Clinical and serologic features of patients with polymyositis or dermatomyositis

Daniel J. Holden,* MD
A. Keith W. Brownell,† MD
Marvin J. Fritzler,‡ PhD, MD

The clinical and serologic features of 36 patients with polymyositis (PM) or dermatomyositis (DM) were observed over a 5-year period. The mean age of the patients at the time of diagnosis was 48.5 years, and 61% were female. According to widely accepted diagnostic criteria 50% had PM (group I), 14% DM (group II), 11% PM or DM associated with malignant disease (group III) and 25% PM or DM associated with a connective tissue disorder (group V). None of the patients had childhood PM or DM associated with vasculitis (group IV). All the patients had muscle weakness, and 94% of the patients tested had an elevated serum level of creatine kinase. The average delay from the onset of symptoms to diagnosis was 14 months overall but only 2.3 months for the DM patients. Of the 30 patients whose serum was tested, 73% had antinuclear antibodies, with antibodies to nuclear ribonucleoprotein being most common in group V patients and antibodies directed against the Jo-1 antigen being restricted to patients with PM alone (group I).

Observation sur 5 ans des caractères cliniques et biologiques de 36 malades souffrant de polymyosite (PM) ou de dermatomyosite (DM) dont l'âge moyen au diagnostic était de 48,5 ans et dont 65% sont du sexe féminin. Selon les critères diagnostiques reconnues, on trouve 50% atteints de PM (groupe I), 14% de DM (groupe II), 11% de PM ou de DM reliée à un néoplasme malin (groupe III) et 25% de PM ou de DM reliée à une maladie du tissu conjonctif (groupe V); le groupe IV, celui de la PM et de la DM ayant débuté dans l'enfance et reliée à une vasculite, n'est pas représenté. Tous les malades accusent une faiblesse musculaire; on trouve une augmentation de la créatine-kinase sérique chez 94% de ceux chez qui on la recherche. Le délai moyen entre l'apparition des premiers symptômes et le diagnostic a été de 14 mois pour l'ensemble des cas, mais de seulement 2,3 mois pour la DM. Parmi les 30 malades chez qui on les recherche, 75% ont des anticorps anti-nucléaires: les anti-ribonucléoprotéines se retrouvent surtout dans le groupe V, les anti-Jo-1 seulement dans le groupe I.

From the departments of medicine, clinical neurosciences and medical biochemistry, University of Calgary

*Current address: 1508 North Lake Blvd., Lorain, OH 44052, USA
†Associate professor, departments of clinical neurosciences and medicine, University of Calgary
‡Associate professor and head, Division of Rheumatology, Department of Medicine, University of Calgary

Reprint requests to: Dr. A. Keith W. Brownell, Department of Clinical Neurosciences, Foothills Hospital, 1403 29th St. NW, Calgary, Alta. T2N 2T9

Polymyositis (PM) and dermatomyositis (DM) are rare diseases, having estimated combined annual incidence and prevalence rates of 5 and 60 cases per million population respectively.[1,2] PM should be considered in a patient of any age who presents with progressive weakness in the shoulder and pelvic girdle muscles when there is no family history of a similar disease. DM has the same clinical picture but is associated with a dermatologic abnormality: a scaly, erythematous skin eruption with elements of dermal atrophy over the forehead, upper torso, elbows, knuckles, knees and medial malleoli.[3] A clinical diagnosis of PM or DM is confirmed by an elevated serum level of creatine kinase (CK), muscle biopsy evidence of an inflammatory myopathy, and myopathic units plus fibrillations in an electromyogram (EMG).[4]

Recent studies in patients with PM or DM have focused on the prevalence of autoantibodies, their association with subsets of the diseases and their utility in predicting outcome.[5-7] For example, antibodies to nuclear ribonucleoprotein (nRNP) are characteristic of a syndrome called mixed connective tissue disease,[8] antibodies to the polymyositis–scleroderma antigen (PM-Scl, formerly called PM-1) are characteristic of a clinical syndrome of polymyositis and scleroderma,[7] and Jo-1 antibodies have been described in PM patients with pulmonary fibrosis.[6]

We have reviewed our experience with PM and DM in patients who presented during a recent 5-year period. In this report we stress aspects of the diseases relating to diagnosis, treatment, disease associations and prognosis, as well as present the patients' autoantibody profiles.

