

CLINICAL REPORT

Dermatomyositis in 132 Patients with Different Clinical Subtypes: Cutaneous Signs, Constitutional Symptoms and Circulating AntibodiesA. PARODI¹, M. CAPRONI², A. V. MARZANO³, C. DE SIMONE⁴, M. LA PLACA⁵, P. QUAGLINO⁶, C. VELLER FORNASEA⁷, C. ZANE⁸, M. VACCARO⁹, M. PAPINI¹⁰, P. FABBRI² and A. REBORA¹

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We retrospectively studied 132 patients with dermatomyositis; 84 had idiopathic, 30 paraneoplastic, 5 juvenile and 13 amyopathic forms of the disease. The commonest features were macular erythema, heliotropic erythema and Gottron's papules. Flagellate erythema occurred in 5% of patients with idiopathic dermatomyositis and correlated with the disease activity. Necrotic lesions were also found in this group of patients but did not always signal malignancy. The prevalence of malignancy was high (23%). Raynaud's phenomenon occurred in 10.6% of patients, also in those with malignancy. Dysphagia, interstitial lung disease and arthralgias affected 20%, 8% and 40% of patients, respectively. Anti-Jo-1 antibodies were found in 5% of patients with idiopathic dermatomyositis and low titre ANA in 1/3 of patients. ANA did not correlate with the disease activity. We confirmed the data from the literature, but no cutaneous sign, constitutional symptom or circulating antibody was found marking a particular subtype of the disease. *Key words: amyopathic dermatomyositis; clinical features; idiopathic; immunological parameters; juvenile; paraneoplastic; systemic symptoms.*

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Dermatomyositis (DM) is characterized by an inflammatory myopathy and includes various subtypes with different age of onset, cutaneous involvement and possible association with a neoplasm. Probably because of the rarity of the disease, there is no consensus about the prevalence of cutaneous lesions and their significance as markers of a particular DM subtype. Furthermore, the prevalence of tumours, concomitant diseases and the importance of circulating antibodies in DM are unclear. We have had the opportunity to study a large cohort of patients with DM and wish to report the results of a

retrospective survey initiated by the Italian Group of Immunodermatology (IGI).

MATERIAL AND METHODS

A questionnaire with clinical, laboratory and immunological items was mailed to IGI centres in Bologna, Brescia, Firenze, Genova, Messina, Milano, Padova, Roma-Catholic University, Terni and Torino. The recruited records from 1990 were then examined. The diagnosis of DM was accepted when patients proved to fulfil Bohan & Peter's diagnostic criteria (1, 2). Juvenile DM was diagnosed when the disease had begun before the patient had reached 15 years of age (3). The diagnoses of the retained records were divided into idiopathic DM, juvenile DM, DM associated with malignancy and amyopathic DM.

The records of 99 females and 33 males were retained. Patients with polymyositis (PM) DM associated with connective tissue diseases were considered inhomogeneous with the remainders and were excluded. The patients with amyopathic DM have been reported in detail elsewhere (4). We registered lesions for each patient as follows:

- heliotrope rash with or without periorbital oedema: violaceous to dusky erythematous rash with or without oedema involving, in a symmetrical distribution, periorbital skin
- erythematous and/or poikilodermatous macules: violaceous macules sometimes with slight scales, telangiectases and epidermal atrophy involving the back, extensor surface of the arms, the "V" of the neck
- Gottron's papules: erythematous papules which can become confluent to form plaques covering bony prominences, usually metacarpophalangeal joints, proximal and distal interphalangeal joints but also elbows, knees, feet
- erythematous lesions arranged radially on the dorsa of the hands: erythematous linear streaking over the extensor tendon sheaths
- periungueal telangiectases and/or cuticular overgrowth: dilated capillary loops of the nail folds and/or thickening, roughness, hyperkeratosis and irregularity of the cuticles and small haemorrhagic areas of the hypertrophic cuticle
- flagellate erythema: linear, violaceous itching and oedematous streaks localized mainly on the trunk resembling bleomycin-induced linear erythema
- necrotic lesions: scaly, erythematous patches with areas of erosions and necrosis.

