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The cutaneous and systemic findings associated with nuclear matrix protein-2 antibodies in adult dermatomyositis patients

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Abstract

Objective—To characterize the cutaneous and systemic clinical phenotype of dermatomyositis patients with anti-NXP-2 antibodies.

Methods—We conducted a retrospective cohort analysis of 178 dermatomyositis patients seen at the Stanford University Clinic. Electronic chart review employing a keyword search strategy was performed to collect clinical and laboratory data. Anti-NXP-2 antibodies were assayed by immunoprecipitation using NXP-2 produced by in vitro transcription/translation.

Results—Antibodies to NXP-2 were detected in 20 (11%) of the 178 patients. Anti-NXP-2 antibodies were associated with male gender (50% vs. 25%, p=0.02), dysphagia (74% vs. 39%, p=0.006), myalgia (89% vs. 52%, p=0.002), peripheral edema (35% vs. 11%, p=0.016), and calcinosis (37% vs. 11%, p=0.007). These patients were less likely to be clinically amyopathic (5% vs 23%, p=0.08). Five of the 20 patients with NXP-2 antibodies (25%) had an associated internal malignancy. No other cutaneous characteristics were associated with anti-NXP-2 antibodies except a decreased frequency of Gottron's sign (44% vs. 75%, p=0.012) and the fact that these patients were more likely to have mild skin disease.

Conclusion—Dermatomyositis patients with anti-NXP2 antibodies have a distinct and often severe systemic phenotype that includes myalgia, peripheral edema and significant dysphagia despite having milder inflammatory skin disease.

Like most rheumatic diseases, dermatomyositis (DM) can have a wide range of target organ manifestations. This heterogeneity of manifestations presents both challenge and opportunity—there is challenge in rendering the correct diagnosis but opportunity to assess if clinical nuance may have pathologic or prognostic significance. Furthermore, if clinical findings tend to cluster in different patient groups, recognition of these patterns can actually improve diagnostic power for presentations that lack "pathognomonic" findings. Recently,

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myositis specific antibodies (MSAs) have been identified in the sera of the majority of patients with DM and have been shown to correlate with specific disease phenotypes within the broader spectrum of clinical presentation(1). Thus, identification of antibody-associated clinical phenotypes can aid in diagnosis and patient assessment.

Nuclear matrix protein 2 (NXP-2), formerly known as MJ, has been described as a target of autoantibodies in DM patients in children and adults(1). NXP-2 is a nuclear matrix protein involved in the regulation of p53-induced cellular senescence in response to oncogenic signals.(2). Anti-NXP-2 autoantibodies, initially termed anti-MJ, were first described in 1999 in patients with juvenile dermatomyositis (JDM) with severe muscle weakness, with some patients also having joint contractures and atrophy, intestinal vasculitis, and polyarthritis(3, 4). Subsequent larger studies in the JDM population associated anti-NXP-2 antibodies with increased risk for muscle cramps, severe weakness, intestinal bleeding, dysphagia, falling episodes(5, 6) and most strikingly an increased risk of calcinosis(5–7). These autoantibodies are present in 20–25% of JDM patients, making them one of the most common DM-specific autoantibodies found in many JDM populations(1). Anti-NXP-2 autoantibodies have also been reported in adult DM, with a wide spectrum of frequencies (1.6%–30%) reported(8–12). In adults, anti-NXP-2 is also associated with calcinosis(10, 13, 14) and possibly with internal malignancy(8, 9, 11). Few studies in adult DM have looked at cutaneous manifestations associated with anti-NXP-2 antibodies—currently published studies involve rather limited patient numbers or are focused on one or two cardinal DM skin features (e.g. Gottron papules and heliotrope rash) (10, 11, 14). Thus, we sought to document skin disease phenotype and outcomes, as well as systemic features, in a large cohort of DM patients in the U.S.

