

Incidence of Dermatomyositis and Clinically Amyopathic Dermatomyositis

A Population-Based Study in Olmsted County, Minnesota

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Objectives: To identify new and existing cases of dermatomyositis and its subtypes in Olmsted County, Minnesota, from 1976 through 2007, and to establish a population-based estimate of the incidence and prevalence of dermatomyositis and amyopathic dermatomyositis.

Design: Retrospective population-based study.

Setting: Community-based epidemiology project.

Patients: Patients with a diagnosis of dermatomyositis were identified from the Rochester Epidemiology Project.

Main Outcome Measures: Incidence of dermatomyositis and clinically amyopathic dermatomyositis and risk of malignancy in clinically amyopathic dermatomyositis.

Results: Of the 29 patients identified, 6 (21%) had the clinically amyopathic subtype of dermatomyositis and 22 (76%) were female. Overall age- and sex-adjusted inci-

dence of dermatomyositis including all subtypes was 9.63 (95% confidence interval [CI], 6.09-13.17) per 1 million persons and 2.08 (95% CI, 0.39-3.77) per 1 million persons for clinically amyopathic dermatomyositis. Age- and sex-adjusted prevalence for all subtypes of dermatomyositis was 21.42 (95% CI, 13.07-29.77) per 100 000 persons. Eight patients (28%) had a malignant condition during the study period; the risk of malignancy (odds ratio) for classic dermatomyositis compared with clinically amyopathic dermatomyositis was 4.61 but was not statistically significant (95% CI, 0.22-96.09) ($P = .44$).

Conclusions: Dermatomyositis is a rare disease, and clinically amyopathic dermatomyositis represents an estimated 20% of all dermatomyositis cases. Larger population-based studies are needed to estimate the risk of malignancy associated with subtypes of dermatomyositis, particularly clinically amyopathic dermatomyositis.

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THE TERM AMYOPATHIC DERMATOMYOSITIS (ADM) was first coined by Pearson¹ in 1979 to describe a rare skin disease that has the same cutaneous symptoms as classic dermatomyositis (CDM) but lacks objective evidence of myopathy. Amyopathic dermatomyositis was not fully recognized as a distinct subset of dermatomyositis until the early 1990s.² Initially thought to carry a favorable prognosis, ADM may in fact be linked with an increased risk of internal malignancy, as suggested by some case reports.^{3,4} Several studies also have indicated an increased risk of lung disease,^{5,6} but the extent of this risk is unclear. It has been estimated that ADM represents approximately 10% of all cases of dermatomyositis; this percentage may be higher in Asian populations.⁷ Multiple studies have reported on the incidence of cancer in patients with dermatomyositis or polymyositis.⁸⁻¹¹ The incidence of dermatomyositis

itself, however, including the subtype ADM, is largely unknown.

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Founded in 1966, the Rochester Epidemiology Project (REP) is a comprehensive medical record-linking database for all residents of Olmsted County, Minnesota.¹² By using the REP, we aimed to ascertain the incidence and prevalence of dermatomyositis and its subtypes, along with the incidence of the subtypes ADM and clinically amyopathic dermatomyositis (CADM).

METHODS

After obtaining Mayo Clinic Institutional Review Board approval, we retrieved from the REP and then reviewed patient records for all newly diagnosed cases of dermatomyositis in Olm-

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sted County from 1976 through 2007. Patients with polymyositis or mixed connective tissue disease and patients who had denied research authorization were excluded from the study.

DEFINITIONS

Patients with a diagnosis of dermatomyositis were subclassified by disease subtype—CDM, ADM, CADM, CADM evolving into CDM, hypomyopathic dermatomyositis (HDM), and juvenile dermatomyositis—according to the definitions described in **Table 1**.^{7,13-15} Because patients with HDM and patients with ADM may have similar initial cutaneous symptoms and a subjective lack of muscle involvement, the term *clinically amyopathic dermatomyositis* (CADM) was designated to describe such patients. Also, because of the broad definitions used in our study, the designations of juvenile dermatomyositis and CADM were not mutually exclusive from the other dermatomyositis subtypes (Table 1).