Materials and methods

Using the widely accepted diagnostic criteria proposed by Bohan and Peter[4] (Table I) we selected

patients from the total population studied by muscle biopsy in the laboratory of one of us (A.K.W.B.) during the 5-year period Jan. 1, 1976 through Dec. 31, 1980. No patients in whom the diagnosis was suspected refused the biopsy. The diagnosis of PM is definite when all except the last criterion are present, probable when three of the first four criteria exist and possible when only two of these criteria exist. The last criterion indicates DM, which is definite in patients who also have three of the first four criteria, probable in those with two and possible in those with one. All the patients were assigned to one of five classes (Table II); established criteria were used for the diagnosis of a connective tissue disorder.[9]

A single muscle biopsy was performed for each patient: frozen and paraffin sections were made of 34 of the specimens and paraffin sections alone of the other 2. One of us (A.K.W.B.) interpreted all of the histologic findings. An inflammatory myopathy was diagnosed on the basis of muscle fibre degeneration, phagocytosis and regeneration plus an inflammatory cell infiltrate. Pathologic variation in muscle fibre diameters, central nuclei and fibre splitting was often present but did not constitute one of the mandatory diagnostic criteria. A diagnosis of a myopathy consistent with a clinical diagnosis of PM or DM was made when some but not all of the enumerated criteria existed.

Electromyography was done in two hospital-based diagnostic laboratories by several neurologists. The precise muscles sampled as well as the actual number of muscles studied in any patient was decided by the electromyographer. The EMG was considered diagnostic for PM/DM when myopathic units plus fibrillations were recorded. An EMG showing only myopathic units was considered consistent with the diagnosis of PM/DM.

Serum from 30 patients was available for analysis and was tested for autoantibodies by indirect immunofluorescence on HEp-2 tissue-culture substrates.[10] Detection of antibodies against double-stranded DNA was done by the *Crithidia luciliae* test,[11] and detection of antibodies to the saline-soluble antigens Sm, nRNP, SS-A/Ro, SS-B/La, PM-Scl and Jo-1 was done by immunodiffusion.[10]

Table I—Diagnostic criteria for polymyositis (PM) and dermatomyositis (DM)[4]

Symmetric, progressive weakness of shoulder and pelvic girdle muscles
Muscle biopsy evidence of an inflammatory myopathy
Elevated serum level of creatine kinase
Myopathic units plus fibrillations in an electromyogram
Typical rash of DM

Results

Demographic features

Of the 36 patients in the study population 22 (61%) were female. The patients' ages at the time of diagnosis ranged from 4 to 76 years, with the average age being 48.5 years. Twenty-six patients (72%) had PM and 10 (28%) DM (Table III). One patient was not tested for an elevated serum level of CK, and five others did not undergo electromyography, facts that may account for these patients' being assigned to the probable or possible categories.

Clinical features

The onset of either disease was defined as acute, subacute or chronic when the interval from the onset of symptoms to the time medical advice was sought was less than 1 month, 1 to 6 months and greater than 6 months respectively. The onset was acute in 3% of the 36 patients, subacute in 67% and chronic in 30%. The rash was the initial symptom in half of the patients with DM. Dysphagia occurred in 31% of the patients, arthritis or arthralgias in 17%, interstitial lung disease in 14% and vitiligo in 6%. No patients had calcinosis.

Malignant disease was found in four (11%) of the patients, all of whom had DM. In other words, 40% of those with DM had a malignant disease. One of these four patients (the only man) had advanced metastatic carcinoma of the prostate at the time DM occurred. One patient, who had been treated 12 years earlier for breast carcinoma, was found to have recurrent malignant disease shortly after the diagnosis of DM was made. A third patient had had DM diagnosed 12 months before a malignant neoplasm was discovered in an ovary. The fourth patient was being treated for DM (length of time uncertain) and was found to have carcinoma of the colon when her DM worsened clinically.

Nine of the patients had an associated connective tissue disorder: three, progressive systemic sclerosis; three, systemic lupus erythematosus; two, mixed connective tissue disease; and one, Sjögren's syndrome.

Laboratory features

Serum levels of CK were measured in 35 of the patients and found to be elevated in 24 (96%) of the 25 with PM and 9 (90%) of the 10 with DM. The elevated levels varied from just beyond the upper limit of normal to more than 20 times normal. An increased erythrocyte sedimentation rate was noted in half the patients. Of the 17 patients for whom serum protein electrophoresis was done, 10 had a polyclonal increase in the level of γ-globulin; 4 of these patients had group I or II disease.

Microscopic examination of muscle biopsy material, carried out for all the patients, clearly showed an

Table II—Classification of 36 patients with PM or DM[9]

Group	Diagnosis	No. (and %) of patients
I	Primary idiopathic PM	18 (50)
II	Primary idiopathic DM	5 (14)
III	PM or DM associated with neoplasia	4 (11)
IV	Childhood PM or DM associated with vasculitis	0
V	PM or DM associated with a connective tissue disorder	9 (25)

inflammatory myopathy consistent with PM/DM in 83% of the patients, and the findings were compatible with the diagnosis of PM/DM in the remaining 17%; no specimen was normal. The results of electromyography, carried out in 31 patients, were diagnostic in 77%, consistent with the diagnosis in 16% and normal in 7%.