PATIENTS AND METHODS

Patients

The Stanford Institutional Review Board approved the collection of plasma and clinical information for this study and all patients provided written informed consent. Patients with DM were seen in the outpatient clinics at the Stanford University Department of Dermatology between 7/20/2004 and 9/8/2014. All DM patients fulfilled Bohan and Peter criteria (classic DM)(15) or the modified Sontheimer criteria (clinically amyopathic DM) (16). All clinical data and labs were obtained during routine dermatology clinic visits. The Cutaneous Dermatomyositis Assesssment and Severity Index (CDASI)(17) was used to score skin severity—specifically, the CDASI-a denotes the “activity” subscore representing a total sum of all elements constituting skin disease activity.

Clinically amyopathic patients were defined as patients with hallmark, biopsy-proven DM skin lesions for at least 6 months who never developed clinically significant muscle weakness during the course of their disease. Interstitial lung disease was considered to be present if there were compatible findings on high-resolution chest CT scanning. Peripheral edema was noted as any swelling of the forearms and/or legs that met the following criteria: it was not due to synovitis; it was not associated with other causes of peripheral edema; it was new with disease onset and its course generally followed that of the dermatomyositis. Dysphagia and myalgia were determined by patient history. Calcinosis was documented if

present on clinical examination, but was typically confirmed by radiography. Cancer-associated DM was defined as any case in which onset of DM was within 3 years of cancer (excluding non-melanoma skin cancer) diagnosis.

Antibody detection

Plasma was collected at the time of the first visit for antibody analysis that was performed as previously described (9). Briefly, antibodies against nuclear matrix protein 2 (NXP-2), melanoma differentiation-associated gene 5 (MDA5), Mi-2 and SUMO-activating enzyme (anti-SAE1/2) were detected by immunoprecipitation using ^{35}S-methionine–labeled recombinant proteins generated from in vitro transcription/translation (VITT) from the appropriate cDNAs. Immunoprecipitates were electrophoresed on 10% SDS-PAGE gels and visualized by fluorography. Antibodies against transcriptional intermediary factor 1-gamma (TIF1- γ) were detected by immunoprecipitation of extracts derived from HeLa cells transiently transfected with cDNA encoding TIF1- γ followed by immunoblotting with a monoclonal antibody against TIF1- γ. Anti–Jo-1 and anti–Ro 52 antibodies were assayed by enzyme-linked immunosorbent assay (Inova Diagnostics).

Statistics

Dichotomous variables are expressed as absolute frequency and percentage while continuous features were reported as mean and standard deviation (SD). The continuous variables representing disease duration at first visit, maximum CK, and maximum aldolase did not follow a normal distribution and are expressed as median with the 25th and 75th percentile ranges. Significance testing was performed using t tests for continuous variables. For the continuous variables representing disease duration at first visit, maximum CK, and maximum aldolase, the distribution of the data were skewed; thus, these data were first base-10 logarithm-transformed before applying the t-test. Categorical variables were analyzed using Fisher's exact test or chi-squared test as applicable. All tests performed were two-tailed, and P values less than .05 were considered statistically significant.

RESULTS

Patient characteristics and autoantibody frequencies

A total of 178 patients with dermatomyositis were seen in the Stanford outpatient dermatology clinic. Patients were followed in our clinic for a median of 2.4 years with median disease duration of 5.6 years (range 0.06–42.5 yr) at their last clinic visit. The median age at diagnosis was 48.3 years (range 4.6–86.9) with 10 patients having disease onset before 18 years. Most (72%) were female and 37 (21%) were clinically amyopathic, and a total of 27 (15%) had cancer-associated DM. One hundred ten (62%) were Caucasian, 27 (15%) Latino, 9 (5%) Pacific Islander, 22 (12%) Asian, and 8 (4%) African American.

Antibodies to NXP-2 were detected in 20 (11%) of the 178 patients in the cohort. Of the anti-NXP-2 positive patients, 2 patients had high titers of one other myositis-specific antibody (1 anti-Mi2 and 1 anti-Jo-1) while 2 additional patients had antibodies to Ro-52.

