Amyopathic Dermatomyositis: A Review

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Jim Gilliam's research interests throughout his career were forced upon better defining the relationships that exist between the cutaneous and systemic manifestations of the rheumatic diseases. Although the majority of his time was spent studying such relationships in lupus erythematosus patients, he was also intensely interested in dermatomyositis (DM) in this regard as well. He was particularly intrigued with the dissociation of the cutaneous and muscular manifestations of this disorder that occasionally occurs. The term "dermatomyositis sine myositis" has been used in the past to describe patients who present with only the cutaneous manifestations of DM; however, very little published data is available from systematic examinations of such patients. For several reasons, we have preferred the term "amyopathic dermatomyositis" to describe that rare patient who for long periods of time suffers from the classical skin lesions of DM as the only clinically significant manifestation of their disease. In this presentation, we review our own personal experience with a group of six such patients and compare and contrast it to that of other workers who have dealt with this subject over the past two decades.
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Any stigmata will do to beat a dogma
—Phillip Guidella (1899–1944) [1]

In any other review of autoimmune connective tissue diseases, the topic of amyopathic dermatomyositis (ADM) would probably not be covered because it is a relatively new concept [2] as well as a rather controversial one [3,4]. However, because this is a memorial to Dr. James N. Gilliam, it is fitting that this subject be reviewed here because it is one in which Dr. Gilliam was much interested and one that he would quite likely have tackled himself had he been allowed more time to pursue his beloved work.

The thesis of this presentation is that florid cutaneous manifestations of dermatomyositis (DM) can occasionally be present in a patient for a prolonged period of time (if not permanently) without any clinical evidence of underlying inflammatory muscle disease. Although this is not a totally new notion to dermatologists (i.e., the ill-defined concept of ''dermatomyositis siné myositis''), it is one that is not at all accepted by physicians outside our specialty because the somewhat dogmatic but widely accepted criteria for the diagnosis of polymyositis/dermatomyositis (PM/DM) formulated by Bohan and Peter in 1975 [5] do not allow for the diagnosis of any form of DM in patients who do not have firm evidence of myositis. It is our view that because such patients clearly exist and because considerable confusion currently surrounds them, they deserve further study in order to determine the most logical and efficient means or managing their particular variety of disease.

NOMENCLATURE

While reviewing this subject after seeing a six-year-old girl with florid cutaneous manifestations of DM but no underlying clinical or enzymatic evidence of muscle disease for over two years, we were quite surprised to find no references in the National Library of Medicine's Medline database (including backfiles through 1966) under the search term ''dermatomyositis siné myositis.'' However, we did find a textbook reference to such patients made by Carl Pearson, M.D. [6], a pioneering rheumatologist, who stated

> Although the diagnosis of polymyositis rarely can be made in the absence of muscular weakness, I have for some time observed five women who show the completely typical erythematous heliotrope eruption as already described in association with erythematous plaques on the elbows and elsewhere. In none can I find any evidence of muscle disease or any other disorder. One woman has been observed repeatedly for thirteen years. Hence, it may be possible to disassociate the dermal from the muscular component in rare instances, whereas in many cases a myositic process occurs without any dermal features. In six other persons (four women and two men), the rash was florid whereas weakness and EMG changes were minimal. This variant could be called amyopathic dermatomyositis.

Hence, in honor of Dr. Pearson for recognizing these patients and for his many other contributions to our current understanding of PM/DM in general, we felt that it would be appropriate to use his term ''amyopathic dermatomyositis'' for patients in whom the cutaneous manifestations of DM was the sole *clinical* manifestation of their disease for prolonged periods of time.

PRIOR OBSERVATIONS BY OTHERS

Dr. Lawrence Krain [7] was the first investigator to formally evaluate the issue of DM without muscle involvement in the modern English medical literature. He described six patients with skin changes of DM and no muscle involvement initially, all of whom later developed myositis. The first case described a 10-year-old girl who had skin disease that preceded muscle weakness by four months. Case 2 concerned a man with cutaneous disease preceding muscle disease by six years. Cases 3 and 4 were two women who had skin disease that preceded muscle disease by five years. Case 5 had concurrent skin changes with mild shoulder weakness. His skin lesions progressed and the weakness became clinically significant after six years. This patient also had associated pulmonary fibrosis. Case 6 was a 72-year-old woman who presented initially with concurrent muscle disease and skin disease, both of which resolved spontaneously. Four years later, her skin changes recurred without muscle disease. Six years after that, her muscle disease recurred. This patient also developed pulmonary fibrosis. Krain pointed out that ''the failure to recognize dermatomyositis in the absence of detectable