COLLECTED DATA

Only patients who were residents of Olmsted County at the time of disease diagnosis were included in the study results. Residents who received a previous diagnosis of dermatomyositis elsewhere but were living in Olmsted County as of the reference date were included only in the calculations of prevalence. Collected data included patient characteristics such as age, sex, race, place of diagnosis, residence at time of diagnosis, date and results of skin and muscle biopsies, electromyography, magnetic resonance imaging, testing for autoantibodies and muscle enzymes, associated symptoms and illnesses, malignant disease during the study period, and clinical follow-up.

STATISTICAL ANALYSIS

The incidence rates of CDM, ADM, and CADM were calculated by dividing the number of CDM events, ADM events, and CADM events, respectively, by the Olmsted County population for 1976 through 2007, as determined by the US decennial census, with linear interpolation for intercensus years. Because of the low percentage of African Americans living in Olmsted County (3.8% in Olmsted County vs 12.8% nationally), the incidence rates were adjusted to the age and sex distribution of the 2000 US white population.¹⁶ Overall prevalence of dermatomyositis in Olmsted County was also calculated using January 1, 2007, as a reference date.

Logistic regression was used to calculate the odds ratios for malignancy in all patients with CDM compared with patients with CADM. Survival was estimated using the Kaplan-Meier method. Models also evaluated the death events as expected survival probabilities based on total Minnesota population from 1970 to 2000. All tests were 2 sided with an α level of .05. Statistical analyses were performed using SAS version 9.1 software (SAS Institute Inc, Cary, North Carolina).

RESULTS

PATIENT POPULATION

Between January 1, 1976, and December 31, 2007, 77 patients were identified from the REP as having a coded preliminary or final diagnosis of dermatomyositis; 4 patients (5%) who denied research authorization were excluded. On review of the medical records, the clinical

Table 1. Dermatomyositis Definitions^a

Type of Dermatomyositis	Definition
Classic (CDM)	Hallmark cutaneous manifestations with evidence of proximal muscle weakness occurring within 6 mo after onset of skin disease
Amyopathic (ADM)	Hallmark cutaneous manifestations of dermatomyositis for ≥ 6 mo without clinical or laboratory evidence of myopathy Exclusion criteria: (1) Use of drugs capable of producing hallmark cutaneous changes characteristic of dermatomyositis (2) Use of systemic immunosuppressive agents for >2 consecutive mo within the 6 mo after skin disease onset
Hypomyopathic (HDM)	Hallmark cutaneous manifestations without subjective muscle weakness for >6 mo but with objective evidence of subclinical muscle weakness on further testing, abnormal muscle enzymes, signs of myopathy on electromyography or muscle biopsy
Clinically amyopathic (CADM)	A term used to describe both ADM and HDM
Clinically amyopathic evolving into classic (CADM \rightarrow CDM)	Patients with cutaneous dermatomyositis with onset of muscle involvement >6 mo after onset of clinically significant skin disease
Juvenile (JDM)	Dermatomyositis of any subset occurring in a patient younger than 18 y

^aAdapted from Gerami et al.¹³ Used with permission.

descriptions and courses of illness were typical of dermatomyositis for 40 patients. Diagnosis of dermatomyositis was excluded for the other 33 patients on the basis of the clinical records, including incorrect preliminary diagnosis of dermatomyositis and coding overlap with polymyositis. For incidence calculations, 11 of the 40 remaining patients were further excluded from the study group because the diagnosis was not made within the designated study dates (3 patients) and because they were not residents of Olmsted County at the time of diagnosis (8 patients). However, those 11 patients were included in prevalence calculations.

