

Classical and Amyopathic Dermatomyositis seen at the National Skin Centre of Singapore: A 3-year Retrospective Review of their Clinical Characteristics and Association with Malignancy

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Abstract

Introduction: Dermatomyositis is a condition well-known to medical physicians, especially rheumatologists and dermatologists. Classically, patients present with typical cutaneous features and proximal muscle weakness. Amyopathic dermatomyositis has been reported in recent literature where patients present with skin changes without muscle involvement. **Materials and Methods:** We reviewed 28 patients diagnosed with dermatomyositis at the National Skin Centre over a 3-year period from 1996 to 1998 to assess the prevalence of this amyopathic variant in our local population and its association with malignancy. **Results:** Out of the 28 patients, 13 (46.4%) had no clinical or laboratory evidence of myositis at presentation. Nine patients (32.1%) had clinical muscle weakness and 6 patients (21.4%) had laboratory evidence of myositis. Malignancies were detected in 12 patients (42.8%), half of which were nasopharyngeal carcinomas. There was no significant difference in the prevalence of malignancy between those with detectable muscle weakness (33.3%) and those without (47.4%). However, there was a significant higher prevalence of malignancy in those with clinical and laboratory evidence of myositis (66.6%) than those without (15.4%). **Conclusion:** We conclude that amyopathic dermatomyositis is a common presentation in our population and may have a lower risk of malignancy than the classical variant. Screening for malignancy, especially nasopharyngeal carcinoma, is recommended for all dermatomyositis patients.

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Key words: Gottron's papules, Gottron's sign, Heliotrope rash, Nasopharyngeal carcinoma

Introduction

Polymyositis/dermatomyositis is a connective tissue disorder with inflammatory muscle disease resulting in muscle weakness. When there is only muscle involvement, the term polymyositis is used. When there is muscle involvement with characteristic skin changes, the term dermatomyositis is used. Both are associated significantly with the presence of underlying internal malignancy.

In recent years, a clinical subset has been recognised where patients present with the typical skin changes of dermatomyositis without any muscle involvement. This has been termed amyopathic dermatomyositis. Amyopathic dermatomyositis is also associated with malignancy and may either remain limited to the skin for long periods of time or progress to classical dermatomyositis. It is important to recognise this variant to avoid misdiagnosis and an unnecessary delay in the search for an underlying malignancy.

The aims of our study were to assess the epidemiology of dermatomyositis in our local population, the clinical

presentation, the prevalence of amyopathic dermatomyositis and its association with malignancy as compared to that of classical dermatomyositis.

Patients and Methods

All patients diagnosed with dermatomyositis at the National Skin Centre from 1996 to 1998 were collated from our computerised database. The diagnosis was made if the patient fulfilled the clinical below criteria: characteristic skin changes with or without a consistent skin biopsy and clinical/laboratory evidence of myositis. Characteristic skin changes included Gottron's papules/sign, heliotrope rash, photosensitivity, poikiloderma and periungual erythema/telangiectasia. Clinical or laboratory evidence of myositis included proximal muscle weakness or dysphagia, raised creatine kinase and/or aldolase, abnormal electromyogram (EMG) and muscle biopsy. Cases of juvenile dermatomyositis (12 years old or less) were excluded. We reviewed and analysed the data with regards to the patient's profile, cutaneous signs, muscle involvement and malignancy.

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Results

A total of 28 patients were studied. There were 15 female and 13 male patients giving a female to male ratio of 1.2:1. There were 25 Chinese (89.3%) and 3 Malays (10.7%). Their ages ranged from 13 to 81 years (mean 49.8 years). Most of the patients ($n = 15$, 53.6%) were in the 41 to 60 years age group.

The presenting symptoms were analysed. All patients complained of rash and most experienced pruritus (78.6%) and photosensitivity (50%). Less than one third had symptoms suggestive of muscle involvement such as weakness (32.1%), breathlessness (10.7%) and dysphagia (3.6%). Four patients presented with loss of appetite and weight (14.3%), 3 with changes in bowel habits (10.7%), 2 with arthralgia (7.1%) and one each with mouth ulcers/blisters, hoarse voice/tinnitus, hair loss and myalgia (3.6%). The duration of symptoms ranged from 0.25 to 48 weeks (mean 6.9 weeks).