In addition, we considered as "other cutaneous manifestations" the following: the mechanic's hands that resemble the calluses of manual labourers, facial swelling, seborrhoeic dermatitis-like lesions, livedo reticularis, lichen planus-like lesions, vasculitis, papular mucinosis, panniculitis and follicular hyperkeratosis (3, 5).

Dysphagia, arthralgias, Raynaud's phenomenon, cardiac and respiratory manifestations as well as the associated diseases were considered. ANA and anti-cytoplasmic antibodies were recorded in the majority of the patients. In particular, anti histidyl-tRNA synthetase (Jo-1) antibodies were looked for in 66 patients. In 87 patients the antibodies for hepatitis C virus (HCV) and hepatitis B virus (HBV), and in 7 those for anti-Epstein-Barr virus (EBV) and cytomegalovirus were studied. Muscle conditions were studied by enzymatic tests, by electromyography in 127 patients and by biopsy in 47. Only in 4 cases were immunohistochemical investigations done.

Cardiac and respiratory functions were studied by electro- and echo-cardiography, chest X-ray, computerized axial tomography and scintigraphy, and by lung spirometry whenever necessary.

Data were analysed statistically by the chi-squared test whenever the expected count in all cells was > 5.

RESULTS

In the 132 retained patients, the female/male ratio was 3:1. The mean age was 53 years, ranging from 2 to 83 years. In all patients, cutaneous manifestations were the presenting symptom of the disease. Cutaneous and muscle involvement were contemporary in most cases, but in 4 patients the muscle involvement became apparent one month after the cutaneous symptoms, in 11 patients after 3 months, in 5 patients after 6 months and in 6 patients after 9 months.

In 21 of the 47 biopsied patients, histology showed a perivascular and/or interfascicular inflammatory cell infiltrate and in 26 cases fibre necrosis. In these 26 patients, degenerating and regenerating fibres were also present. Perifascicular atrophy was found in 4 cases. In all but 3 patients electromyography revealed specific myopathic alterations and all patients had at least one of the muscle enzyme values elevated in particular creatine-phosphokinase.

Eighty-four patients (24 males and 60 females) had idiopathic DM. They averaged 51 years of age, ranging from 18 to 78 years. The prevalence of their cutaneous manifestations is summarized in Table I.

Table I. Prevalence of cutaneous manifestations in 84 patients with idiopathic dermatomyositis

Cutaneous signs	Gender		
	F	M	Both (%)
Heliotrope erythema	44	14	58 (68)
Erythematous/poikilodermatous macules	47	19	66 (78)
Flagellate erythema	2	2	4 (5)
Gottron's papules	20	13	33 (39)
Linear erythema of the back of the hands	9	5	14 (16)
Periungual telangiectases/cuticular overgrowth	15	5	20 (23)
Necrotic lesions	2	1	3 (3.5)
Livedo reticularis	1	0	1 (1)
Lichen planus-like lesions	2	0	2 (2)
Vasculitis	0	1	1 (1)

Because the expected count in some cells was < 5, the chi-squared test was applied to a table in which the rows were reduced to 6 by gathering flagellate erythema, necrotic lesions, livedo reticularis, lichen planus-like lesions and vasculitis into a single row. There was no significant statistical difference between the two sexes ($\chi^2 = 3.059$; $p = 0.691$).

As for the associated diseases, 4 patients (2 females and 2 males) also had psoriasis, 1 female had lichen planus, 7 (3 females, 4 males) had pulmonary fibrosis, 2 females had hyperthyroidism, 7 (6 females, 1 male) had hypothyroidism, 7 (6 females, 1 male) had chronic obstructive pneumopathy, 1 female had chronic hepatitis, 3 (2 females, 1 male) had cardiovascular diseases, 3 females had hypertension, 3 (1 female, 2 males) had diabetes. Nine patients (8 females, 1 male) had Raynaud's phenomenon, 12 (6 females, 6 males) had dysphagia, and 40 (31 females, 9 males) had arthralgias. In no case was DM reported to begin after a viral disease.