Serologic results

Serum from 30 patients was available for analysis. A positive result for antinuclear antibody (ANA) with indirect immunofluorescence on HEp-2 substrate (in our laboratory a titre greater than 1/40 in a patient younger than 50 years or greater than 1/80 in a patient older than 50 years) was obtained for 22 (73%) of the patients (Table IV). The titres in these 22 patients ranged from 1/80 to 1/5120. The immunofluorescence demonstrated a variety of patterns — homogeneous, nucleolar, speckled and homogeneous cytoplasmic being the most commonly observed (Fig. 1). Other less commonly observed patterns were fine nuclear speckled and fibrous or granular cytoplasmic. When the serum of the patients with negative results for ANA was tested on other substrates (mouse kidney and liver, monkey stomach), ANA was not detected, although high titres of antibodies to smooth muscle were present in the serum from one patient.

The serum was also tested for specific autoantibodies in an attempt to determine whether specific reactivities were associated with any of the disease groups; none of the four children with PM or DM had associated vasculitis, so all were included in other groups (Table IV). Antibodies directed against the Jo-1 antigen were found in 3 of the 10 patients tested in group I who had a positive result for ANA but not in patients in the other groups. Of these three patients two showed strong cytoplasmic staining of HEp-2 cells (Fig. 1). Patients in group V had the widest variety of autoantibodies, the most common of which were anti-PM-Scl and anti-nRNP (each detected in four patients). Antibodies against both SS-A/Ro and SS-B/La were found in one patient. None of the patients in any group had anti-DNA or anti-Sm antibodies.

Table III—Category of PM/DM in the 36 patients

Diagnosis and category	No. (and %) of patients
PM	
Definite	17 (47)
Probable	6 (17)
Possible	3 (8)
DM	
Definite	7 (19)
Probable	3 (8)
Possible	0

Diagnostic delay

The average interval between the onset of symptoms and diagnosis was 14 months, although in those with serum CK levels at least five times normal the interval was only 2 months, and in the patients with DM it was 2.3 months.

Treatment and patient status

As this was a retrospective study and many physicians were involved in the management of the patients, different treatment plans were used. In most instances the initial treatment consisted of the administration of prednisone, in dosages of more than 40 mg/d. Any decision to alter the prednisone dosage or to give other drugs, such as azathioprine or methotrexate, was made by the attending physician. One patient refused treatment and is not considered further in this report.

At the end of the study period 8 patients had died, and of the 27 living patients 17 had been followed for more than 1 year. Of these 17 patients only 1 had no symptoms, showed no clinical signs of disease activity and was not receiving drug therapy. Of the other 16, 11 (69%) were taking only prednisone: 7, less than 20 mg/d; 3, 20 to 40 mg/d; and 1, 60 mg/d. Nine (56%) of the 16 had had exacerbations of their disease, and in 5 of the 9 the exacerbation occurred when the prednisone dosage was being tapered and they were receiving less than 20 mg/d.

Three deaths (two caused by aspiration pneumonia and one by respiratory failure due to muscle weakness) were judged directly related to the disease, and two deaths (both caused by pulmonary emboli) were judged indirectly related; thus, the disease-related mortality rate was 14%. The other three deaths were judged unrelated to the diseases; they were due to intractable congestive heart failure, metastatic carcinoma and an intracerebral hemorrhage. Overall, 22% of the study population died during the period of follow-up.

Cushingoid features and weight gain occurred in all the prednisone-treated patients. Other prednisone-related complications included vertebral body compression fractures in four patients, diabetes mellitus in two, hair loss in two, encephalopathy in two, and bilateral avascular necrosis of the femoral head, amen-

Table IV—Antinuclear antibody (ANA) profile of the 30 patients for whom serum was available for analysis

Diagnostic group (no. tested)	No. (and %) of patients with ANA in serum	ANA pattern*	ANA specificity† (no. of patients‡)
I (12)	10 (83)	H, Nu, S, Cy	Jo-1 (3)
II (5)	1 (20)	H, S	U
III (4)	2 (50)	H	U
V (9)	9 (100)	H, Nu, S, Cy	PM-Scl (4), nRNP (4), SS-A/Ro (1), SS-B/La (1)

*H = homogeneous; Nu = nucleolar; S = speckled; Cy = cytoplasmic.
†U = unidentified; PM–Scl = polymyositis–scleroderma antigen; nRNP = nuclear ribonucleoprotein; SS-A/Ro = Sjögren's syndrome antigen A; SS-B/La = Sjögren's syndrome antigen B(La).
‡The same patient had both SS antigens.

orrhea and fatty liver in one patient each.