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Abbreviations: ADM, amyopathic dermatomyositis; CK, creatine kinase; DM, dermatomyositis; EMG, electromyogram; PM, polymyositis

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muscle weakness, despite a characteristic skin eruption, resulted in a considerable delay in diagnosis.'' He also concluded that the resistance of the cutaneous findings to corticosteroid therapy generally indicated a poorer prognosis.

The same year that Krain's article was published (1975), Bohan and Peter [5] published their landmark article in which criteria were presented that must be met in order to make a diagnosis of PM/DM (symmetrical proximal muscle weakness with or without dysphagia or respiratory muscle involvement, abnormal muscle biopsy, elevation of skeletal muscle-derived enzymes, abnormal electromyo-gram, typical skin rash; confidence limits for diagnosis of definite DM are rash and three or four other criteria, for probable DM are rash and 2 other criteria, and for possible DM are rash and one other criteria [5]). As a result of this article as well as their later work [8], almost every published report of DM patients since 1975 has used these criteria to select patients for review. Because these criteria employ muscle disease as the siné qua non for the diagnosis of DM, patients who have DM skin disease but lack muscle disease have been excluded from these reviews. Hence, there has been a bias towards not reporting ADM patients that has resulted in a dearth of information in the modern literature on this subject. What follows is a chronologic review of the data concerning ADM that has appeared since the Bohan and Peter criteria were presented in 1975.

In 1977, Bohan *et al* [8] used their published criteria to select patients for a study entitled ''A Computer Assisted Analysis of 153 Patients with Polymyositis and Dermatomyositis.'' In this article, they described three patients (2%) who ''failed to develop evidence of significant muscle weakness while clearly meeting other diagnostic criteria.'' They also stated that muscle strength was normal in 48 patients (31%) upon initial presentation. Unfortunately, they did not specify the length of time between skin disease presentation and onset of muscle disease in this subgroup of patients. Several other groups of workers have suggested that this interval is usually less than 2 years and often less than six months [9–13].

Fernandes *et al* [14] in 1979 described a 48-year-old West Indian patient who had DM skin disease and pulmonary disease but no muscle disease who died of his fibrosing alveolitis just ten months after coming under observation.

In 1981, Braverman [15] described a 13-year-old caucasoid female with classic cutaneous changes of DM without muscle disease for 10 years and a 16-year-old female with characteristic DM skin lesions without evidence of myositis. In this last patient, oral and topical corticosteroids provided no relief and the skin eruption disappeared spontaneously after 2 years. He also described another patient who had only the cutaneous findings of DM as a manifestation of underlying lung cancer.

Three years later, Woo *et al* [16] reported seven patients with DM whose skin lesions had not responded to oral corticosteroids but did improve with the addition of hydroxychloroquine. One of these patients did not have myositis. In 1985, Taieb *et al* [17] reviewed their experience with childhood DM and found eight individuals in their review of 70 cases whom they retained in their study as possible DM patients—patients who had the typical cutaneous changes of DM without clinical or laboratory evidence of muscle involvement at the time of their initial evaluation.

Gertner and Urowitz [18] also reported in 1985 a 24-year-old woman who initially presented with concordance of muscle and skin involvement. She was treated with prednisone with resolution of the myositic component of her disease with persistence of the cutaneous component for 17 years before once again developing myositis.

Caro [19], in 1988, alluded to following a patient for several years who had all the typical skin findings of DM but no clinical or enzymatic evidence of muscle disease.

