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Oxford University Press
2023-12-01

Demortier, J, Vautier, M, Chosidow, O, Gallay, L, Bessis, D, Berezne, A, Cordel, N, Schmidt, J, Smail, A, Duffau, P, Jachiet, M, Begon, E, Gottlieb, J, Chasset, F, Graveleau, J, Marque, M, Cesbron, E, Forestier, A, Josse, S, Kluger, N, Beauchêne, C, Le Corre, Y, Pagis, V, Rigolet, A, Guillaume-Jugnot, P, Authier, F J, Guilain, N, Streichenberger, N, Leonard-Louis, S, Boussouar, S, Landon-Cardinal, O, Benveniste, O & Allenbach, Y 2023, 'Anti-SAE autoantibody in dermatomyositis : original comparative study and review of the literature', Rheumatology (Oxford, England), vol. 62, no. 12, pp. 3932-3939. https://doi.org/10.1093/rheumatology/kead154

http://hdl.handle.net/10138/576380
10.1093/rheumatology/kead154

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acceptedVersion

Anti-SAE autoantibody in dermatomyositis: original comparative study and review of the literature

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Abstract

Objective: Among specific autoantibodies in dermatomyositis, the anti-SAE antibody is rare. We aim to describe clinical characteristics, cancer prevalence, and muscle pathology of anti-SAE positive dermatomyositis.

Methods: Patients with a diagnosis of dermatomyositis and sera positive for the anti-SAE antibody were recruited from 19 centers in this retrospective observational study. Available muscular biopsies were reviewed. We conducted comparison to anti-SAE negative dermatomyositis and a review of the literature.

Results: Patients (n=49) were 84 % women. Skin involvement was typical in 96 %, with 10 % calcinosis, 18 % ulceration, 12 % necrosis; 35 % presented with a widespread skin rash. Muscular disease concerned 84 % of patients, with mild weakness (MRC-scale 4 (3;5)), although with 39 % of dysphagia. Muscular biopsies showed typical DM lesions. Interstitial lung disease was found in 21 %, mainly of organizing pneumonia pattern, 26 % of patients showed dyspnea. Cancer associated-myositis was diagnosed in 16 % and responsible for the majority of deaths, its prevalence is five times that of the general population. Intravenous immunoglobulin therapy was administered to 51 % of patients during course evolution. Comparison to anti-SAE negative dermatomyostis (n=85) show less and milder muscle weakness (p=0.02 and p=0.006 respectively), lower creatinine kinase levels (p<0.0001), less dyspnea (p=0.003).

Conclusion: Anti-SAE positive dermatomyositis is a rare subgroup associated with typical skin features but a potentially diffuse rash, a mild myopathy. Interstitial lung disease defines an organizing pneumonia pattern. Cancer associated dermatomyositis prevalence is five times that of the general population.

Trial registration number: ClinicalTrials.gov, https://clinicaltrials.gov/, NCT04637672.

Keywords: Myositis, Dermatomyositis, Small Ubiquitin like modifier activating enzyme, cancer, interstitial lung disease

Key messages:

- Dermatomyositis associated with the anti-SAE autoantibody present with a commonly mild myopathy.
- Interstitial lung disease frequently defines an organizing pneumonia pattern.
- The risk of malignancy is five times higher than in the general population of France.

INTRODUCTION

Dermatomyositis (DM) is a rare idiopathic inflammatory disorder characterized by the association of typical skin and skeletal muscles features (1). This systemic disease may be associated with interstitial lung disease (ILD) and/or malignancy, which are both the leading cause of death in myositis patients (2).

Five mutually exclusive DM specific autoantibodies (anti-Mi2, anti-melanoma differentiation-associated protein 5 (MDA5), anti-nuclear matrix protein-2 (NXP2), anti-transcriptional intermediary factor-1 (TIF1g), anti-Small Ubiquitin like modifier activating enzyme (SAE)) have been described thus far. In addition to their importance for the diagnosis (3), DM specific auto-antibodies help delineate more homogeneous subgroups of patients associated with distinct clinical phenotypes and prognosis (eg. presence of ILD or cancer) (4).