From an immunological point of view, 7 patients (4 females, 3 males) had antibodies anti-HBV and 3 (2 females, 1 male) anti-HCV. ANA and/or anti-cytoplasmic antibodies were positive in 38 patients and negative in 35 patients. In 11 patients they were not detected. In indirect immunofluorescence (IIF), their pattern was homogeneous in 2 patients and speckled in 31. Five patients also had positive anti-extractable nuclear antigens. Five patients had anti-histidyl-tRNA synthetase (Jo-1) antibodies.

Thirty patients (22 females and 8 males) had paraneoplastic DM. They averaged 66 years of age, ranging from 43 to 83 years. Their clinical features are summarized in Table II.

The associated neoplasm affected breasts (5 females), lung (4 females, 2 males), stomach (3 females, 2 males), uterus, ovary, vulva (3, 2 and 1, respectively), liver (1 female), Kaposi's sarcoma (1 female), multiple myeloma (1 female), metastatic melanoma (1 female), prostate (1), pharynx (2 males). In this group, 2 patients (1 female, 1 male) had diabetes, 3 females hyperthyroidism, 2 females hypertension, 1 female psoriasis, 1 female chronic hepatitis and 1 female pulmonary emphysema.

Table II. Clinical features of 30 patients with paraneoplastic dermatomyositis

Clinical features	Gender		
	F	M	Both (%)
Heliotrope erythema	17	3	20 (67)
Erythematous/poikilodermatous macules	11	5	16 (53)
Flagellate erythema	0	0	0
Gottron's papules	10	4	14 (47)
Linear erythema of the back of the hands	3	0	3 (10)
Periungual telangiectases/cuticular overgrowth	6	0	6 (20)
Necrotic lesions	1	1	2 (7)

Three patients (females) had Raynaud's phenomenon, 6 (3 females, 3 males) dysphagia and 9 (7 females, 2 males) arthralgias.

Only 2 of 30 patients with paraneoplastic DM had anti-HBV (1 female) and anti-HCV (1 female) antibodies. In 5 patients ANA/anti-cytoplasmic antibodies were not detected. In 11 patients (8 females, 3 males) the IIF pattern was speckled, in 2 (females) homogeneous and in 1 nucleolar. One patient (female) had PM/Scl antibodies. Ten patients had no ANA.

As for juvenile DM, only 5 patients (all females) had such diagnosis. Their mean age was 9 years. The cutaneous lesions are summarized in Table III.

One patient had Raynaud's phenomenon and one dysphagia. In one patient, DM occurred after an episode of influenza and in another one after a streptococcal infection. On IIF, 3 patients had speckled ANA and in 2 ANA were absent.

Thirteen patients (12 females and 1 male) had amyopathic DM. They averaged 53 years of age and ranged from 19 to 86 years. Their cutaneous features are given in Table IV.

Arthralgias occurred in 2 patients and Raynaud's phenomenon in 4. Anti-HBV antibodies were found in 3 patients, speckled antinuclear antibodies in 7 and anti-Ro/SSA and anti-mitochondria antibodies in one case each. None of our patients had evidence of internal malignancy, but one had primary biliary cirrhosis and one a multinodular goitre. Neither cardio-pulmonary nor oesophageal dysfunction were demonstrated. EMG showed a protopathic muscle pathology in 3 patients. Muscle biopsy revealed myositis and a neurogenic myopathy in another one.

Table III. *Clinical features of 5 female patients with juvenile dermatomyositis*

Clinical features	No. of patients (%)
Heliotrope erythema	4 (80)
Erythematous/poikilodermatous macules	4 (80)
Flagellate erythema	0
Gottron's papules	2 (40)
Linear erythema of the back of the hands	3 (60)
Periungual telangiectases/cuticular overgrowth	3 (60)

Table IV. *Clinical features of 13 patients with amyopathic dermatomyositis*

Clinical features	Both sexes (%)
Heliotrope erythema	9 (69)
Erythematous/poikilodermatous macules	7 (54)
Flagellate erythema	0
Gottron's papules	7 (54)
Linear erythema of the back of the hands	3 (23)
Periungual telangiectases/cuticular overgrowth	6 (46)
Necrotic lesions	2 (15)

DISCUSSION

This is one of the largest series of patients with DM studied so far. The most commonly detectable cutaneous features were the violaceous macular erythema often distributed symmetrically, the heliotrope erythema and Gottron's papules. About 50% of patients with idiopathic DM exhibited telangiectases and cuticular overgrowth which, furthermore, were present in about 1/5 of the patients with paraneoplastic DM and only in females.