The presenting signs are shown in Table I. The commonest sign in our series was Gottron's papules or Gottron's sign (75.0%). The other common cutaneous signs were nail-fold telangiectasia/erythema (64.3%), poikiloderma (60.7%), facial erythema (57.1%), photosensitivity (50.0%) and heliotrope rash (50.0%). One patient each had alopecia, blisters together with oral ulcers, and vasculitic lesions on the fingertips (3.6%). Nine out of 28 patients (39.4%) had proximal muscle weakness on initial presentation. Out of the other 19 patients, 6 developed muscle weakness eventually (31.5%) over a period of 1 to 7 months (mean 2.5 months). Creatine kinase (CK) levels were measured in 25 patients and found to be increased in 8 patients (Table II). Four out of 9 patients (44.4%) with weakness and 4/19

patients (21.1%) without weakness had raised CK levels. Aldolase levels were measured in 24 patients and were increased in 6/9 patients with muscle weakness (66.7%), and 3/19 patients without muscle weakness (15.8%). Electromyograms (EMG) were performed in 15 patients and showed a myopathic pattern in 7, including 2 patients without muscle weakness. Muscle biopsies were performed in 3 patients, all of which showed changes consistent with myositis. Two out of these 3 patients had no muscle weakness on presentation. In summary, the patients were divided into 3 groups. There were 9/28 patients (32.1%) with clinical muscle weakness, 6/28 patients (21.4%) with no clinical muscle weakness at presentation but had laboratory evidence of myositis (abnormal muscle enzymes and/or EMG), and 13/28 patients (46.4%) without clinical or laboratory evidence of myositis, i.e. truly amyopathic at presentation. Six more patients went on to develop clinical muscle weakness (4 from the second group and 2 from the amyopathic group).

Four patients (14.3%) were found to have interstitial lung disease, 2 of whom had concurrent muscle weakness at presentation and 2 developed muscle weakness one month later. No other organ systems were involved in this series.

Skin biopsies were performed in 25 patients, out of which 20 (76.9%) had histological features suggestive of dermatomyositis. The others were reported as superficial perivascular dermatitis (3), scleroderma (1) and subacute lupus erythematosus (1). However, they were all diagnosed as dermatomyositis based on typical cutaneous signs and clinical/laboratory evidence of myositis. Direct immunofluorescence tests (DIF) were non-specific. Out of 21 DIF performed, 9 were negative (42.9%), 5 were reported as interface dermatitis, 2 showed fibrinogen in upper dermal blood vessels, 2 reported as vasculitis, 1 each as pemphigus, bullous pemphigoid and mixed connective tissue disease, respectively.

The anti-nuclear antibody (ANA) was measured in 22 patients and was positive in 11 (50%). Antibodies to Ro antigen, La antigen, ribonucleoprotein (RNP), double-stranded DNA (dsDNA) and Smith antigen (Sm) were measured in 11 patients, all of which were negative. Anti Jo-1 was measured in 6 patients (3 of whom had interstitial lung disease) and were negative in all.

There were malignancies detected in 12/28 patients

TABLE I: PRESENTING SIGNS

Signs	n	%
Gottron's papules/sign	21	75.0
Nail-fold telangiectasia/erythema	18	64.3
Poikiloderma	17	60.7
Facial erythema	16	57.1
Photosensitivity	14	50.0
Heliotrope rash	14	50.0
Alopecia	1	3.6
Calcinosis	1	3.6
Blisters with oral erosions	1	3.6

TABLE II: RESULTS OF MUSCLE ENZYME MEASUREMENTS

	Creatinine kinase ($n = 25$)			Aldolase ($n = 24$)		
	Increased	Normal	Not done	Increased	Normal	Not done
Weakness ($n = 9$)	4	3	2	6	1	2
No weakness ($n = 19$)	4	14	1	3	14	2

(42.8%), 6 of which were nasopharyngeal carcinomas (50%) and the rest were carcinomas of the breast, brain, liver, stomach, lung and rectum (Table III). Most of the malignancies were detected at the same time as the dermatomyositis (75%). There was no significant difference in the prevalence of malignancy between those presenting with detectable muscle weakness ($3/9 = 33.3\%$) and those without ($9/19 = 47.4\%$) (Table IVa). However, when laboratory evidence of myositis was included in the analysis, there was a significant higher prevalence of malignancy in the group with myositis ($10/15 = 66.6\%$) as compared to those without ($2/13 = 15.4\%$) (Table IVb).