Anti-SAE antibody has been first described in 2007 by Betteridge and al. (5). Its prevalence is low, ranging from less than 1% to 8% of DM patients (5,6). Only few case reports or case series have been published, reporting a late-onset myositis with a mild severity but with high frequency of dysphagia (5,7–10) sometimes in association with ILD (5,6,8,11–16). These studies raise awareness about a diffuse skin rash (8,10,16,17) or potential ethnic disparities (7,8,10), and no reliable phenotypic description can yet be made (18). Prevalence of cancer varies between studies (6,7,12,16,19) and its prognosis remains uncertain. Finally, its myopathological features have yet to be described. This study aims to characterize the clinical and pathological features of anti-SAE antibody positive DM (anti-SAE+ DM) patients, clarify its association with cancer and evaluate its outcome.

PATIENTS AND METHODS

Patients

Through the French networks in systemic diseases and dermatology, we identified anti-SAE+ DM patients and data collection occurred between January 2018 and April 2021, with clinical follow-up until May 2021.

Patients were enrolled if (i) they fulfilled the 239th European NeuroMuscular Centre (ENMC) DM classification criteria (18) and (ii) had a positive anti-SAE autoantibody testing. Anti-SAE negative DM (Anti-SAE- DM) were used as controls.

Anti-SAE antibody detection as well as other DM-specific auto-antibodies (anti-NXP-2, anti-Mi2, anti-TIF1-γ and anti-MDA5) were performed using commercial dot immunoassays (D-Tek ®, Belgium or Euroline ®, Germany).

Data collection

The following were collected for each patient using a standardised form: demographic data, clinical presentation, laboratory test results and paraclinical evaluation (Chest computed tomography, Pulmonary function tests (PFT), magnetic resonance imaging (MRI), skin and muscle biopsies) at diagnosis, longitudinal clinical evolution and lines of treatment.

Cutaneous manifestations were classified according to the ENMC criteria (20). 'Typical' DM lesions were defined as either a heliotrope (red to violaceous) rash and/or eyelid oedema, Gottron's sign or papules at bony prominences, an erythema of the chest and neck (V-sign) or the upper back (shawl sign). 'Classical DM' lesions

included a photosensitive erythema (face and/or trunk and/or extension face of the arms and/or lateral hips (holster sign)), a periungual telangiectatic erythema or dystrophic cuticles ; and 'secondary DM' lesions were panniculitis, alopecia, poikilodermia, ulceration, cutaneous necrosis, and calcinosis.

Muscle involvement was defined as proximal limb muscle weakness (evaluated by Medical Research Council (MRC)-5 scale ≤ 5), and/or dysphagia, and/or increase of creatinine phosphokinase (CK) levels and/or T2/Short-TI Inversion Recovery hypersignal on magnetic resonance imaging (MRI), and/or pathological DM features on muscle biopsy including either perifascicular atrophy, perimysial inflammatory infiltrate, diffuse positive HLA1 immunostaining, capillary dropout and/or dilatation and/or capillary C5b-9 deposition, or muscle infarction.

The diagnosis of interstitial lung disease (ILD) was based on radiological assessment of chest computed tomography (CT) scan by a radiologist (expert in chest radiology) and features were classified according to the American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias (21). A restrictive pulmonary pattern was defined by a decrease in total lung capacity under 80% of the theoretical value on pulmonary function tests. Cancer-associated DM was defined if a malignancy occurred within 3 years (before or after) of the diagnosis of DM (22).

Pathological analysis

Muscle biopsies were reviewed by muscle expert pathologists using a standardized approach. Muscle involvement was assessed in 3 domains (inflammatory, vascular, muscle fiber), using the following stains : haematoxylin and eosin, anti-HLA class I (Mouse, clone CR3/43, Dako), C5b-9 (Mouse, clone aE11, Dako), CD31 (clone JC70A, Dako ®), MxA (Mx1/2/3 [H-285, sc-50509], 1:100 dilution, Santa Cruz Biotechnology, USA), CD3 (Rabbit, clone 2GV6, Roche), CD20 (Mouse, clone L26, Dako), CD68 (Mouse, clone KP1, Dako).

