Supplementary Table 1 | **Diagnostic and autoantibodies details of the cohort of patients.**

Sex	Age	Raynaud	Diagnosis	ANA/nDNA	MAA	MSA w/o tRNA synthetase	tRNA synthetase	PS	Calc	ILD	MSA	tRNA
Patients with paraneoplastic syndrome and calcinosis												
M	31	Yes	DM	0	Ro52, Scl75	MDA-5 SAE1 NXP2	0	1	1	0	1	0
F	57	Yes	DM	1:320	0	0	0	1	1	0	0	0
F	75	Yes	DM	0	0	0	0	1	1	0	0	0
Patients with paraneoplastic syndrome												
F	57	No	DM	1:80	Ro52	TIF-1γ	0	1	0	0	1	0
F	64	No	DM	1:320	0	0	Jo-1	1	0	0	1	1
M	78	Yes	DM	0	Ku	TIF-1	0	1	0	0	1	0
F	58	Yes	Overlap DM/RA	1:80	Ku	0	Jo-1	1	0	0	1	1
Patients with calcinosis												
F	50	Yes	Overlap DM/Scl	1:640	0	NXP-2 MDA05 SRP	0	0	1	0	1	0
F	54	No	DM	0	0	NXP2 MDA5	0	0	1	0	0	0
F	27	No	DM	1:80	0	0	Jo-1	0	1	0	1	1
F	56	Yes	DM	0	0	NXP2 MDA5	0	0	1	0	0	0
F	43	Yes	DM	0	0	0	0	0	1	0	0	0
F	58	Yes	DM	1:1,280	0	NXP2 MDA5	0	0	1	0	0	0
Patients with interstitial lung disease												
F	44	No	DM	0	0	MDA-5	0	0	0	1	1	0
F	43	No	DM	0	Ro52	Mi-2α	EJ	0	0	1	1	1
F	67	No	Overlap DM/Scl	0	0	TIF-1γ	Jo-1	0	0	1	—	1
F	57	No	Overlap DM/LES	1:160	Ro52	0	PL-7	0	0	1	1	1
F	76	Yes	DM	1:1,280	0	0	Jo-1	0	0	1	1	1
M	84	No	DM	0	0	0	0	0	0	1	0	0
F	57	Yes	DM	1:320	0	SRP SAE-1	0	0	0	1	0	0
F	52	Yes	DM	1:80	0	0	PL-12	0	0	1	1	1
F	50	No	DM	0	0	Mi-2α Mi-2β	Jo-1	0	0	1	1	1
M	70	Yes	DM	0	0	Mi-2α	PL-7	0	0	1	1	1
F	59	Yes	DM	0	0	MDA-5	Jo-1	0	0	1	1	1

