Amyopathic Dermatomyositis

A Review by the Italian Group of Immunodermatology

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Objective: To analyze the average age, sex distribution, duration of follow-up, clinical course, serologic abnormalities, and incidence of possibly associated malignancy in patients with amyopathic dermatomyositis.

Design: Retrospective study.

Setting: University hospitals.

Patients: Thirteen patients with amyopathic dermatomyositis.

Results: The 13 patients represented 8.2% of 157 patients with dermatomyositis seen retrospectively in a 10-year period by the Italian Group of Immunodermatology of the Italian Society of Dermatology and Venereology. Gottron papules and sign and periungual telangiectasias were found in approximately 50% of cases (papules in 7 patients, Gottron sign and periungual telangiectasias in 6), while periorbital violaceous erythema was seen in 70% (9 patients). Arthralgias occurred in 2 patients and Raynaud phenomenon in 4. An elevated erythrocyte sedimentation rate was detected in 6 patients, hepatitis B virus antigen in 3, speckled antinuclear antibodies in 7, and anti-Ro and antimitochondrial antibodies in 1 case each. None of our patients had evidence of internal malignancy. Neither cardiopulmonary nor esophageal dysfunction was demonstrated. Electromyography showed a protopathic muscle abnormality in 3 patients. Muscle biopsy disclosed myositis and a neurogenic myopathy in another one.

Conclusions: Amyopathic dermatomyositis is a rare disease. So far, only 2 series of a few cases each have been reported. The “amyopathic” subset of dermatomyositis is peculiar in that its cutaneous lesions are predominant for long periods or even permanently, although they are indistinguishable from those of classic dermatomyositis. The minimal or absent muscle disease and the rarity of serum immunologic findings imply a favorable prognosis in white patients.

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The term amyopathic dermatomyositis (ADM) (or dermatomyositis sine myositis) refers to patients who, after 2 years of biopsy-confirmed classic cutaneous manifestations of dermatomyositis (DM), have “minimal” muscle disease (after complete evaluation with electromyography [EMG], muscle biopsy, and magnetic resonance imaging) or no evidence of inflammatory myopathy. Amyopathic dermatomyositis is a rare disease. Only 2 series of a few cases each have been reported so far. Rarity, however, may be only apparent depending in part on the lack of qualitative differences in the clinical features and immunohisto-pathologic findings between the cutaneous manifestations of ADM and those of classic DM. Other reasons are the diagnostic difficulty in patients in whom concurrent treatment with drugs, such as hydroxyurea, alfuzosin hydrochloride, and phenytoin, may induce DM-like reactions, and the racial differences in the published reports. In fact, 1 of the 2 series comprised only Chinese patients and the other a mixed population of blacks and whites.

To determine whether the conclusions of the 2 mentioned series could also apply to Mediterranean patients, the Italian Group of Immunodermatology of the Italian Society of Dermatology and Venereology reviewed retrospectively the cases of ADM observed during the last 10 years. For editorial comment see page 114

Gottron papules (Figure 1) and sign (Figure 2) were found in 7 (54%) and 6 (46%) of our patients, respectively. Among

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**PATIENTS AND METHODS**

Thirteen patients (12 women and 1 man; mean age, 53 years; range, 19-86 years) from the centers (Florence, Genoa, Messina, Milan, Rome, and Terni) of the Italian Group of Immunodermatology were reviewed. They belonged to a series of 157 consecutive patients with DM (8.2%). A questionnaire with clinical, laboratory, and immunologic items was sent to the study centers. The recruited records were then examined. The diagnosis of DM was accepted when patients proved to fulfill Bohan and Peter’s clinicopathologic criteria⁵ and satisfied the exclusion and Sontheimer’s additional criteria.⁶

Eleven patients had had their skin disease for at least 2 years (confirmed ADM),⁴ while 2 had it for longer than 6 months but shorter than 24 months (provisional ADM).⁴ In the juvenile case, the disease had begun at age 13 years; no familial cases were included. All patients had the characteristic histopathologic changes of DM, with basal keratinocyte liquefaction degeneration and lymphohistiocytic inflammation of papillary dermis. Patients were observed during a mean follow-up of 6.8 years.