Comparison to cancer prevalence in the general population

Incidence of malignancy in the general population of France was obtained from the Association of the French Cancer Registries (FRANCIM, a French registry was chosen as only two patients were recruited from another country). The number of cancer-associated DM in anti-SAE+ DM patients was compared to the expected number of malignancies in the general population matched for sex and age, and reported by a standardized incidence ratio (SIR, number of observed incident cancers divided by the number of the expected). Deceased patients and malignancies occurring 3 years before or after the diagnosis of DM were censored at the time of death or malignancy diagnosis, every other patient accounted for 6 person-years. Non-French patients and patients with cancer diagnosed more than 3 years before DM diagnosis were excluded from the SIR analysis.

Statistical analysis

Statistical analyses were performed using Prism 9.0 (GraphPad Software). Quantitative variables are reported as medians and interquartile range [IQR]. Qualitative variables are reported as percentages of the total of the available data. The characteristics of anti-SAE+ and anti-SAE- patients were compared using Fisher's exact test

for categorical variables and Student's t-test for continuous variables. P-value estimate for the standardized incidence ratio of cancer used a Poisson modeling (appropriate for uncommon events). Tests were two-sided, differences were considered statistically significant for p values ≤ 0.05.

Review of the literature

We searched PUBMED, EMBASE, EMprenium, LiSSA, BDSP, and Cochrane Library databases for articles related to the association of dermatomyositis and the anti-SAE autoantibody up until January 2022. We included all papers with anti-SAE+ DM case(s) description and/or comparison to anti-SAE- DM patients.

Ethics

This work has been approved by the French Ministry of research (CCTIRS no. 14.323 and AC-2013-1868) and the Research Ethics Comittee of the Pitié Salpêtrière University Hospital (Paris, France) in compliance with the Declaration of Helsinki. Registration number in ClinicalTrials.gov is NCT04637672. Written informed consent is not necessary for this type of study under current legislation in France.

RESULTS

Patients' characteristics

A total of 49 anti-SAE+ DM patients from 18 French and 1 Finnish centers were included in this study. Anti-SAE autoantibody subtypes were represented as follows: anti-SAE type 1 n=48/49, anti-SAE type 2 n=2/49. The control group was composed of 85 anti-SAE negative DM patients, consisting in 32 anti-Mi2 DM, 5 anti-TIF1g DM, 5 anti- NXP2 DM, 9 anti-MDA5 DM and 34 seronegative DM.

Patients were mostly females (83.7 %, n=41/49) and were 53 years old [43-62 years], including 3 juvenile cases. In comparison, the control group (anti-SAE- DM) comprised 65.9 % of females (n=56/85, p=0.03) and age at diagnosis was not statistically different (anti-SAE- DM 50 years, p=0.39). Comparison of anti-SAE+ and anti-SAE- DM patients is shown in Table 1.

Skin manifestations

All patients, but two, presented with DM skin lesions. Two patients presented a sine dermatitis DM and were diagnosed as DM based on myopathological criteria. All anti-SAE+ DM patients with skin changes (n=47/49) had a typical DM skin rash, 91.8 % (n=45/49) of patients had a classical skin rash. Detailed skin manifestations are shown in Table 2.

Among secondary DM lesions, 18.4 % (n=9/49) of anti-SAE+ DM presented with cutaneous (n=6/9) or mucosal (n=3/9) ulcerations (Figure 1a). Prevalence of ulceration was not statistically different in the control group (anti-SAE+ 18.4 % vs anti-SAE- 11.8 % (n=10/85), p=0.31) (Table 1). Skin necrosis and calcinosis were each observed in more than 10 % of anti-SAE+ DM (Figure 1b and 1c). Calcinosis was not statistically different in the control group (anti-SAE+ 10.2 % vs anti-SAE- 5.9 % (n=5/85), p= 0.50). Widespread skin involvement (beyond photoexposed areas) was described in 34.7 % (n=17/49) of anti-SAE+ DM patients (Figure 1d).