After all exclusions, 29 patients with a new diagnosis of dermatomyositis were included in the study analysis. We grouped patients into the following subclassifications: 20 patients with CDM (2 juvenile), 3 with ADM (1 juvenile), 3 with HDM, and 3 with CADM evolving into CDM (**Table 2**). Combining the patients with ADM and HDM resulted in 6 patients with CADM. Three patients had juvenile dermatomyositis (2 CDM and 1 ADM). Excluding the 3 juvenile cases (patients aged 2, 5, and 11 years), the mean age was 57.4 years (range, 30.5-95.0 years). Most patients were female (22 of 29 [76%]) and the majority were white (24 of 29 [83%]); 1 patient was Asian, 1 patient was Hispanic, and race was unknown for 3 patients. Clinical characteristics of the 6 patients with CADM are given in the eTable (<http://www.archdermatol.com>).

Table 2. Patient Characteristics by Subtype of Dermatomyositis

Characteristic	Dermatomyositis Subtype, ^a No. (%)					
	CDM (n=20)	ADM (n=3)	HDM (n=3)	CADM (n=6)	CADM→CDM (n=3)	JDM (n=3)
% of the total group (N=29)	69	10	10	21	10	10
Mean age at diagnosis, y	51.9	44.1	64.4	54.3	49.3	6.8
Positive diagnostic studies						
Skin biopsy	9/10 (90)	2/2 (100) 3/3 (100)	5/5 (100)	2/2 (100)	0/0	
EMG	18/19 (95)	0/2	2/3 (67)	2/5 (40)	3/3 (100)	1/1 (100)
Muscle biopsy	11/12 (92)	0/0	0/0	0/0	1/1 (100)	2/2 (100)
MRI	1/2 (50)	0/1	0/0	0/1	0/0	0/1
Malignant condition	6/20 (30)	0/3 (25)	1/3 (33)	1/6 (17)	1/3 (33)	0/3

Abbreviations: ADM, amyopathic dermatomyositis; CADM, clinically amyopathic dermatomyositis; CADM→CDM, CADM evolving into CDM; CDM, classic dermatomyositis; EMG, electromyography; HDM, hypomyopathic dermatomyositis; JDM, juvenile dermatomyositis; MRI, magnetic resonance imaging.

^aSubtypes are not mutually exclusive.

Table 3. Age- and Sex-Adjusted Incidence of Dermatomyositis per 1 Million Persons in Olmsted County, Minnesota, 1976 to 2007

Calendar Decade	No. of Cases	Incidence (95% CI)
1976-1985	3	4.4 (0-9.4)
1986-1995	9	9.4 (3.2-15.7)
1996-2007	17	12.5 (6.5-18.5)
Overall	29	9.6 (6.1-13.2)

Abbreviation: CI, confidence interval.

EPIDEMIOLOGY

The overall age- and sex-adjusted incidence of dermatomyositis including all subtypes was 9.63 per 1 million persons (95% confidence interval [CI], 6.09-13.17); age-adjusted incidence was 13.98 per 1 million (95% CI, 8.08-19.89) for females and 4.68 per 1 million (95% CI, 1.15-8.20) for males. Overall age- and sex-adjusted incidence of ADM including the juvenile case was 0.95 per 1 million persons (95% CI, 0-2.04); age-adjusted incidence was 1.39 per 1 million (95% CI, 0-4.41) for females and 0.45 per 1 million (95% CI, 0-3.31) for males. Overall age- and sex-adjusted incidence of CADM was 2.08 per 1 million persons (95% CI, 0.39-3.77); age-adjusted incidence of CADM was 3.50 per 1 million (95% CI, 0.43-6.58) for females and 0.45 per 1 million (95% CI, 0-1.32) for males. Age- and sex-adjusted incidence of dermatomyositis per 1 million persons by decade of diagnosis is given in **Table 3**.

Prevalence was calculated using January 1, 2007, as a reference date; 26 cases were used to calculate prevalence. Age- and sex-adjusted overall prevalence of all subtypes of dermatomyositis was 21.42 per 100 000 persons (95% CI, 13.07-29.77). Age-adjusted prevalence was 33.08 per 100 000 (95% CI, 18.83-47.33) for females and 8.35 per 100 000 (95% CI, 0.81-15.90) for males.