Azathioprine had to be discontinued in two patients because of a rash and in one patient each because of cholestasis and leukopenia. Methotrexate-induced oral ulcerations, cholestasis and gastrointestinal upset occurred in one patient each and necessitated discontinuation of the drug.

Discussion

Weakness, the commonest symptom of patients with PM/DM,[12,13] is frequently the reason that patients consult their primary care physician;[14,15] therefore, these diseases must be considered in the differential diagnosis each time a patient is being assessed for weakness, regardless of the acuteness or chronicity of the symptom. In our series of patients, although the majority (67%) had noted weakness for 1 to 6 months, a small number (3%) had had weakness for less than a month, and 30% had had it for more than 6 months prior to seeking medical advice. The average time from symptom onset to diagnosis was 14 months, although the diagnosis was made more rapidly in two subgroups: patients with serum levels of CK at least five times as high as normal and patients with DM. In these categories the intervals between the onset of symptoms and diagnosis were 2 and 2.3 months respectively. The patients with markedly elevated CK values all had noted fairly rapid deterioration in their strength. This group comprised eight patients with PM and four with DM. Physicians may be more likely to investigate rapidly developing symptoms because the changes are more noticeable than are chronically developing symptoms. Also, markedly abnormal laboratory test results are probably pursued more vigorously than are slightly abnormal results. Whatever the reason, the average delay in diagnosis was too great; physicians evaluating complaints of weakness should consider PM/DM early on.

In the 10 patients with DM the rash was the feature that seems to have accelerated the diagnostic process, which suggests that patients and physicians react more readily to what they see than to what is felt.

A higher rate of diagnostically abnormal results of electromyography and muscle biopsy might have been obtained if wider sampling had been undertaken in each patient. Inflammatory myopathies are multifocal rather than diffuse,[12,13] so the results of these procedures can be normal in patients with active disease.

The overall mortality rate of 22% is similar to the rates reported in three other series of polymyositis patients: 20%,[13] 28%[16] and 30%.[1] Because no series to date has looked at mortality in relation to clinical subgroups (Table II) or according to