Muscular manifestations

Two third (69.4 %, n=34/49) of patients had a proximal weakness. Muscle weakness was mild in most patients and only 30.6 % (n=15/49) were scored ≤ 3 on the MRC scale (including 4 patients ≤ 2). Compare to controls, anti-SAE+ DM presented more frequently with normal strength (anti-SAE+ 30.6 % vs anti-SAE- 12.9 % (n=11/85), p=0.02), and muscle weakness, when present, was milder (worst proximal MRC in anti-SAE+ is 4 [3-5] vs antiSAE- is 3 [3-4], p=0.006). (Table 1). Dysphagia was reported in 38.8 % (n=19/49) including seventeen patients at baseline and two other patients during followup. Frequency of dysphagia in the control group was not statistically different (anti-SAE+ 38.8 % vs anti-SAE- 41.2 % (n=35/85), p=0.85). Of note, when data was available 86.7 % (n=13/15) had muscle disease that occurred after skin lesions with a delay of 92 days [11-212]. Creatinine-kinase (CK) level was 200 UI/L [94-440], with 59.2 % (n=29/49) of patients remaining inferior to twice the norm (N < 130 UI/L). CK level was statistically lower in the anti-SAE+ DM compared to the anti-SAE- DM (anti-SAE- CK 1967 [786-7592], p<0.0001; anti-SAE- with CK<2N in 16.4 % (n=13/79), p<0.0001) (Table 1). Detailed muscle features of the anti-SAE+ DM patients are shown in Table 3.

Fifteen muscular biopsies were reviewed. Most (80.0 %, n=12/15) showed myofiber atrophy, prevailing in perifascicular areas (53.3 %; n=8/15), and 60 % (n=9/15) presented diffuse HLA-1 immunostaining. Myofiber necrosis was observed in 53.3 % (n=8/15). (Figure 2a and 2b). More than a half of cases showed capillary C5b-9 deposition (57.1 %, n=8/14), capillary dilatation (53.3 %, n=8/15) and dropout (58.3 %, n=7/12) (Figure 2c); infarction was found in 20.0 % (n=3/15). There was a perimysial inflammatory infiltrate in 46.7 % of the biopsies (n=7/15). (Table 3).

Extra-cutaneomuscular manifestations

Among patients who underwent chest CT, 21 % (n=8/39) revealed an ILD, associated with clinical dyspnea in 5 out of the 8 patients. All ILD, but one (nonspecific interstitial pneumonia), presented with an organizing pneumonia pattern (87.5 % (n=7/8)) (Figure 3). Prevalence of ILD did not differ compared to the control group (anti-SAE- ILD 27.9 % (n=19/68), p=0.49). The rate of dyspnea was, however, statistically higher in the control group than the anti-SAE+ DM (anti-SAE+ 26.5 % (n=13/49) vs anti-SAE- 56.1 % (n=32/57), p=0.003).

A minority of patients (12.5 %, n=4/32) displayed a restricted pulmonary disease. Forced vital capacity (FVC) was decreased in 15.4 % (FCV <80 %, n=4/26). Diffusing capacity for carbon monoxyde (DLCO) was reduced in 26.7 % (DLCO <70 %, n= 8/30). Of note, anti-SAE+ DM with ILD were more frequently African (62.5 % , n=5/8) compared to anti-SAE positive DM without ILD (0 %, n=0/39; p<0.0001).

Articular manifestations (arthralgia and/or synovitis) were found in 24.5 % (n=12/49) of patients, most commonly in distal joints of the upper limbs, the difference with the control group was not statistically significant (anti-SAE- 50 % (n=31/62), p=0.07).

Malignancy association

Median follow-up duration was 39 months [27-62]. Eight out of ten malignancies fulfilled the definition of cancer-associated DM, representing 16.3 % (n=8/49) of our anti-SAE+ DM patients (colorectal (n=2, aged 57 and 67 years-old (y-o) at diagnosis), lung (n=2, aged 62 and 77 y-o at diagnosis), ovarian (n=2, aged 71 and 76 y-o at diagnosis), melanoma (n=1, aged 37 y-o at diagnosis), haematologic (n=1, aged 81 y-o at diagnosis)).