MALIGNANT CONDITIONS

Among the 29 patients with dermatomyositis, 8 (28%) had a diagnosis of cancer at some time during the study period. Cancer was diagnosed after dermatomyositis onset

in 6 of the 29 patients (21%), including 1 patient with CADM evolving into CDM who received a diagnosis of esophageal adenocarcinoma 12 years after dermatomyositis was diagnosed. Endometrial cancer was diagnosed and treated in 1 patient 1.5 years before the onset of HDM but was no longer an active disease process at the time of dermatomyositis diagnosis. In addition, dermatomyositis developed in 1 patient during chemotherapy for metastatic colon cancer. The odds ratio for concurrent or future development of malignancy in patients who have CDM compared with those who have CADM was 4.61 but was not statistically significant (95% CI, 0.22-96.09; *P* = .44).

LUNG DISEASE

Of the 29 study patients, 5 (17%) had evidence of lung disease. Results from computed tomography of the chest were available for 4 of these patients. Of the 5 patients, 3 (2 with CDM and 1 with CADM evolving into CDM) had interstitial fibrosis, 1 (with CDM) had interstitial muscle weakness, and 1 (with CDM) received a diagnosis of bronchitis obliterans-organized pneumonia. No patients with CADM had evidence of lung disease.

SURVIVAL

Follow-up data were available for all 29 patients. The mean duration of follow-up from the date of diagnosis was 6.85 years (range, 0.07-19.56 years). At the end of the study period, 8 of the 29 adult patients had died (28%). For 6 of these patients, the cause of death was attributed to metastatic disease (in the setting of dermatomyositis with associated malignancy). Kaplan-Meier estimates of overall 5- and 10-year survival for patients with a diagnosis of dermatomyositis was 0.80 (95% CI, 0.66-0.97) and 0.73 (95% CI, 0.56-0.96), respectively; expected 5- and 10-year survival for the age- and sex-matched general Minnesota population was 0.92 and 0.85, respectively.

COMMENT

In 1990, Oddis et al¹⁷ reported an incidence of 5.5 cases of dermatomyositis per million; of interest, that study

showed a significant increase in incidence from the first to the second decade of the study: 2.5 per 1 million persons in the first decade, increasing to 8.9 per 1 million persons in the second.¹⁷ We also sought to examine whether our study showed a similar increasing frequency of dermatomyositis over time (Table 3), but our patient population was too small to yield any significant conclusions. Our overall incidence of 9.63 per 1 million persons from 1976 through 2007 is only slightly higher than the rate reported in the second decade by Oddis et al¹⁷ and may more accurately reflect true incidence because ours is a population-based study.

Approximately 20% of the patients in our study (6 of 29) had CADM, which correlates with previously reported rates of 10% to 20%.¹³ Of these 6 patients with CADM, 5 received their diagnosis since 2000 (the other patient, in 1981). It remains unclear whether the incidence of ADM is truly increasing or whether this represents increased awareness and clinician knowledge of this rare subtype of dermatomyositis.

In accordance with the classification scheme by Sontheimer,^{7,13-15} we defined CADM evolving into CDM as the presence of skin manifestations for more than 6 months before the onset of clinical or subclinical evidence of myopathy. Case studies suggest that, for some patients, ADM may progress to frank myopathy up to 10 years after the onset of cutaneous symptoms.^{3,7} Our study identified 3 patients with CADM that progressed to CDM, but only 1 patient had CADM that progressed to myopathy (CDM) after a long period (14 years), with only cutaneous manifestations. This finding is consistent with those of previous reports indicating that progression of CADM to CDM after a long period of cutaneous-only disease is a relatively rare occurrence in the spectrum of CADM disease.¹³ However, we acknowledge that the true classification of disease in a patient may perhaps be known only after an entire lifetime.