Rockerbie *et al* [20] in an article entitled ''Cutaneous Changes of Dermatomyositis Precede Muscle Weakness'' retrospectively reviewed 50 patients with DM. All patients included in this analysis met at least four or more of the five Bohan and Peter criteria and were thus classified as having at least definite DM by that classification scheme. The onset of skin lesions in these patients ranged from 51 months before to 14 months after the onset of muscle weakness. In those patients whose skin disease preceded muscle disease (56% of the entire group), the mean interval (± one standard deviation) between onset of cutaneous changes and muscle weakness was 4 (±11 months). Four patients (12%) had cutaneous changes greater than 1.75 years before onset of muscle weakness. Interestingly, although not statistically significant, the mean skin/muscle discordance for the female group of patients was 5 months (±12 months) compared with 1 (± 8 months) for the male group. These workers also examined the relationship between skin and muscle discordance and patient outcome. Of the four deaths during the follow-up period, none of the patients had a history of skin/muscle discordance greater than 3 months. There was only one documented malignancy in this series, occurring in a patient with no history of skin/muscie discordance. Of their 50 patients, 41 (82%) were less than 25 years old. In this younger subgroup, the mean skin/muscle discordance was 4 months compared to a mean skin/muscle discordance of 8 months in the 9 patients over 25 years of age.

OBSERVATIONS ON OUR OWN PATIENTS

In our own study [2], we reviewed six patients with the classic cutaneous findings of DM who did not develop clinical or laboratory evidence of muscle disease for at least 2 years following the onset of their skin disease. The decision to use 2 years as a cut-off time was an arbitrary one based on the experience of other investigators, suggesting that most patients with classical DM usually develop muscle disease within two years after onset of their skin disease [9–13,20].

Unlike previous studies, the criteria set forth by Bohan and Peter [5] were not used as inclusion criteria for our study. To the contrary, if those criteria had been used, these patients would not have been included as they did not meet the requirements for the diagnosis of definite DM. Even if an electromyogram (EMG) and muscle biopsy had been performed and had been positive, our patients would have only met the criteria for probable or possible DM because they lacked proximal muscle weakness and elevated muscle enzymes. We did not believe these procedures were clinically indicated because the results either positive or negative would not have influenced our treatment approach. All five of our adult ADM patients had failed conservative topical treatment and all had long-standing, disabling cutaneous symptoms severe enough in our opinion to warrant a trial of more aggressive systemic medical management. When one sees a patient with the unequivocally classical cutaneous changes of DM with no muscle weakness by history or exam and normal skeletal muscle enzymes, we have found that it is often difficult to convince that patient to undergo a muscle biopsy (not a trivial procedure either medically or economically), when this information is quite unlikely to change what one is going to recommend concerning treatment.

Patients were included in our review only if they met all four of the following criteria that we are here proposing for the diagnosis of ADM: 1) presence of pathognomonic clinical changes of cutaneous DM (to be considered for the diagnosis of ADM, each patient had to have fully established or incipient Gottron's papules, periungual nailfold erythema/telangiectasia, and violaceous erythema/edema of the face including a periorbital distribution), 2) a skin biopsy specimen compatible with DM, 3) no clinical evidence of proximal motor weakness in the shoulders or hips within 2 years of skin disease onset, and 4) normal skeletal muscle enzyme levels (creatine kinase [CK] and aldolase) within the first 2 years of their illness. Six of the fifty DM patients (11%) seen by one of the authors (RDS) in our department during the past 15 years met these criteria. This prevalence rate is similar to that of the four patients with skin/muscle discordance of 1.75 years or greater reported in the study by Rockerbie *et al* [20]. However, since all of their patients ultimately met criteria for definite DM, all of their patients ultimately developed muscle disease.

At the time of publication, our patients had skin disease for a mean duration of 3.8 years (range 2–8 years). The pediatric patient began to

complain of intermittent muscle pain in her proximal thighs after 3 years of skin disease. Physical exam revealed normal muscle strength but an EMG was abnormal although her muscle enzymes remained normal. Of the adult patients, one has been followed for four years, two for five years, and one each for seven and ten years respectively with no muscle disease.

All five of the adult patients in our series were treated initially by us with moderate to high-dose prednisone (40–60 mg/d) for their increasingly symptomatic skin disease. These patients had skin disease resistant to topical therapy (including corticosteroids and sunscreens) for a mean duration of 14 months prior to seeing us. All patients began to respond within 4–6 weeks of treatment, at which point tapering of the prednisone was begun and adjusted on the basis of clinical response. One year after starting prednisone, all five patients had none-to-minimal skin disease and were taking no more than one-half their original dose of prednisone daily. This slow rate of corticosteroid taper is generally required in DM to prevent recrudescence of disease activity. Hydroxychloroquine was added as a steroid-sparing agent in three patients. One patient had to discontinue this drug because of a cutaneous hypersensitivity reaction. One of the oldest patients in our series did develop a minimal degree of glucose intolerance while on corticosteroids. None of the other patients had significant side effects from corticosteroids.