Comparison of cancer incidence in the age and sex-matched general population in France found an increased risk of cancer in our anti-SAE+ DM patients with a SIR of 5.0 (observed n=8 vs expected n=1.59 in n=229.5 person-years, [2.5-10.1] p<0.001). This association was present in women (SIR=6.6 [3.3-13.2] p<0.001), but this study could not estimate the risk in the male subset because of its limited number (0 cancer cases in 8 patients).
Of note as expected, anti-SAE+ DM with malignancy were older (70 years old) compared to anti-SAE positive DM without (50 years old ; p=0.02).

Treatments and outcomes

First line of treatment consisted of oral corticosteroids for a majority of patients (87.7 %, n=43/49), and another systemic therapy in 91.8 % (n=45/49) (methotrexate n=27, hydroxychloroquine n=21, azathioprine n=6, rituximab n=2, mycophenolate mofetil n=2, cyclophosphamide n=1, and intravenous immunoglobulins (IVIG) n=18). Overall, 51 % (n=25/49) received IVIG, the clinical indication being dysphagia in 64 % of them. Lines of systemic treatments used are detailed in Supplementary Table S1, available at *Rheumatology* online.

At the last follow-up (median of 39 months since diagnosis), 58.3 % (n=28/48) of patients were in physician-assessed complete remission, including 9 patients without any systemic treatment. Eighteen percent (n=9/48) had a persistent muscular disease, 35.4 % (n=17/48) a persistent cutaneous disease (presence of at least 1 typical skin lesion). Among the half of patients with follow-up of at least 39 months, none had an active muscular disease and three patients had a persistent cutaneous disease.

Five patients died during the follow-up period : one of disseminated tuberculosis, three from evolutive malignancy, one from the evolution of her DM in a bedridden 76 years-old. The death rate in the control group was not statistically different (anti-SAE- : 8.2 % (n=7/85), p=0.76).

Review of the literature

Twenty seven articles met our inclusion criteria. Three case reports were excluded for insufficient data for diagnosis of DM (n=2) or insufficient description of the case (n=1). Criteria of interest in each selected study are reported in Supplementary Table S2, available at *Rheumatology* online. Results are discussed in the following section.

DISCUSSION

This cohort of 49 cases of anti-SAE+ DM shows that (i) cutaneous manifestations are 'typical' and rarely severe however sometimes associated with a diffuse erythema; (ii) muscle involvement is frequently mild, with expected myopathological changes, (iii) ILD occurs in the same proportion as in other DM, with a characteristic

pattern of organizing pneumonia and (iv) the risk of malignancy is increased compared with the general population, and was responsible for the majority of fatal outcomes.

Our results are consistent with previously published data including 166 cases reported in 24 articles (4–17,19,23–31) (Supplementary Table S2). All reported case series, but one (Betteridge and al. in 2019 (4)), reported no more than twenty patients. The largest of case series (n=42), comparing anti-SAE+ versus anti-SAE- myositis (not only DM) demonstrated that anti-SAE antibody is DM specific (rash and periungueal erythema) but no further description of cases is available.

According to our review of the literature, skin features are reported as follows : 100 % cutaneous involvement (n=111/111), with a prevalence of 80 % heliotrope rash (n=88/110), 93 % Gottron's sign or papules (n=102/110), 66 % periungueal changes (n=49/74), 69 % V-neck sign (n=51/74), 65 % shawl sign (n=44/68), 62 % diffuse erythema (n=26/42), 27 % alopecia (n=8/30), 11 % calcinosis (n=5/44), 28 % ulceration (n=12/42) (Supplementary Table S2). Proportion of calcinosis was consistent among cohorts, although seldomly recorded (total n=44), and ranged between 0 and 40 % (7,25).

Despite the discrepancies among cohorts, a diffuse erythema has been consistently reported. Among studies reporting this feature, ours has the lowest prevalence, and Albayda and al.'s work (16) in a North American cohort found a close prevalence of 42 %. Inoue and al. (17) recently reported an erythema of the back respecting the interscapular region (n=6), characterization of this entity would benefit a prospective setting.