Among our 29 patients with dermatomyositis, 8 (28%) had a diagnosis of cancer at some time during the study period. This rate is higher than that in previous reports: in 1992, Sigurgeirsson et al¹⁰ reported a malignancy rate of 15% associated with dermatomyositis in a population-based study in Sweden. Of note, our calculations included cancers diagnosed before the onset of dermatomyositis; if only those cancers diagnosed at or after the onset of dermatomyositis are included, our malignancy rate would be 21%, closer to the rate reported by Sigurgeirsson et al.¹⁰

We sought to examine the incidence of malignancy in patients with CADM compared with their CDM counterparts; however, with only 6 patients in our study population having CADM, our comparisons of malignancy incidence between the 2 groups were not statistically significant. Only 1 patient with CADM had a malignant condition, and this cancer occurred 1.5 years before the diagnosis of dermatomyositis. In addition, of the 5 patients with lung disease, none had the CADM subtype. Case reports of a decreased risk of both malignancy and lung disease in patients with CADM exist in the medical literature.¹³ However, a comparison of 120 patients with dermatomyositis by Klein et al¹⁸ found no significant differences in risk of malignancy or lung disease between

patients with CDM and CADM. The risk remains unclear, and screening for both malignancy and lung disease continues to be essential for all dermatomyositis patients regardless of disease subtype.

In our patients with CADM, 3 of 6 (50%) had elevated levels of anti-Jo-1 IgG antibodies. This antibody has been shown to be present in some patients with polymyositis and dermatomyositis. A review by Gerami et al¹³ showed that 3 of 85 patients with CADM (3.5%) and 1 of 21 patients with CADM and coexisting lung disease (4.8%) were positive for anti-Jo-1 antibodies. With 3 of 6 patients testing positive for this antibody, our yield is higher than previously reported results and is at variance with published reports to date. Reasons for this discrepancy are unknown but may be related to our epidemiologic patient population in Olmsted County.

The strength of this report is that it is a population-based study performed using the REP, a well-validated medical record database for Olmsted County. However, it is possible that patients may have been excluded from our study because of lack of disease recognition by clinicians; even today, ADM continues to be a clinically difficult diagnosis. Given the small patient numbers in this population-based study, limited conclusions can be derived regarding associations of dermatomyositis and its subtypes with malignancy, lung disease, and prognosis. The retrospective nature of the study and reliance on the medical record precluded comprehensive clinical data on all patients in our analysis. Dermatomyositis manifesting in nonwhite skin is an important clinical entity; our analysis is limited by the predominantly white population of Olmsted County.

In conclusion, CADM represents approximately 20% of all cases of dermatomyositis. Although our rate of malignancy associated with dermatomyositis is similar to that in previous reports in the literature, larger population-based studies are needed to estimate the risk of malignancy associated with subtypes of dermatomyositis, particularly with CADM.

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Author Contributions: Drs Bendewald and Davis had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Bendewald and Davis. *Acquisition of data:* Bendewald and Davis. *Analysis and interpretation of data:* Bendewald, Wetter, Li, and Davis. *Drafting of the manuscript:* Bendewald, Li, and Davis. *Critical revision of the manuscript for important intellectual content:* Bendewald, Wetter, and Davis. *Statistical analysis:* Li and Davis. *Obtained funding:* Davis. *Administrative, technical, and material support:* Bendewald and Davis. *Study supervision:* Wetter and Davis.

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Online-Only Material: The eTable is available at <http://www.archdermatol.com>.

Additional Information: The rationale for this study arose from discussions between members of the organizing committee of the North American Rheumatologic Dermatology Society concerning priorities for research in connective tissue diseases, particularly dermatomyositis.

Additional Contributions: Richard D. Sontheimer, MD, the current president of the North American Rheumatologic Dermatology Society, provided specific comments concerning the manuscript.