Laboratory tests included erythrocyte sedimentation rate, serum muscle enzyme levels (creatine kinase, lactate dehydrogenase, aspartate aminotransferase, and aldolase), antinuclear antibodies, anti-double-strand DNA, anti-extractable nuclear antigens, and antimitochondria, anti–smooth muscle, and antithyroid antibodies. Serologic tests for hepatitis B and C virus were also performed.

Electromyography was performed on deltoids and quadriceps in 8 of 13 patients. Muscle biopsy specimens were obtained from 2 cases. Complaints of Raynaud phenomenon and arthralgias were also recorded. Pulmonary investigations (x-ray films, carbon monoxide diffusion capacity) and esophageal motility studies were performed in all patients.

Search for neoplasia included clinical examination, standard biological tests, and chest x-ray films. Specific investigations were also performed only if indicated by direct abnormal symptoms.

The characteristic skin lesions, periorbital violaceous erythema (Figure 3 and Figure 4) was seen in 9 patients (69%) and periungual telangiectasias (Figure 1) in 6 patients (46%). Poikiloderma was observed in only 1 case. Two patients complained of photosensitivity, while in 3 the cutaneous lesions were accompanied by severe pruritus. Arthralgias occurred in 2 patients (15%) and Raynaud phenomenon in 4 (31%).

An elevated erythrocyte sedimentation rate was detected in 6 patients (46%). Hepatitis B virus antigen was present in 3 patients (23%). Speckled antinuclear antibodies were found in 7 patients (54%) with a titer ranging between 1:80 and 1:640. Anti-Ro and antimitochondrial antibodies were found in 1 case each. Antithyroid and anti–smooth muscle antibodies were detected in another one.

None of our patients had evidence of internal malignancy. Neither cardiopulmonary nor esophageal dysfunction was demonstrated.

The EMG showed no signs of muscle involvement in 5 of the 8 cases in which it was performed, while a protopathic muscle abnormality was demonstrated in 3 patients. Muscle biopsy showed myositis in 1 patient who was not in the positive EMG group, while in
COMMENT

Only 8% of our 157 patients with DM had ADM. This prevalence is lower than reported elsewhere (10%-20%). Recently, an even higher incidence of ADM (25%) has been reported in a Chinese study. Apparently, ADM is less common in the Mediterranean area.

Most cases have been reported in middle-aged adults. Until now, juvenile patients have been described only in case reports and small case series, but, in a recent study, 27 juvenile-onset cases of ADM have been analyzed. Elderly patients have also been described, including an 84-year-old man presenting with blisters on the neck and oral ulcers in association with the typical skin manifestations of DM. We observed an 86-year-old woman.

Most patients with ADM are said to be women, only the Chinese series showed a prevalence of men. In our series, the female predominance was almost absolute (92%) (Table). The characteristic heliotrope erythema was slightly more frequent than the pathognomonic Gottron papules (69% vs 54%). Although the difference was not statistically significant, we support Callen’s opinion that heliotrope erythema is a pathognomonic lesion.

Periungual alterations affected only 46% of our patients. In a previous study, periungual nailfold telangiectasias were present in the 3 cases studied. In contrast, all 6 patients described by Euwer and Sontheimer presented with Gottron papules, periungual erythema telangiectasias, and violaceous discoloration of the face, neck, and upper part of the chest, or had had them at some time during the course of the disease. Also, in the study by Rockerbie et al., Gottron papules and heliotrope erythema were the most frequent lesions (80%). On the contrary, in the patients with associated malignancies in the Chinese series, the most common cutaneous lesions (83%) were erythematous, violaceous macules or papules on the face, limbs, and trunk (Table).