COMPARISON OF OUR EXPERIENCE TO THAT OF OTHERS

Similarities between the patients described in the Rockerbie *et al* study [20] and our own [2] included a greater female-to-male ratio (3:1) than has been reported in other DM patient series (i.e., 2:1) [8]. In addition, underlying malignancies did not occur in patients described by Rockerbie *et al* whose skin disease preceded their muscle disease nor were malignancies present in our six patients (subsequent to the publication of our report we have seen an additional female ADM patient who developed ductal carcinoma of the breast approximately two and one-half years following the onset of her skin disease [4]). We have also recently been made aware of several other cases of ADM that have been associated with internal malignancy (Dr. T.T. Provost, personal communication, August, 1991). Interestingly, it appeared that although the majority of the DM patients in the Rockerbie study were less than 25 years of age, those with the greatest discordance between the onset of skin and muscle disease were older than 25. Among our six patients, there was one six-year-old pediatric patient. The average age of the remaining five patients was 53.6 years old. The mean time in months between onset of skin disease and presentation to our department in our series of patients was 14 months (range 5–24 months). In Krain's study, it was 18 months (range, 2–50 months).

The most common erroneous initial diagnoses given our patients before seeing us were 1) lupus erythematosus, 2) contact dermatitis, 3) lichen planus, 4) psoriasis, and 5) seborrheic dermatitis. Other erroneous initial diagnoses reported in Krain's study were polymorphous light eruption, atopic dermatitis, and erythroderma. All patients in our series had moderate-to-severe pruritus, which can help distinguish DM patients from patients with cutaneous lupus erythematosus who generally do not complain of severe itching. All six of our ADM patients also complained of photosensitivity.

All of our patients responded to systemic corticosteroids. This is somewhat different from the experience of other observers who have noted that DM skin lesions can at times be quite refractory to systemic corticosteroid therapy [16]. We too have seen patients with classical DM whose skin disease has been refractory to high-dose corticosteroids. Perhaps our good fortune with our ADM patients in this regard was due only to the small number of patients we studied or, perhaps, concurrent muscle weakness in some way increases the likelihood of therapeutically refractory skin disease. None of the corticosteroid-treated patients in our series developed muscle disease as did all of Krain's patients and, presumably, Rock-erbie's patients as well. A comparison of our series with Krain's, although admittedly not the ideal control group, suggests that our more aggressive approach to treating the skin disease might have prevented the development of myositis in our patients. We, however, do not have firm data at this time to support this view. Furthermore, early treatment with systemic corticosteroids potentially could allow lower doses and shorter courses to be used to control the disease, thereby resulting in fewer side effects. It should be emphasized that we only treated patients with ADM for severely symptomatic skin disease in whom the benefits appeared to outweigh the risks. We believed the risks of corticosteroids in our pediatric patient with ADM were not justified and, hence, this patient was treated more conservatively with antimalarials alone without benefit. Interestingly, the more conservatively treated pediatric patient was the only one to ultimately develop signs and symptoms of muscle disease.

A SURVEY OF OTHER DERMATOLOGISTS

While analyzing the results of our study, we were intrigued to know how other practicing dermatologists dealt with patients such as ours. Therefore, in 1988 we designed a questionnaire addressing several issues concerning ADM and mailed it along with a standardized case report form to all 90 members of the Dallas Dermato-logical Society as well as to a total of 29 other dermatologists around the country whom, because of their clinical interests, we felt might have seen such patients. Unfortunately, the response to this preliminary polling was somewhat disappointing. Although a number of individuals reported having seen such patients, only five case report forms of patients meeting our criteria were returned (three cases from a single local dermatologist, one case from another local dermatologist, and a single case from a dermatologist practicing in another part of the country). The clinical features of these five additional cases of ADM were quite similar to those of our six patients [2]. There were mixed opinions among the three physicians who formally responded to our questionnaire regarding the need for EMG and muscle biopsies in such patients as well as the justification for the type of aggressive systemic therapy with corticosteroids that was used in our five adult patients.