Flagellate erythema, which is said to be rare in DM (4, 5), occurred in 5% of our patients with the idiopathic subtype and in none of those with paraneoplastic, juvenile or amyopathic DM. As reported previously, flagellate erythema was associated with an active disease and heralded a relapse.

Necrotic lesions were also noted in patients (3.5%) with idiopathic DM. In contrast to the literature (6), which considers them a sign of malignancy, they developed only in two of the patients with paraneoplastic DM.

Cutaneous features (7), such as the mechanic's hands, seborrhoea-like dermatitis, vasculitis, lichen planus-like papules and livedo reticularis were seen in only a minority of patients. Because of the retrospective nature of our study and their clinical inconspicuousness, however, some of those features may have escaped our survey, i.e. not being registered in the records. Overall, 16% of our patients had a thyroid pathology, which is quite a high prevalence especially considering that not all patients have been investigated from this point of view.

The prevalence of malignancy in our patients is high (22%), but similar to that reported earlier (8). Likewise, the type of associated neoplasms is as expected. In women, breast, uterus and ovary and in both sexes lung and stomach cancers were the most frequent, as they are in the general population.

Raynaud's phenomenon is reported to occur in 10–20% of individuals with DM. In our study, it occurred in 10.5% of patients with both idiopathic and paraneoplastic DM, and also in 1 of 5 patients with juvenile DM. None of the patients with Raynaud's phenomenon developed sclerodactily or cutaneous signs of scleroderma. Bohan & Peter (1, 2) did not report Raynaud's phenomenon in patients with paraneoplastic DM. We found it in 10% of these patients.

Dysphagia is said to be a common symptom in DM (9), and, in fact, we found it in about 20% of our patients. Interstitial lung disease was found only in the group of idiopathic DM (8%). Only 2 of these patients had anti-synthetase antibodies, though a larger number was to be expected because of the alleged prevalence (40%) of such antibodies in DM associated with interstitial pneumonitis (10). Although arthralgias are reported in a minority of patients (7), we found them

in as many as about 50% of patients with idiopathic DM and in 31% of those with DM and cancer.

Calcinosis cutis (7, 9) and gingival telangiectases (11) are considered a common occurrence in children with DM (30–70% versus less than 10% in adults), but this was not our experience. Other skin lesions of juvenile DM were similar to those in adult DM. In 2 young patients, a febrile illness preceded the onset of DM as was expected in juvenile DM.

Antibodies directed to histidyl-tRNA synthetase (anti-Jo 1) were detected in only 5 cases (5%) of idiopathic DM and in none of those with paraneoplastic or juvenile DM. This prevalence is slightly lower than reported in the literature (20–30%) (10), probably because the more sensitive confirmatory ELISA was not used in all centres. These antibodies are rarely found in juvenile DM/PM and are reported in DM associated with interstitial pneumonitis. In fact, 2 of our 5 anti-Jo-1-positive patients had interstitial fibrosis. Anti PM/Scl antibodies usually define a subset associated with scleroderma (12). We found them in one patient with paraneoplastic DM without Raynaud's phenomenon, sclerodactily or other signs of scleroderma. She died one year after the diagnosis of DM because of lung carcinoma. In all of our ANA-positive patients, the titres were low or mild and their presence did not correlate with the disease activity.

In conclusion, we confirmed the prevalence of the typical cutaneous lesions and of the tumours and concomitant diseases, but failed to detect any cutaneous sign, constitutional symptoms or circulating antibodies which may be considered markers of a particular subtype of the disease. A possible exception was the flagellate erythema which, in our patients, was a clear sign of disease activity. Necrotic lesions were not found to signal malignancy.

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