Considering the muscle domain, our review shows a global prevalence of myopathy of 79 % (n=69/87), with 45 % myalgia (n=10/22), 71 % paresia (n=58/82), 51 % having elevation of CK levels (n=49/97), and 50 % dysphagia (n=42/84). Dysphagia prevalence may reach 64 % (8) or even 78 % (6) in some cases series. Frequently (58 %, n=57/98) patients presented either with clinically amyopathic DM or delayed muscle disease onset after skin involvement ("skin first"). Amyopathic DM concerned 20.7 % (n=18/87) of anti-SAE + DM. Severity of muscle weakness found in our study is shared with Peterson's work (36 % moderate to severe)(25) whereas other series did not semi-quantitatively measure the strength. IVIG use in our study was in correlation with its expected efficacy in muscle involvment in a selected population (32).

One previous study described muscle biopsy findings in anti-SAE+ DM (n=7)(8). It reported perimysial inflammatory infiltrates without the characteristic DM pattern (18). Our findings delineate perifascicular atrophy, vasculopathic changes and inflammatory infiltrate in only about half of anti-SAE+ DM patients. These results suggest that anti-SAE+ DM muscle damage could be moderate, which would be consistent with the milder clinical muscle features. Of note, only one patient who was biopsied was amyopathic.

Our review identified a total of 53 % (n=49/92) of ILD in anti-SAE+ DM, ranging from 17 to 77 % (excluding studies where pulmonary involvement was an inclusion criteria or studies reporting 2 or less cases). Particularly, evidences of preserved pulmonary function, absent respiratory failure, and presence of organizing pneumonia

pattern (statistically more frequent than with other myositis specific autoantibodies (15)) are reported in Zuo and al. (15), Gono and al. (11) and Albayda and al. (16)'s work. The majority (79.6 %) of patients we studied performed a CT-scan. The discrepancy between the ILD rate in our study compared to those in the literature may be explained by the fact none systematically performed CT evaluation, and some authors have raised queries about potential ethnic disparities between Asian and Caucasian patients in the phenotypic expression of anti-SAE+ DM (8,10). Our study population only comprised 5 patients of Asian and African ethnicity each, and lacked power to draw any conclusions.

Cancer association found in our study is consistent with the other published cohorts ranging from 6 % to 25 % (6–9,16,19,25), excluding Muro and al. (12)'s little series 57 % rate. The total malignancy rate in our review is 18 % (n=17/96). In our series, we were able to measure standardized index ratio, showing for the first time an increased risk of malignancy in anti-SAE positive DM compared to the general population. Patients with cancer-associated DM were older, which is concordant with previous population-based studies in dermatomyostis (33,34).

We conducted a retrospective study with all related limitations. Nevertheless, our results are consistent with those of the literature. The multicenter design allows for minimization of possible referal bias, and prolonged follow-up duration may limit the risk of incomplete phenotypic description (eg delayed muscle signs). Our review identified only one small (n=6) prospective study (23). The trust in our review's phenotypic description of the disease should take into account each feature's number of missing data in the literature ; whereas our study was dedicated to minimizing them.

CONCLUSION

The anti-SAE autoantibody in dermatomyositis is associated with « typical » skin disease and potentially diffuse erythema with a mild muscle involvement that may present with a delayed onset. ILD most commonly present with an organizing pneumonia pattern, yet it does not worsen the overall prognosis whereas cancer prevalence is higher than in the general population.

Acknowledgements.

To the Study Group of Systemic Diseases in Dermatology (Étude des Maladies Systémiques en Dermatologie, EMSED group) who provided help for cases' identification. This work was presented as an abstract at the 83rd SNFMI Conference 2021.

Data availability statement: The data that support the findings of this study are available from the corresponding author, J.D, upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure: The authors have declared no conflicts of interest.

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Table 1: Characteristics of anti-SAE+ compared to anti-SAE- DM patients.