Clinical characteristics associated with anti-NXP-2 antibodies

We first compared the demographic and systemic characteristics of patients with or without anti-NXP-2 antibodies (Table I). Patients with anti-NXP-2 antibodies were more likely to be male (50% vs. 25%, p =0.02). The presence of NXP-2 antibodies was not significantly associated with age at diagnosis or race. There was a trend for anti-NXP-2 positive patients to have less clinically amyopathic disease (5% vs 23%, p=0.08). Consistent with this, anti-NXP-2 positive patients had significantly higher peak creatine kinase (CK) levels (p=0.0003). Although there was an increase in the prevalence of internal malignancy in the anti-NXP-2 patients, this was not statistically significant (p=0.2).

Patients with anti-NXP-2 antibodies had a higher prevalence of myalgias and dysphagia (p=0.002 and 0.006, respectively), with myalgias occurring in 89% of the patients and were often the primary patient complaint. By defining severe dysphagia as that requiring feeding tube placement and/or hospital admission for inability to handle oral intake or secretions, five out of 14 (35.7%) of dysphagic anti-NXP-2 patients were severe compared to 6 out of 61 (9.8%) dysphagic patients without NXP-2 antibodies (p=0.03). It is possible that the increased risk of myalgia and dysphagia in the anti-NXP-2 population is related to a lower prevalence of clinically amyopathic patients. When we excluded all clinically amyopathic patients from the analysis, we found that dysphagia and myalgia were still more common in the anti-NXP-2 population (78% vs 50%, p=0.041, and 94% vs 62%, p=0.006, respectively).

Cutaneous Manifestations

We next wished to determine if any cutaneous findings are associated with anti-NXP-2 antibodies (Table II). Most of the classic cutaneous manifestations of dermatomyositis were seen at the expected frequently in anti-NXP-2 patients, including Gottron’s papules, heliotrope rash and periungual telangiectasias. Erythema and/or scale of the elbows and/or knees were seen at a reduced frequency in anti-NXP-2+ patients (44% versus 75%, p=0.012). Interestingly, peripheral edema was more commonly seen in patients with anti-NXP-2 antibodies (35% versus 11%, p=0.016). There was a clear association of NXP-2 antibodies with calcinosis—found in 7/19 (37%) versus 17/152 (11%), of anti-NXP-2-positive versus negative patients, respectively (p=0.007), consistent with prior reports(5–7). There was no significant difference between the time of onset, location, or pattern (superficial, deep, plate-like) of calcinosis between patients with and without anti-NXP-2 antibodies (not shown). There was no significant correlation (positive or negative) among the findings of myalgia, cancer, peripheral edema, or dysphagia in the anti-NXP-2 population (not shown).

We also wished to characterize both the severity as well as the clinical course of skin disease activity in patients with anti-NXP-2 antibodies. We used the CDASI-a (activity) score as a quantitative measure of severity—CDASI-a scores were available for 159/178 (89%) of patients. The maximum CDASI-a score for NXP-2 positive patients had a median value of 15 (range 0–41) compared to a median of 24 (range 0–57) for NXP-2 negative patients (p= 0.048). This result persisted after accounting for disease duration (Table 1) and the number or types of systemic medications used to control skin disease in the two populations (not

shown). These data suggest that patients with anti-NXP-2 antibodies have less severe skin disease than other DM patients.

In order to look at longer term outcomes of skin disease, we first calculated how many patients were able to achieve clinically satisfactory control of their skin disease, defined as physician assessment of no or minimal clinical evidence of skin disease activity with no plan to escalate or change therapy for skin disease. We found that 14/18 (78%) of NXP-2 positive patients versus 84/142 (59%) of NXP-2 negative patients were able to achieve this level of disease control by the time of their last visit (p=0.20). A quantitative approach was also taken using the CDASI-activity data by defining clinical control as a CDASI-a less than 10, based on prior studies(17). This approach revealed that 71% vs 46% of anti-NXP-2 positive and negative patients, respectively, achieved remission at their final visit (p=0.09).

DISCUSSION

The reported frequency and phenotypic implications of anti-NXP-2 antibodies in adults with DM have varied significantly across studies. This might be due to both differences in study populations as well as differences in methods for detecting anti-NXP-2 antibodies. In addition, many of the studies have included a small number of NXP-2+ patients, so characterizing phenotypic findings has been challenging. We found NXP-2 antibodies in 11% of our patients—previously reported frequencies in adult DM range from 1.6% to 30%.