As for treatment, all were treated with topical steroid preparations and sunscreen. Those with cutaneous features who responded poorly to topical treatment were prescribed systemic therapy like chloroquine ($n = 6$) and hydroxychloroquine ($n = 7$). Twenty out of 28 patients (71.4%) were also given systemic corticosteroids for severe

cutaneous involvement or muscle involvement. There were also 3 patients on methotrexate. Fifteen patients improved with treatment (53.6%), 4 remained the same (14.3%), 6 defaulted follow-up (21.4%) and 2 died, 1 of carcinoma of the stomach and the other from interstitial lung disease. None of the patients worsened with treatment. The duration of follow-up ranged from 1 to 31 months (mean 9.1 months).

Discussion

The term “dermatomyositis” was first coined by Unverricht in 1887¹ with the first report of the condition. In 1913, Stertz and Kankeleit^{2,3} described the first case of dermatomyositis associated with malignancy. In 1975, Bohan and Peter⁴ published their landmark article in which they formulated diagnostic criteria for the condition which remain widely accepted by most authorities today. These criteria include symmetric proximal muscle weakness with or without dysphagia or respiratory muscle involvement, abnormal muscle biopsy, raised muscle enzymes, abnormal EMG and a typical skin rash (Gottron’s papules or sign, heliotrope rash). Their criteria require the concurrent presence of characteristic cutaneous features with clinical and laboratory evidence of myositis. As a result of their work, almost every report since 1975 has used these criteria to select patients for review. On the basis of these criteria, muscle involvement is a prerequisite for the diagnosis of dermatomyositis and excludes all cases with only skin changes. Thus, most early reviews of dermatomyositis have been biased towards those with myositis and there was a scarcity of literature on dermatomyositis without muscle involvement. However, patients with typical skin changes of dermatomyositis without apparent muscle involvement have been observed since the 1970s. In the same year that Bohan and Peter published their paper, Krain⁵ described 6 patients without initial muscle weakness but who developed myositis later. He also noted that a failure to recognise this variant may lead to a delay in diagnosis. This variant was termed “amyopathic dermatomyositis” by Pearson, a leading rheumatologist in 1979.⁶ It was not until 1991 when Euwer and Sontheimer⁷ formally proposed diagnostic criteria for amyopathic dermatomyositis that the condition received greater recognition. Finally, Stonecipher et al⁸ were the first to report the association of amyopathic dermatomyositis with malignancy in 1993.

Euwer and Sontheimer’s criteria state that a person has amyopathic dermatomyositis if he has pathognomonic cutaneous signs (Gottron’s papules or sign, heliotrope rash), a skin biopsy consistent with dermatomyositis, no clinical evidence of proximal muscle weakness within 2 years of skin disease and normal muscle enzymes within 2 years of their illness.⁷

In our series, the female to male ratio was 1.2:1 as compared to most reports which quote a slightly higher

TABLE III: DERMATOMYOSITIS PATIENTS WITH MALIGNANCY

Type of carcinoma	n	Antecedent (n)	Concurrent (n)	Evidence of myositis (n)	No evidence of myositis (n)
Nasopharyngeal	6	1	5	5	1
Brain	1	1	-	1	-
Breast	1	1	-	1	-
Liver	1	-	1	1	-
Lung	1	-	1	1	-
Stomach	1	-	1	1	-
Rectum	1	-	1	-	1
Total	12	3	9	10	2