Characteristics	Anti-SAE+ DM n=49	Anti-SAE- DM n=86	Univariate analysis p-value
Sex ratio (F/M)	5.12 (41/8)	1.93 (56/29)	p=0.03
Age at diagnosis, years	53 (43;62)	50 (38;62)	p=0.39
Skin disease, yes	95.9 (47/49)	92.9 (79/85)	p=0.71
Calcinosis	10.2 (5/49)	5.9 (5/85)	p=0.50
Ulceration	18.4 (9/49)	11.8 (10/85)	p= 0.31
Proximal weakness	69.4 (34/49)	87.0 (74/85)	p= 0.02
Worst proximal MRC evaluation (deltoid or psoas)	4 (3;5)	3 (3;4)	p=0.006
CK levels	200 (94 ; 440)	1967 (786;7592)	p<0.0001
Dysphagia	38.8 (19/49)	41.2 (35/85)	p=0.85
Dyspnea	26.5 (13/49)	56.1 (32/57)	p=0.003
Interstitial lung disease	21.0 (8/39)	27.9 (19/68)	p=0.49
Arthralgia and/or arthritis	24.5 (12/49)	50.0 (31/62)	p= 0.07
Death from any cause	10.2 (5/49)	8.2 (7/85)	p=0.76

Quantitative variables are reported as medians and interquartile range (IQR). Qualitative variables are reported in percentages of the total of the available data. Univariate analysis was conducted through Fisher's exact test for categorical variables and Student's t-test for continuous variables. Difference was considered statistically significant for p values < 0.05. F=female. M=male. MRC = Medical research council scale. CK= creatinine kinase. CK levels are reported in UI/L.

Table 2: Cutaneous features in anti-SAE+ DM patients.

Characteristic	Anti-SAE + DM, n= 49
Skin manifestations, yes	95.9 (47/49)
Erythema of the eyelids	71.4 (35/49)
Periorbital oedema	44.9 (22/49)
Gottron's sign or papules	77.5 (38/49)
Periungual erythema	77.5 (38/49)
Erythema of the upper back (shawl sign)	57.1 (28/49)
Erythema of the upper trunk (V sign)	77.5 (38/49)
Lateral hip erythema (holster sign)	34.7 (17/49)
Panniculitis	8.2 (4/49)
Poikiloderma	12.2 (6/49)
Alopecia	8.2 (4/49)
Calcinosis	10.2 (5/49)
Necrosis	12.2 (6/49)
Cutaneous or mucosal ulceration	18.4 (9/49)
Only skin disease at onset, (n=15)*	86.7 (13/15)
Raynaud phenomenom	14.3 (7/49)

Quantitative variables are reported as medians and interquartile range (IQR). Qualitative variables are reported in percentages of the total of the available data. *Indicates the number of patients for whom data was available.

Table 3: Muscular characteristics of anti-SAE+ DM patients.

Characteristic	SAE + DM , n= 49
Muscular manifestations, yes	83.7 (41/49)
Myalgia	55.1 (27/49)
Dysphagia	38.8 (19/49)
Proximal weakness (MRC <5)	69.4 (34/49)
Worst proximal MRC evaluation (deltoid or psoas)	4 (3;5)
CK levels	200 (94 ; 440)
Muscular biopsy	34.7 (17/49)
Reviewing of available biopsies, (n=15)*	
Muscle fiber necrosis	53.3 (8/15)
Muscle fiber atrophy	80.0 (12/15)
Perimysial fragmentation, (n=13)*	7.7 (1/13)
Perimysial inflammatory infiltrates	46.7 (7/15)
Diffuse positive HLA1 immunostaining	60.0 (9/15)
Sarcolemmal positivity for C5b9, (n=13)*	23.1 (3/13)
C5-B9 endocapillaries, (n=14)*	57.1 (8/14)

Capillaries dilatation	53.3 (8/15)
CD31 (capillary rarefaction upon atrophic areas), (n=12)*	58.3 (7/12)
Infarction	20.0 (3/15)
Predomience of CD3 over CD20, (n=12)*	50.0 (6/12)
CD68, (n=12)*	58.3 (7/12)

Quantitative variables are reported as medians and interquartile range (IQR). Qualitative variables are reported in percentages of the total of the available data. MRC = Medical research council scale. CK= creatinine kinase. CK levels are reported in UI/L. *Indicates the number of patients for whom data was available.

Figure 1: Cutaneous lesions in anti-SAE+ DM patients.

A) Ulceration located on the upper thigh. B) Skin necrosis. C) Calcinosis in a juvenile DM patient. D) Diffuse erythema of the back.

Figure 2: Muscle pathology in anti-SAE+ DM patients.