We found that NXP-2 antibodies are associated with increased risk of dysphagia, which is in agreement with some(4, 5) but not all(7) studies. Dysphagia was only scored as a subjective complaint, however, and was not always documented by more objective means. Significantly, a higher proportion of these patients with dysphagia required hospitalization and/or feeding tube placement for swallowing issues than patients without NXP-2 antibodies. Our results do not necessarily contradict those of a recent Japanese study reporting that dysphagia is more common in patients with anti- TIF1-γ antibodies(18), given that NXP-2 antibodies are very rarely found in Japanese patients and thus were likely not well represented in the study population(11).

Myalgia also appears to be more common in anti-NXP-2 positive patients. These may correspond to the cramps that Rider et al describe associated with NXP-2 antibodies in patients with juvenile DM (5). The pathologic causes of myalgia are unclear, but it is interesting to note that two other autoantibodies, anti-SRP (signal recognition particle) and anti-HMGCR (3-hydroxy-3-methylglutaryl-coenzyme A reductase), are also associated with prominent myalgia. These antibodies are commonly associated with a necrotizing myopathy on muscle histology, which is typically pauci-inflammatory. Recent work has similarly shown that muscle biopsies from DM patients with anti-NXP-2 antibodies have less primary inflammation that those from patients without this antibody, and many show necrosis on histology(19). It is conceivable that mechanisms of muscle injury that are associated with myalgia do not coincide with the traditional inflammation on muscle biopsy that characterizes DM patients with mostly weakness (versus myalgia).

Our results are in agreement with prior work showing that NXP-2 antibodies are associated with calcinosis and malignancy(5–7, 9). Although more commonly seen in anti-NXP-2 patients, calcinosis did not appear to differ in the location or morphology from that found in anti-NXP-2 negative patients (not shown). Patients with NXP-2 antibodies also had an increased risk of malignancy than their comparator group, although this was not statistically significant (Table 1). This is consistent with our previously reported data(9), and the lack of statistical significance is likely due to under powering, especially in light of the fact that the non-NXP-2 comparator group is largely made up of patients with TIF1-γ antibodies, which are strongly associated with malignancy. Other published data regarding risk of malignancy in anti-NXP-2 patients are difficult to interpret given their small size, as the three adult cohorts reported had only 4, 5, and 8 DM patients with anti-NXP-2 antibodies(8, 10, 14).

We describe a novel association of peripheral edema with anti-NXP-2 antibodies. Soft tissue edema is a well-known manifestation of DM, but typically this manifests as periorbital edema and/or subclinical edema that is seen diffusely in the muscle and soft tissues on imaging studies. However, there are over 25 cases in the literature reporting clinically severe subcutaneous edema as a (sometimes only) cutaneous manifestation of dermatomyositis(20–23). This edema can be generalized or localized to the limbs, occurs early in the disease, is typically non-pitting and is described as having the appearance of changes following deep venous thrombosis (26). Interestingly, these patients have many other features associated with anti-NXP-2 antibodies. A significant proportion of these patients had prominent dysphagia (16/23, or 70%) and myalgia (7/21, or 33%) while ILD was distinctly uncommon(20, 21, 23). In addition, of the data reported, five of the 15 (33%) had an internal malignancy (20). Severe edema and/or anasarca has also been reported in JDM patients, with the largest series showing 20/21 (95%) with myalgia, 11/18 (61%) with dysphagia, and 7/21 (33%) with calcinosis(24). Furthermore, up to 7/10 of these patients had gastrointestinal ulcerations(27), a finding that has also been associated with anti-NXP-2 antibodies(4, 28).