Supplementary Table 1 | **Continued.**

Sex	Age	Raynaud	Diagnosis	ANA/nDNA	MAA	MSA w/o tRNA synthetase	tRNA synthetase	PS	Calc	ILD	MSA	tRNA
Patients with pure DM or overlap syndrome												
F	53	Yes	Overlap DM/Scl	1:80	0	SRP	PL-7 PL-12	0	0	0	1	1
F	71	Yes	Overlap DM/Scl	0	Ku	NXP-2	PL-7 PL-12	0	0	0	1	1
F	56	Yes	DM	1:640	0	0	PL-7	0	0	0	1	1
F	42	Yes	DM	1:640	0	0	0	0	0	0	0	0
M	43	Yes	DM	0	Ku	0	PL-7 PL-12	0	0	0	1	1
F	68	Yes	DM	0	0	0	0	0	0	0	0	0
M	58	Yes	DM	0	0	Mi-2α	0	0	0	0	1	0
F	69	No	DM	0	Ku	SRP Mi-2α Mi-2β	0	0	0	0	1	0
M	49	Yes	Overlap DM/LES	1:160 nDNA+	Ro52	0	0	0	0	0	0	0
F	72	Yes	DM	1:160	Ro52	Mi-2α	Jo-1	0	0	0	1	1
F	43	Yes	DM	0	0	0	0	0	0	0	0	0
M	24	Yes	DM	0	0	SRP	0	0	0	0	0	0
F	37	Yes	Overlap DM/Scl	0	0	SAE-1, NXP2 MDA-5	0	0	0	0	1	0
F	55	Yes	DM	0	0	0	0	0	0	0	0	0
F	45	Yes	Overlap DM/LES	1:80 nDNA+	Ro52	0	0	0	0	0	0	0
F	55	Yes	Overlap DM/Scl	0	0	SRP MDA-5 TIF-1γ Mi-2α	0	0	0	0	1	0
F	73	Yes	DM	0	0	0	0	0	0	0	0	0
F	4	No	DM	0	0	0	0	0	0	0	0	0
F	39	No	Overlap DM/LES	1:160 nDNA+	Ro52	0	0	0	0	0	0	0
F	53	Yes	Overlap DM/RA	1:160	Ro52 PM/Scl-100	Mi-2α Mi-2β	PL-7 PL-12	0	0	0	1	1
M	53	Yes	DM	0	0	0	0	0	0	0	0	0
F	39	Yes	DM	0	0	0	0	0	0	0	0	0
F	49	Yes	DM	0	0	SRP	PL-7 PL-12	0	0	0	1	1
F	60	Yes	Overlap DM/Scl	1:1,280	0	0	0	0	0	0	0	0
M	31	No	DM	1:160	PM-Scl75	0	Jo-1	0	0	0	1	1
F	48	Yes	DM	0	PM-Scl75	Mi-2β MDA-5	PL-12 Jo-1	0	0	0	1	1
F	37	Yes	DM	1:80	PM/Scl75	TIF-1γ	PL-7 PL-12	0	0	0	1	1
M	53	Yes	DM	1:1,280	0	Mi-2α MDA-5	PL-12	0	0	0	1	1
M	62	Yes	DM	0	0	0	0	0	0	0	0	0
F	44	Yes	DM	0	0	0	0	0	0	0	0	0

F = female, M = male, MAA = myositis-associated autoantibodies, MSA = myositis specific autoantibodies, PS = paraneoplastic syndrome, Calc. = calcinosis, ILD = interstitial lung disease, Scl = scleroderma, LES = lupus erythematosus, RA = rheumatoid arthritis, tRNA = tRNA synthetase antibodies, Ro52 = anti-Ro52 antibody, Scl75 = anti-topoisomerase I antibody, MDA-5 = anti-melanoma differentiation-associated protein 5 antibody, SAE1 = anti-small ubiquitin-like modifier activating enzyme antibody, NXP2 = anti-nuclear matrix protein 2 antibody, TIF-1γ = anti-transcription intermediary factor 1-gamma antibody, Jo-1 = anti-histidyl tRNA synthetase antibody, Ku = anti-Ku antibody, SRP = anti-signal recognition particle antibody, Mi-2α = anti-Mi-2 alpha antibody, Mi-2β = anti-Mi-2 beta antibody, PL-7 = anti-threonyl tRNA synthetase antibody, PL-12 = anti-alanyl tRNA synthetase antibody, PM/Scl-100 = anti-PM/Scl-100 antibody, ANA/nDNA = antinuclear antibodies and anti-double-stranded DNA antibodies, ANA = antinuclear antibodies, nDNA = anti-double-stranded DNA antibodies, MSA w/o tRNA synthetase = myositis-specific antibodies without tRNA synthetase antibodies.
*Patients with overlap syndrome are reported with an asterix.

Supplementary Table 2 | **Capillaroscopic features in patients with interstitial lung disease.**

Sex	Age at diagnosis	Engorged venous plexuses	Ramified capillaries	Hemorrhages	Edema
Female	44	Yes	No	Yes	Pericapillary
Female	43	Yes	Yes	No	Diffuse
Female	67	Yes	Yes	Yes	Diffuse
Female	57	Yes	No	No	Diffuse
Female	76	Yes	Yes	Yes	Diffuse
Male	84	Yes	Yes	No	Diffuse
Female	57	Yes	Yes	Yes	Diffuse
Female	52	Yes	Yes	No	Diffuse
Female	50	Yes	Yes	Yes	Diffuse
Male	70	Yes	No	Yes	Diffuse
Female	59	Yes	Yes	No	Diffuse