A) Perifascicular atrophy and necrosis. B) HLA1 perifascicular positivity. C) Capillary microthrombosis with C5b9 endocapillaries, the little number of thrombi is explained by a global capillary rarefaction seen on CD31 immunostaining.

Figure 3: Thorax CT scans with interstitial lung disease in anti-SAE+ DM patients.

Thorax CT-scan evaluation found an interstitial lung disease defining an organizing pneumonia pattern.

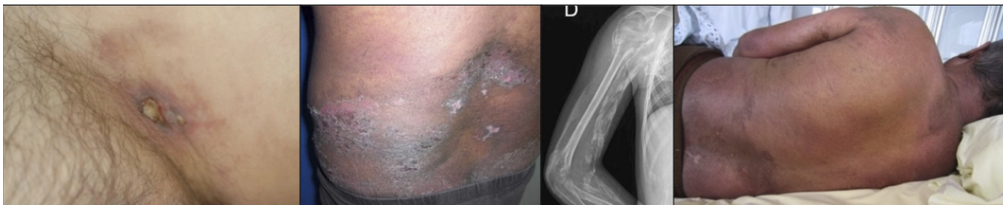

Figure 1

89x17mm (300 x 300 DPI)

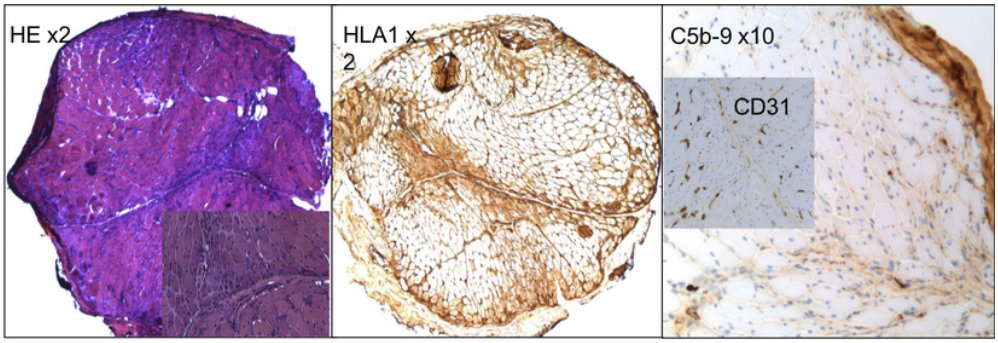

Figure 2

70x23mm (300 x 300 DPI)

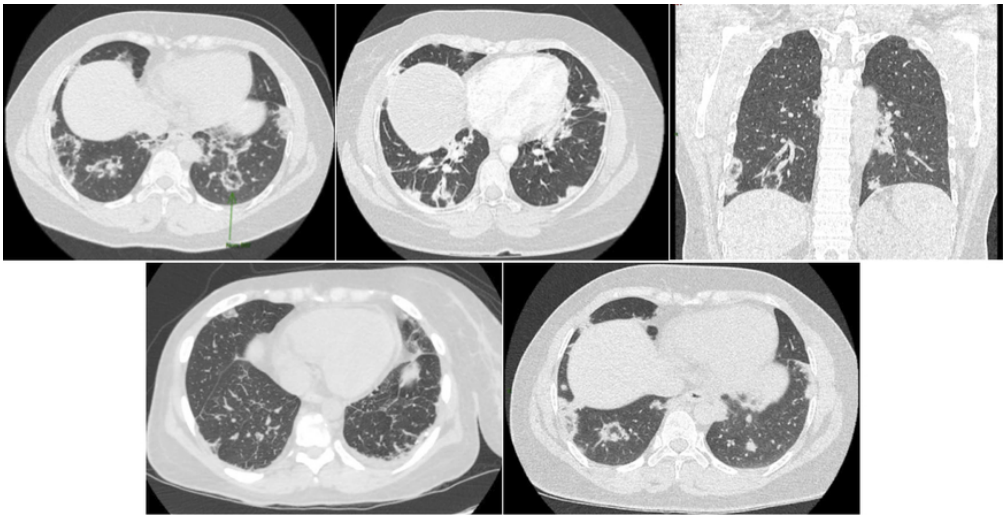

Figure 3

73x37mm (300 x 300 DPI)