Finally, our data suggest that, on the whole, skin disease in the anti-NXP-2 population is milder than in their seronegative counterparts. Given our dataset and the fact that we have very few little data regarding severity in patients before treatment, we cannot discern if these patients have milder disease versus having disease that is more responsive to our therapies. In addition, we followed the NXP-2 positive patients longer than the NXP-2 negative patients (median 3.6 versus 2.2 years, respectively, p=0.13)—it is possible that the longer follow-up time gave the patients more time to get the skin into remission. Larger prospective studies of treatment-naive patients at disease onset will be required to answer this question with more clarity.

Limitations of this study include the retrospective design and limited generalizability, given that these patients were managed at a tertiary referral center. In addition, high-resolution chest CT scans were only performed on symptomatic patients or on patients with abnormal pulmonary function testing, and thus we might have not detected some mild cases of ILD. The retrospective design may introduce bias given that certain features were hypothesized to be of particular interest before actual chart review was performed—however, all charts are electronic and were interrogated objectively using a key word search algorithm for each clinical symptom. In addition, power is limited given that the number of anti-NXP-2-positive

patients is still relatively small. Finally, detailed and complete information regarding muscle strength and/or muscle histology were not available for analysis in our cohort. Despite these limitations, we feel these data provide further evidence that clinical features, both common and rare, can be associated with antigen-specific immune responses and, when viewed as a collection, can help define an anti-NXP-2 “core phenotype” which is variably expressed but often still recognizable in many patients.

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References

1. Betteridge Z, McHugh N. Myositis-specific autoantibodies: an important tool to support diagnosis of myositis. J Intern Med. 2016; 280:8–23. [PubMed: 26602539]
2. Takahashi K, Yoshida N, Murakami N, Kawata K, Ishizaki H, Tanaka-Okamoto M, et al. Dynamic regulation of p53 subnuclear localization and senescence by MORC3. Mol Biol Cell. 2007; 18:1701–9. [PubMed: 17332504]
3. Oddis C, Fertig N, Goel A, Espada G, Confalone Gregorian M, Maldonado Cocco JA. Clinical and serological characterisation of the anti-MJ antibody in childhood myositis. Arthritis Rheum. 1997; 40:139.
4. Espada G, Maldonado Cocco JA, Fertig N, Oddis CV. Clinical and serologic characterization of an Argentine pediatric myositis cohort: identification of a novel autoantibody (anti-MJ) to a 142-kDa protein. The Journal of rheumatology. 2009; 36:2547–51. [PubMed: 19833756]
5. Rider LG, Shah M, Mamyrova G, Huber AM, Rice MM, Targoff IN, et al. The myositis autoantibody phenotypes of the juvenile idiopathic inflammatory myopathies. Medicine (Baltimore). 2013; 92:223–43. [PubMed: 23877355]
6. Tansley SL, Betteridge ZE, Shaddick G, Gunawardena H, Arnold K, Wedderburn LR, et al. Calcinosis in juvenile dermatomyositis is influenced by both anti-NXP2 autoantibody status and age at disease onset. Rheumatology (Oxford). 2014; 53:2204–8. [PubMed: 24987158]
7. Gunawardena H, Wedderburn LR, Chinoy H, Betteridge ZE, North J, Ollier WE, et al. Autoantibodies to a 140-kd protein in juvenile dermatomyositis are associated with calcinosis. Arthritis Rheum. 2009; 60:1807–14. [PubMed: 19479859]
8. Bodoki L, Nagy-Vincze M, Griger Z, Betteridge Z, Szollosi L, Danko K. Four dermatomyositis-specific autoantibodies-anti-TIF1gamma, anti-NXP2, anti-SAE and anti-MDA5-in adult and juvenile patients with idiopathic inflammatory myopathies in a Hungarian cohort. Autoimmun Rev. 2014; 13:1211–9. [PubMed: 25182203]
9. Fiorentino DF, Chung LS, Christopher-Stine L, Zaba L, Li S, Mammen AL, et al. Most patients with cancer-associated dermatomyositis have antibodies to nuclear matrix protein NXP-2 or transcription intermediary factor 1gamma. Arthritis Rheum. 2013; 65:2954–62. [PubMed: 24037894]
10. Ceribelli A, Fredi M, Taraborelli M, Cavazzana I, Franceschini F, Quinzanini M, et al. Anti-MJ/NXP-2 autoantibody specificity in a cohort of adult Italian patients with polymyositis/dermatomyositis. Arthritis Res Ther. 2012; 14:R97. [PubMed: 22546500]
11. Ichimura Y, Matsushita T, Hamaguchi Y, Kaji K, Hasegawa M, Tanino Y, et al. Anti-NXP2 autoantibodies in adult patients with idiopathic inflammatory myopathies: possible association with malignancy. Ann Rheum Dis. 2012; 71:710–3. [PubMed: 22258483]