REFERENCES

1. Pearson C. Polymyositis and dermatomyositis. In: McCarty DJ, ed. *Arthritis and Allied Conditions: A Textbook of Rheumatology*. 9th ed. Philadelphia, PA: Lea & Febiger; 1979:742.
2. Euwer RL, Sontheimer RD. Amyopathic dermatomyositis (dermatomyositis sine myositis): presentation of six new cases and review of the literature. *J Am Acad Dermatol*. 1991;24(6, pt 1):959-966.
3. el-Azhary RA, Pakzad SY. Amyopathic dermatomyositis: retrospective review of 37 cases. *J Am Acad Dermatol*. 2002;46(4):560-565.
4. Finger DR, Dunn CL, Gilliland WR, James WD. Amyopathic dermatomyositis associated with malignancy. *Int J Dermatol*. 1996;35(9):663-664.
5. Nanke Y, Tateisi M, Yamagata H, Hara M, Kamatani N. A case of amyopathic dermatomyositis with rapidly progressive interstitial pneumonia [in Japanese]. *Ryumachi*. 2000;40(4):705-710.
6. Tahara K, Nishiya K, Hisakawa N, Hashimoto K, Hara I, Kodama H. A case of amyopathic dermatomyositis associated with interstitial pneumonitis [in Japanese]. *Ryumachi*. 1997;37(5):714-718.
7. Sontheimer RD. Dermatomyositis: an overview of recent progress with emphasis on dermatologic aspects. *Dermatol Clin*. 2002;20(3):387-408.
8. Airio A, Pukkala E, Isomaki H. Elevated cancer incidence in patients with dermatomyositis: a population based study. *J Rheumatol*. 1995;22(7):1300-1303.
9. Chow WH, Gridley G, Mellekjaer L, McLaughlin JK, Olsen JH, Fraumeni JF Jr. Cancer risk following polymyositis and dermatomyositis: a nationwide cohort study in Denmark. *Cancer Causes Control*. 1995;6(1):9-13.
10. Sigurgeirsson B, Lindelof B, Edhag O, Allander E. Risk of cancer in patients with dermatomyositis or polymyositis: a population-based study. *N Engl J Med*. 1992;326(6):363-367.
11. Wakata N, Kurihara T, Saito E, Kinoshita M. Polymyositis and dermatomyositis associated with malignancy: a 30-year retrospective study. *Int J Dermatol*. 2002;41(11):729-734.
12. Melton LJ III. History of the Rochester Epidemiology Project. *Mayo Clin Proc*. 1996;71(3):266-274.
13. Gerami P, Schope JM, McDonald L, Walling HW, Sontheimer RD. A systematic review of adult-onset clinically amyopathic dermatomyositis (dermatomyositis sine myositis): a missing link within the spectrum of the idiopathic inflammatory myopathies. *J Am Acad Dermatol*. 2006;54(4):597-613.
14. Sontheimer RD. Cutaneous features of classic dermatomyositis and amyopathic dermatomyositis. *Curr Opin Rheumatol*. 1999;11(6):475-482.
15. Sontheimer RD. Would a new name hasten the acceptance of amyopathic dermatomyositis (dermatomyositis sine myositis) as a distinctive subset within the idiopathic inflammatory dermatomyopathies spectrum of clinical illness [published correction appeared in *J Am Acad Dermatol*. 2002;46(5):699]? *J Am Acad Dermatol*. 2002;46(4):626-636.
16. US Census Bureau. State and county quickfacts. US Census Bureau Web site [cited October 31, 2008]. <http://quickfacts.census.gov/>. Accessed October 31, 2008.
17. Oddis CV, Conte CG, Steen VD, Medsger TA Jr. Incidence of polymyositis-dermatomyositis: a 20-year study of hospital diagnosed cases in Allegheny County, PA, 1963-1982. *J Rheumatol*. 1990;17(10):1329-1334.
18. Klein RQ, Teal V, Taylor L, Troxel AB, Werth VP. Number, characteristics, and classification of patients with dermatomyositis seen by dermatology and rheumatology departments at a large tertiary medical center. *J Am Acad Dermatol*. 2007;57(6):937-943.