All patients described by Euwer and Sontheimer had moderate to severe pruritus and complained of photosensitivity. These symptoms have been reported more rarely elsewhere and were uncommon in our series, with 2 patients complaining of photosensitivity and 3 of severe pruritus. Arthralgias and Raynaud phenomenon (15% and 31% of our cases, respectively) have not been previously reported, except by Euwer and Sontheimer (1 patient with arthralgias).

As for the laboratory findings, positive antinuclear antibodies were found in half of our patients, in agreement with previous data. In other series, however, they were positive in almost all patients. The speckled pattern was prevalent in all of the studies, with lower titers only in Stonecipher and coworkers’ series. We confirmed the speckled pattern of other reports and elevated titers as well. No correlation was demonstrated between the presence of Raynaud phenomenon and positive antinuclear antibodies, but only a fortuitous association was made in 2 cases.

Anti–double-strand DNA autoantibodies were absent (as in other ADM reports), and antineutropilic nuclear antigen autoantibodies were found in only 1 case. In addition, another patient had positive antithyroid and anti–smooth muscle autoantibodies. In fact, we had also found antithyroid antibodies in 2 of the 3 patients with ADM studied previously. Although other authors have encountered several diagnostic autoantibodies (anti–Jo-1, anti–Mi-2, anti–PML, and anti–Ku) in classic DM, we failed to do so.

First Braverman and Bohan et al suggested the possible association with malignancy in patients with ADM, and later Stonecipher et al recommended examining patients with ADM, like those with classic DM. In fact, in the Chinese series, 60% of patients had malignancy. None of our patients had such evidence, in agreement with other Western series. In the Chinese series, nasopharyngeal carcinoma was the most common malignant disease. Chinese findings may be coincidental given the small number of their ADM cases and the fact that nasopharyngeal carcinoma is frequent in Southeast Asia. Other cases of ADM have been reported in association with breast cancer, transformed malignant lymphoma, and papillary serous ovarian cancer. We agree with other authors that the risk of malignancy should be considered low in white patients.

Some patients with ADM have subclinical evidence of muscle inflammation if investigated thoroughly with EMG, muscle biopsy, or noninvasive procedures that can assess muscle anatomy and physiology, such as ultrasound and magnetic resonance imaging. Four of 10 of our patients who fulfilled the diagnostic criteria for ADM underwent some of those investigations, demonstrating minimal, subclinical muscle involvement without subjective and laboratory (normal serum levels of muscle enzymes) evidence of muscle weakness.

These findings reveal the necessity of proper classification of these patients, and, in this regard, the use of noninvasive tests might be helpful because a complete and reliable evaluation of muscle involvement is not possible on the basis of only EMG and muscle biopsy. In fact, EMG is a sensitive but not specific procedure, while muscle...
biopsy may give confusing results because of sampling error. In the absence of these important noninvasive procedures, as in our study, we treated the patients conservatively without using immunosuppressive drugs.

In conclusion, the amyopathic subset of DM is unusual in that its cutaneous lesions are predominant for long periods or even permanently, although they are indistinguishable from those of classic DM. The minimal