ISSUES THAT DESERVE FURTHER ATTENTION

Although ADM patients are admittedly rare, they do exist and it is important that their condition be recognized in order to identify differences that might distinguish their form of disease from that of more classical DM patients. For example, what is the diagnostic yield and incremental clinical benefit of EMG and muscle biopsies in ADM patients who have no clinical or enzymatic evidence of muscle disease? Can predictive factors be identified in those ADM patients who are destined to develop muscle disease? Is there a significant association between ADM and internal malignancy, and if so what features correlate with tumor development in such patients? What is the optimal treatment approach for ADM patients? What percentage of ADM patients managed conservatively never develop muscle disease? Does early aggressive treatment of skin disease significantly alter the risk for eventually developing muscle disease? Because of the rarity of this condition, only an appropriately designed, multicenter study will be able to answer these questions effectively.

At the very least, ADM patients need to be recognized in order that they can be followed more closely for the development of muscle disease so that appropriate treatment can be instituted during the earliest phases of this complication. In addition it is our opinion that such patients need to be monitored for the development of internal malignancy.

SUMMARY AND CONCLUSIONS

If patients with ADM, DM, and PM are grouped together, this disease can be viewed as a spectrum or continuum much like lupus erythematosus with primary involvement of the skin at one extreme (ADM) and primary muscle involvement at the other (PM) with the combination of skin and muscle disease (more typical DM) somewhere in the middle (Fig 1). Currently, the majority of patients who express the cutaneous manifestations of DM appear to fall within the mid part of this spectrum. Perhaps with earlier, aggressive treatment of patients during the amyopathic phase of their illness, there might be a decrease in patients

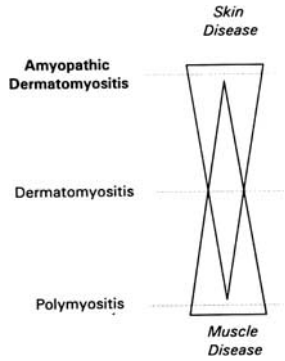

Figure 1. Spectrum of clinical disease in polymyositis/dermatomyositis. The term ''amyopathic dermatomyositis'' is used here to designate those patients who for at least 2 years express only the classical cutaneous manifestations of this disorder.

who go on to develop significant muscle involvement. We have previously suggested [2] that the diagnostic criteria set forth for DM by Bohan and Peter be altered to include a sixth diagnostic category, amyopathic dermatomyositis, that would allow the diagnosis of ADM to be made on the basis of fully-expressed, histopathologically-compatible, classical cutaneous findings alone. The recently defined condition of inclusion body myositis [21,22] should also be included in any such reclassifi-cation. The types and designations we propose are I, polymyositis; II, dermatomyositis; III, myositis with malignancy; IV, childhood myositis; V, myositis with other autoimmune connective tissue disorders (i.e., overlap syndromes); *VI, amyopathic dermatomyositis;* and VII, inclusion body myositis.

Taking a broader view, perhaps the diagnosis of ADM need not be limited to patients who have only skin disease for 2 years; rather, any patient with classical DM skin disease having only equivocal evidence of muscle disease at presentation might also warrant this designation as a provisional diagnosis. This approach would logically lead to the division of ADM into two subtypes—*confirmed ADM* representing pure ADM patients who have only skin disease for at least 2 years, and *provisional ADM* representing patients with classical skin disease who have subjective myalgia and/or subjective weakness but no laboratory evidence of muscle disease, patients with suggestive but not classical skin disease (i.e., poikiloderma atrophicans vasculare, violacelous erythema over the extensor aspects of the arms), or patients with no clinical signs or symptoms of muscle disease but who have abnormal laboratory tests indicative of myositis at some time during their course. Provisional ADM patients would obviously deserve stronger consideration for EMG and/or muscle biopsy to discern the basis of their symptoms and laboratory abnormalities. The unifying feature among both subtypes of ADM would be the presence of prominent skin disease and relative lack of clinical muscle disease.

There are few dermatologic entities that are as clinically distinctive and recognizable as are the fully expressed skin changes of DM. As dermatologists we are trained to trust, beyond all others, our eyes. Let us not be confused or apologetic for what our eyes are telling us when confronted with patients whose only *clinical* problem is the presence of the classical cutaneous manifestations of this disorder.

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