TABLE IV: PREVALENCE OF MALIGNANCY IN DERMATOMYOSITIS PATIENTS WITH AND WITHOUT MUSCLE INVOLVEMENT

Table IVa

	Detectable weakness (clinical only)(n = 9)	No detectable weakness (n = 19)
Malignancy (n = 12)	3	9
No malignancy (n = 16)	6	10

$P = 0.3884$

Table IVb

	Myositis (clinical and/or laboratory evidence) (n = 15)	No myositis (n = 13)
Malignancy (n = 12)	10	2
No malignancy (n = 16)	5	11

$P = 0.0083$

ratio of 2:1.⁹ The peak age group was 41 to 60 years, which is consistent with most reports.⁹ The high prevalence of Chinese patients is consistent with the high proportion of Chinese in our local population. All our patients had rash as a presenting complaint and most also complained of itch and photosensitivity. Interestingly, less than a third of the patients had symptoms suggestive of myositis such as weakness, breathlessness or dysphagia. Pathognomonic cutaneous signs for dermatomyositis include Gottron's papules or sign and heliotrope rash.⁹ Gottron's papules are defined as erythematous papules (or plaques) which are often scaly, located over bony prominences like the knuckles, dorsum of interphalangeal joints, elbows and knees. If only erythema is present, it is known as Gottron's sign. The heliotrope rash is a violaceous eruption over the eyelids and periorbital region and can be associated with oedema. Gottron's papules or sign were found in 75% of our patients and is the most common cutaneous sign. The other cutaneous signs present in our patients were nail-fold telangiectasia/erythema (64.3%), poikiloderma (60.7%), facial erythema (57.1%), a photodistributed eruption (50%) and heliotrope rash (50%). These signs are characteristic but not pathognomonic of dermatomyositis. There was also 1 patient who presented with blisters and oral ulcers. This is an unusual variant of bullous dermatomyositis which has been reported to be more highly associated with malignancy and hence, a poorer prognosis¹⁰ (the patient was found to have nasopharyngeal carcinoma). In a similar local review of dermatomyositis from 1989 to 1994, the commonest cutaneous signs were photosensitivity (86.8%), heliotrope rash (84.2%), Gottron's papules (68.4%), periungual telangiectasia (52.6%) and poikiloderma (29.0%), in order of decreasing frequency.¹¹

It is interesting that only about 40 % of the patients had detectable proximal muscle weakness on presentation. In Bohan et al's¹² review of 153 patients with dermatomyositis, they noted that 31% had normal muscle strength on initial presentation. They did not specify the interval between skin disease presentation and that of muscle disease. Rockerbie et al¹³ found that 56% of their 50 patients had skin disease preceding muscle disease and the mean interval was 4 months. In these studies, Bohan's criteria were used for the selection of patients, hence there is a bias against patients without myositis. In our series, only 32.1% of our patients had weakness on presentation. This is similar to an earlier local study where the figure was 44.7%.¹¹ However, when laboratory investigations were taken into consideration, we found that 21.4% had raised muscle enzymes, abnormal EMG or muscle biopsies without detectable clinical muscle weakness. This group may be called subclinical myositis or occult myositis. 46.4% of all patients had no evidence of myositis at all, either clinical or laboratory, on initial presentation. This group may be

called amyopathic dermatomyositis. Six of our patients later developed myositis; 4/6 (66.7%) of the subclinical myositis group and 2/13 (15.4%) of the amyopathic group. It is questionable whether we should only call these patients amyopathic dermatomyositis if they do not develop myositis for 2 years, as proposed originally by Euwer and Sontheimer or whether they may be given the diagnosis at presentation. However, Euwer and Sontheimer⁷ themselves conceded that the diagnosis of amyopathic dermatomyositis should not be restricted to patients with skin disease for 2 years but that any patient with only skin changes with minimal muscle disease should warrant this diagnosis. Indeed, the time frame is only arbitrary and while useful as selection criteria for retrospective studies, it does not aid in the diagnosis of the condition at first presentation.