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<tbody>
<tr>
<td>Total population of DM</td>
<td>157</td>
<td>40</td>
<td>. . .</td>
<td>65</td>
<td>19</td>
<td>. . .</td>
<td>50</td>
<td>. . .</td>
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<tr>
<td>No. (%) with ADM</td>
<td>13 (8)</td>
<td>10 (25)</td>
<td>3 (. . .)</td>
<td>12 (18)</td>
<td>12 (. . .)</td>
<td>13 (. . .)</td>
<td>6 (11)</td>
<td>50 (. . .)</td>
<td>. . .</td>
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<tr>
<td>Age range, y</td>
<td>19-86</td>
<td>25-72</td>
<td>20-76</td>
<td>26-70</td>
<td>33-72</td>
<td>20-72</td>
<td>ND</td>
<td>2-83</td>
<td>ND</td>
</tr>
<tr>
<td>Median age, y</td>
<td>53.0</td>
<td>ND</td>
<td>51.3</td>
<td>48.6</td>
<td>59.0</td>
<td>45.0</td>
<td>53.6</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Juvenile cases, No.</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Sex, No. M:F</td>
<td>12:1</td>
<td>2:8</td>
<td>3:0</td>
<td>11:1</td>
<td>10:2</td>
<td>10:3</td>
<td>5:1</td>
<td>3:1</td>
<td></td>
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<tr>
<td>Mean follow-up</td>
<td>6.5 y</td>
<td>20-90 mo</td>
<td>5 y</td>
<td>4.8 y</td>
<td>4.2 y</td>
<td>1-6 y</td>
<td>3 y</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Gottron papules, No./total (%)</td>
<td>7/13</td>
<td>4/6</td>
<td>3/3</td>
<td>. . .</td>
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<tr>
<td>Heliotrope erythema, No./total (%)</td>
<td>9/13</td>
<td>2/6</td>
<td>3/3</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
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<tr>
<td>Periungual alteration (erythema, telangiectasia), No./total (%)</td>
<td>6/13</td>
<td>4/6</td>
<td>3/3</td>
<td>ND</td>
<td>0</td>
<td>0</td>
<td>6/6</td>
<td>3/50</td>
<td></td>
</tr>
<tr>
<td>Polikidderma, No./total (%)</td>
<td>1/13</td>
<td>2/6</td>
<td>0</td>
<td>ND</td>
<td>0</td>
<td>0</td>
<td>2/6</td>
<td>(33)</td>
<td>5/50</td>
</tr>
<tr>
<td>Positive ANA, No./total (%)</td>
<td>7/13</td>
<td>5/6</td>
<td>2/3</td>
<td>ND</td>
<td>11 or</td>
<td>12/12</td>
<td>3/6</td>
<td>ND</td>
<td></td>
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<tr>
<td>Positive anti-native DNA, No.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>0</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Anti-ENA (Ro/SSA+)</td>
<td>1/13</td>
<td>0</td>
<td>0</td>
<td>ND</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>ND</td>
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<tr>
<td>Antithyroid antibody, No./total</td>
<td>1/13</td>
<td>ND</td>
<td>2/3</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Enzyme levels</td>
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<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
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<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
<td>Elevated ESR, No./total (%)</td>
<td>6/13</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>0</td>
<td>3/5</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Positive HBV, No./total (%)</td>
<td>3/13</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Frequency of malignancy, No./total (%)</td>
<td>0</td>
<td>6/10</td>
<td>0</td>
<td>1/12</td>
<td>4/12</td>
<td>2/13</td>
<td>0</td>
<td>0</td>
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<tr>
<td>EMG</td>
<td>Normal</td>
<td>No signs of muscle involvement</td>
<td>Normal findings</td>
<td>ND</td>
<td>Positive C/W DM in 4/11 patients</td>
<td></td>
<td></td>
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<td>Muscle biopsy</td>
<td>ND</td>
<td>Not described</td>
<td>Not described</td>
<td>Oral hydroxychloroquine, oral methotrexate, topical corticosteroids</td>
<td>Not described</td>
<td>Not described</td>
<td>Oral corticosteroids</td>
<td>Not described</td>
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*DM indicates dermatomyositis; ADM, amyopathic DM; ND, not determined; ANA, antinuclear antibody; ENA, extractable nuclear antigen; ESR, erythrocyte sedimentation rate; HBV, hepatitis B virus; EMG, electromyogram; and C/W, consistent with.
†Data referred to the 6 patients with malignancies.
‡Ellipses indicate patients had the typical cutaneous features of DM.
§Ellipses indicate diagnosis made on the basis of pathognomonic cutaneous changes (heliotrope eyelid rash and Gottron papules).
||Enzyme levels included creatine kinase, lactate dehydrogenase, aspartate aminotransferase, and aldolase.
or absent muscle disease and the rarity of serum immunologic findings all imply a favorable prognosis in the white population.

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REFERENCES