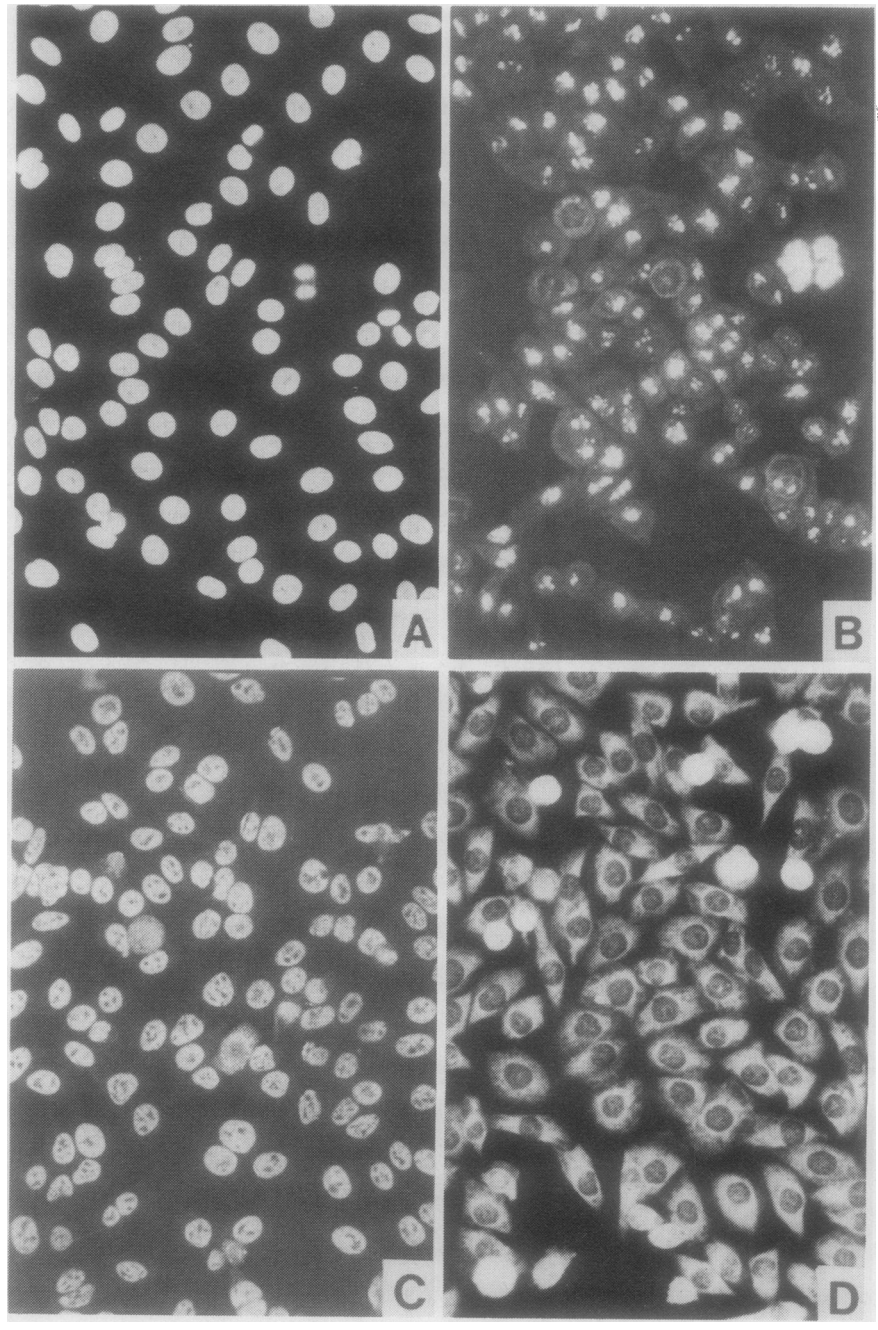

Fig. 1—Patterns of indirect immunofluorescence commonly seen when HEp-2 cells are used as a substrate to test serum from patients with polymyositis or dermatomyositis (PM/DM): (A) homogeneous, seen in all groups of patients with PM or DM; (B) nucleolar, seen in patients with PM (group I) and those with PM-Scl antibodies (group V); (C) speckled, representative of anti-nRNP and most commonly seen in patients with PM or DM and a connective tissue disorder (group V); and (D) cytoplasmic, typically seen in patients with anti-Jo-1 (original magnification ×250).

the degree or distribution of weakness, one should be cautious about using these figures prognostically for individual patients.

The association of malignant disease with PM/DM has been a subject of much debate. In a review Barnes[17] concluded that there was an increased incidence of malignant disease in older women with DM. Although the numbers in our study were small, our findings that 40% of our DM patients had malignant disease, that all were older than 50 years and that 75% were female support her conclusion. On the basis of our experience we cannot say how extensively one should investigate individuals older than 50 years with DM, but we support Callen and associates' recommendation that these patients undergo thorough history-taking and physical examination as well as basic laboratory tests, such as complete blood count, multiphasic biochemical analysis of the blood, urinalysis, stool guaiac test and chest roentgenography.[18] Further studies should be performed only if abnormalities are discovered with any of these screening tests.

No single laboratory test confirms the diagnosis of PM or DM. Thus, continued reliance must be placed on the use of the combined results of serum CK testing, muscle biopsy and electromyography. The CK level was elevated in 33 (94%) of the 35 of our patients in whom it was measured. Although all the muscle biopsy specimens were abnormal, they could be said to be diagnostic only in 83% of the patients. The EMG was diagnostic in 77%, abnormal but not diagnostic in another 16% and normal in 7% of the 31 patients studied.

The use of autoantibody testing as a means of confirming the diagnosis and determining the prognosis has potential. In our study antibodies directed against the Jo-1 antigen were found only in patients with group I PM. This observation agrees with that of Yoshida and colleagues,[6] although we were not able to confirm their observation that these patients also have pulmonary fibrosis. The PM antibody was found only in the group V patients in our series and was most often seen in the patients with PM and early scleroderma.

In our patients there was no consistent change in the ANA titre with disease remission or progression. In general the titre decreased with remission, although that of some of the specific autoantibodies (anti-nRNP and anti-SS-B/La) did not change with treatment. Therefore, the use of ANA titres as a guide to treatment should be considered unreliable.

Our findings, as well as those from several other series,[3,13,16] indicate that all patients with PM/DM require prolonged treatment and that a sustained remission without continuing therapy is uncommon. Our experience is similar to that reported by Bohan and colleagues[3] in that exacerbations of the disease occur frequently and often coincide with reduction in steroid dosage. The need for prolonged corticosteroid therapy, which often results in treatment-related side effects, and the high rate of death directly associated with PM/DM underline the importance of continued monitoring and care of these patients.

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