12. Betteridge Z, Gunawardena H, Chinoy H, Venkovsky J, Allard S, Gordon P, et al. Autoantibodies to the p140 autoantigen NXP-2 in adult dermatomyositis. Arthritis Rheum. 2009; 60:S304.
13. Valenzuela A, Chung L, Casciola-Rosen L, Fiorentino D. Identification of clinical features and autoantibodies associated with calcinosis in dermatomyositis. JAMA dermatology. 2014; 150:724–9. [PubMed: 24869801]
14. Ishikawa A, Muro Y, Sugiura K, Akiyama M. Development of an ELISA for detection of autoantibodies to nuclear matrix protein 2. Rheumatology. 2012; 51:1181–7. [PubMed: 22427409]
15. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med. 1975; 292:344–7. [PubMed: 1090839]
16. Sontheimer RD. Dermatomyositis: an overview of recent progress with emphasis on dermatologic aspects. Dermatol Clin. 2002; 20:387–408. [PubMed: 12170874]
17. Anyanwu CO, Fiorentino D, Chung L, Dzuong C, Wang Y, Okawa J, et al. Validation of the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI): characterizing disease severity and assessing responsiveness to clinical change. Br J Dermatol. 2015
18. Mugii N, Hasegawa M, Matsushita T, Hamaguchi Y, Oohata S, Okita H, et al. Oropharyngeal Dysphagia in Dermatomyositis: Associations with Clinical and Laboratory Features Including Autoantibodies. PLoS ONE. 2016; 11:e0154746. [PubMed: 27167831]
19. Pinal-Fernandez I, Casciola-Rosen LA, Christopher-Stine L, Corse AM, Mammen AL. The Prevalence of Individual Histopathologic Features Varies according to Autoantibody Status in Muscle Biopsies from Patients with Dermatomyositis. J Rheumatol. 2015; 42:1448–54. [PubMed: 26443871]
20. Milisenda JC, Doti PI, Prieto-Gonzalez S, Grau JM. Dermatomyositis presenting with severe subcutaneous edema: five additional cases and review of the literature. Semin Arthritis Rheum. 2014; 44:228–33. [PubMed: 24830790]
21. Tu J, McLean-Tooke A, Junckerstorff R. Increasing recognition of dermatomyositis with subcutaneous edema - is this a poorer prognostic marker? Dermatol Online J. 2014; 20:21244. [PubMed: 24456947]
22. Goussot R, Wettle C, Le Coz C, Cribier B, Lipsker D. Severe edematous dermatomyositis. Ann Dermatol Venereol. 2016; 143:202–9. [PubMed: 26718900]
23. Watanabe M, Natsuga K, Arita K, Abe R, Shimizu H. Generalized acute subcutaneous edema as a rare cutaneous manifestation of severe dermatomyositis. J Eur Acad Dermatol Venereol. 2015
24. Zedan M, El-Ayouty M, Abdel-Hady H, Shouman B, El-Assmy M, Fouda A. Anasarca: not a nephrotic syndrome but dermatomyositis. Eur J Pediatr. 2008; 167:831–4. [PubMed: 18414893]
25. Sherry DD, Haas JE, Milstein JM. Childhood polymyositis as a paraneoplastic phenomenon. Pediatr Neurol. 1993; 9:155–6. [PubMed: 8499047]
26. Mroue KH, Sharara NH, Rbeiz JG, Arayssi TK. A case of edematous dermatomyositis. J Rheumatol. 2003; 30:2722–3. [PubMed: 14719223]
27. Mitchell JP, Dennis GJ, Rider LG. Juvenile dermatomyositis presenting with anasarca: A possible indicator of severe disease activity. J Pediatr. 2001; 138:942–5. [PubMed: 11391348]
28. Rider LG, Nistala K. The juvenile idiopathic inflammatory myopathies: pathogenesis, clinical and autoantibody phenotypes, and outcomes. J Intern Med. 2016; 280:24–38. [PubMed: 27028907]