Pulmonary disease occurs in 15% to 30% of patients with polymyositis and dermatomyositis. We found only 14.3% of our patients had interstitial lung disease. This may be an inherent bias of a dermatology-based review and patients with symptomatic lung disease would more likely present first to the respiratory or general physician. Interestingly, none had anti-Jo1 positivity which is a marker for lung disease.

Reported malignancy prevalence rates in the literature ranged from 15% to 34% in Western centres.^{14,15} Three previous local studies found prevalence rates of 31%,¹¹ 41%¹⁶ and 60%.¹⁷ In all these studies, nasopharyngeal carcinoma (NPC) featured prominently, accounting for up to two-thirds of the cancers detected.¹⁷ In this review, malignancy was found in 42.9% of our patients; 50% of which were NPCs. Seventy-five per cent of the cancers were diagnosed at the same time as the dermatomyositis upon screening; the rest were known cancer patients before presenting with dermatomyositis. We propose screening all patients with suspected dermatomyositis with or without muscle involvement for underlying malignancy which entails a detailed history, physical examination (including breast and pelvic examination for females), tumour markers, chest X-ray, pelvic ultrasound for females and a nasopharyngeal screen by the otorhinolaryngologist in view of the high prevalence rate of NPC in our local population. These patients need to be followed up for further progression of myositis as well as continued tumour surveillance.

We wanted to see if there was any significant difference in the prevalence of malignancy between those with myositis and those without. So far in the literature, the reported prevalence rates of malignancy in amyopathic dermatomyositis ranged from 0% to 83%.^{5,7,13,18-20} In our study, we found that there was no significant difference if only clinical weakness was considered. However, when laboratory evidence of myositis were included, there appears

to be a higher prevalence of malignancy in those with myositis than those without. This suggests that amyopathic dermatomyositis may have a better prognosis. Further studies are required to investigate this.

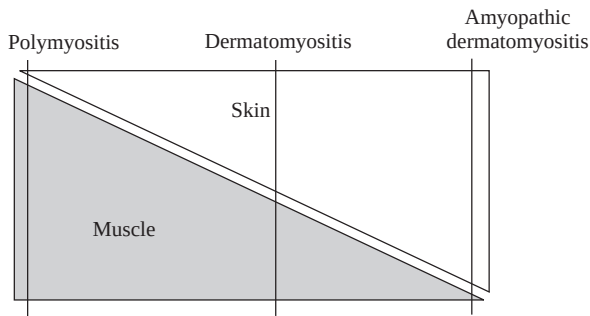


Fig. 1. Clinical spectrum of dermatomyositis.

Conclusion

We believe that at present, there needs to be unifying criteria for the diagnosis of polymyositis, classical dermatomyositis and amyopathic dermatomyositis. These subsets constitute a clinical spectrum where at one end, there is only muscle involvement (polymyositis) and at the other, only cutaneous (amyopathic dermatomyositis) (Fig. 1). Ideally, a set of diagnostic criteria should be employed purely for the cutaneous features of dermatomyositis and another set of criteria for polymyositis. If only the former is satisfied, then the disease is termed cutaneous or amyopathic dermatomyositis; if only the latter is met, then the diagnosis is polymyositis. If both sets of criteria are met, then dermatomyositis can be diagnosed. It is important to remember however, that all subsets are part of a clinical spectrum and may present in varying proportions of muscle and cutaneous disease. Each subset may progress from one to another and all subsets are associated with malignancy. The practical implication from this subclassification into amyopathic and classical dermatomyositis lies from the therapeutic point of view. Generally, those with purely skin disease may be managed with sun protection, topical steroids and anti-malarial drugs. Systemic corticosteroids and other immunosuppressive drugs are reserved for those with severe skin disease refractory to treatment and those with myositis and systemic involvement. Another point of contention is whether early treatment of cutaneous disease with corticosteroids will halt progression to myositis. Euwer and Sontheimer started 5 of their 6 patients with amyopathic dermatomyositis on systemic corticosteroids for severe skin disease and found that none progressed to myositis.⁷ As for prognosis, it is still questionable at present whether there is any prognostic

difference between those with and without myositis as suggested by our study. All these issues need to be further elucidated in future studies.

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