Significance and Innovations

- Dermatomyositis patients with anti-NXP2 antibodies have a typical skin presentation with the exception that skin disease is often have more mild and more commonly complicated with calcinosis.
- Autoantibodies to NXP-2 are associated with peripheral edema, myalgia and often severe dysphagia.

Table I

Patient characteristics of anti-NXP2 positive patients

Variable	NXP-2 positive (n= 20), n (%)	NXP-2 negative (n=158), n (%)	*p* value
Gender, n (%)			
Male	10 (50)	39 (25)	0.017
Female	10 (50)	119 (75)	
Race, n (%)			0.90
Caucasian	14 (70)	96 (61)	
Latino	2 (10)	25 (16)	
Pacific Islander	1 (5)	8 (5)	
Asian	3 (15)	19 (12)	
African American	0 (0)	8 (5)	
Tobacco use, n (%)			0.57
None	13 (65)	116 (73)	
Past	5 (25)	25 (16)	
Current	1 (5)	10 (6)	
Age at diagnosis, yr[2]	51.7 (17.5)	47.3 (16.6)	0.27
Duration of disease at initial visit, yr[3]	0.97 (0.49–1.6)	1.52 (0.63–4.3)	0.18
Length of follow-up, yr[3]	3.6 (0.99–6.1)	2.2 (0.48–4.8)	0.13
Internal malignancy, n (%)	5 (25)	22 (14)	0.20
Interstitial lung disease, n (%)	2 (10)	33 (21)	0.53
Clinically amyopathic, n (%)	1 (5)	36 (23)	0.08
CK, maximum[3]	1410 (343–5518)	225 (87–1194)	0.0003
Aldolase, maximum[3]	11.7 (9.1–19.1)	8.8 (6.0–14.7)	0.21
Review of systems, n (%)			
Raynaud phenomenon	2 (10)	34 (22)	0.36
Dysphagia	14 (74)	61 (39)	0.006
Myalgia	17 (89)	77 (52)	0.002
Arthritis/arthralgia	5 (25)	69 (44)	0.12

CK, creatine kinase; *NXP-2*, nuclear matrix protein 2

[1] Fisher's exact test was used to compare categorical variables and unpaired student *t* test was used to compare continuous variables.

[2] Data expressed as mean (standard deviation).

[3] Data expressed as median (Q1–Q3).

Table II

Cutaneous signs/symptoms of anti-NXP2 positive patients

Variable	NXP-2 positive (n=20), n (%)	NXP-2 negative (n= 158), n (%)	*p* value
Gottron's papules	7 (41)	84 (54)	0.32
Heliotrope	14 (78)	114 (75)	1.0
Elbow or knee rash	8 (44)	112 (75)	0.012
Lateral hip rash (holster)	6 (40)	69 (51)	0.59
V-neck rash	18 (90)	116 (73)	0.25
Facial rash	16 (80)	130 (82)	0.52
Scalp rash	14 (74)	107 (71)	1.0
Back rash	12 (60)	100 (63)	0.82
Periungual telangiectasias	17 (85)	130 (86)	1.0
"Red on white"	2 (11)	16 (11)	1.0
Cutaneous ulceration	4 (20)	57 (37)	0.21
Palmar erythematous papules	0 (0)	17 (11)	0.22
Alopecia	7 (39)	67 (46)	0.62
Pruritus	12 (60)	110 (70)	0.77
Peripheral edema	6 (35)	16 (11)	0.016
Calcinosis	7 (37)	17 (11)	0.007

NXP-2, nuclear matrix protein 2; *CDASI,* Cutaneous Dermatomyositis Disease Area and Severity Index

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Fisher's exact test