



# Diffuse pruritic erythema as a clinical manifestation in anti-SAE antibody-associated dermatomyositis: a case report and literature review

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## Abstract

Anti-small ubiquitin-like modifier-1 activating enzyme (anti-SAE) antibodies have been recently discovered especially for myosin and identified as dermatomyositis (DM) marker. The frequency of anti-SAE antibodies in DM patients is extremely low. Diffuse pruritic erythema may be one kind of clinical manifestations of DM with anti-SAE antibodies. In this report, a 48-year-old female patient with amyopathic dermatomyositis (ADM) carrying anti-SAE antibodies presented diffuse pruritic erythema for 5 months. Diffuse pruritic erythema improved after treatment with prednisolone, cyclosporine, and thalidomide. The clinical characteristics of 75 previously reported cases with anti-SAE antibody-positive DM were reviewed, and the manifestations of the Asian and Western cohorts were compared. It was revealed that the Asian patients were more susceptible to diffuse erythema (17/34 vs. 3/41,  $P = 0.000$ ), dysphagia (16/34 vs. 10/41,  $P = 0.040$ ), and interstitial lung disease (ILD) (21/34 vs. 5/41,  $P = 0.000$ ) compared with the Western patients. The frequency of malignancy in the Asian cohort was significantly higher than that in the Western cohort (10/34 vs. 4/41,  $P = 0.030$ ).

**Keywords** Anti-SAE antibody · Anti-small ubiquitin-like modifier-1 activating enzyme antibody · Dermatomyositis · Diffuse erythema · Literature review · Malignancy

## Introduction

Anti-small ubiquitin-like modifier-1 activating enzyme (anti-SAE) antibodies have been recently discovered as myosin-

specific autoantibodies [1] and identified as dermatomyositis (DM) marker. The frequency of anti-SAE antibodies in DM patients is extremely low, ranging from 1.5 to 8.0%. The antibodies are often associated with the initial presentation of amyopathic dermatomyositis (ADM). However, whether diffuse erythema is a kind of clinical manifestations of DM with anti-SAE antibodies remains unclear [2]. In this study, a Chinese patient with anti-SAE antibody-positive ADM who suffered from diffuse pruritic erythema was reported. The clinical characteristics of 75 previously reported cases were reviewed, and the manifestations of the Asian and Western cohorts were compared.

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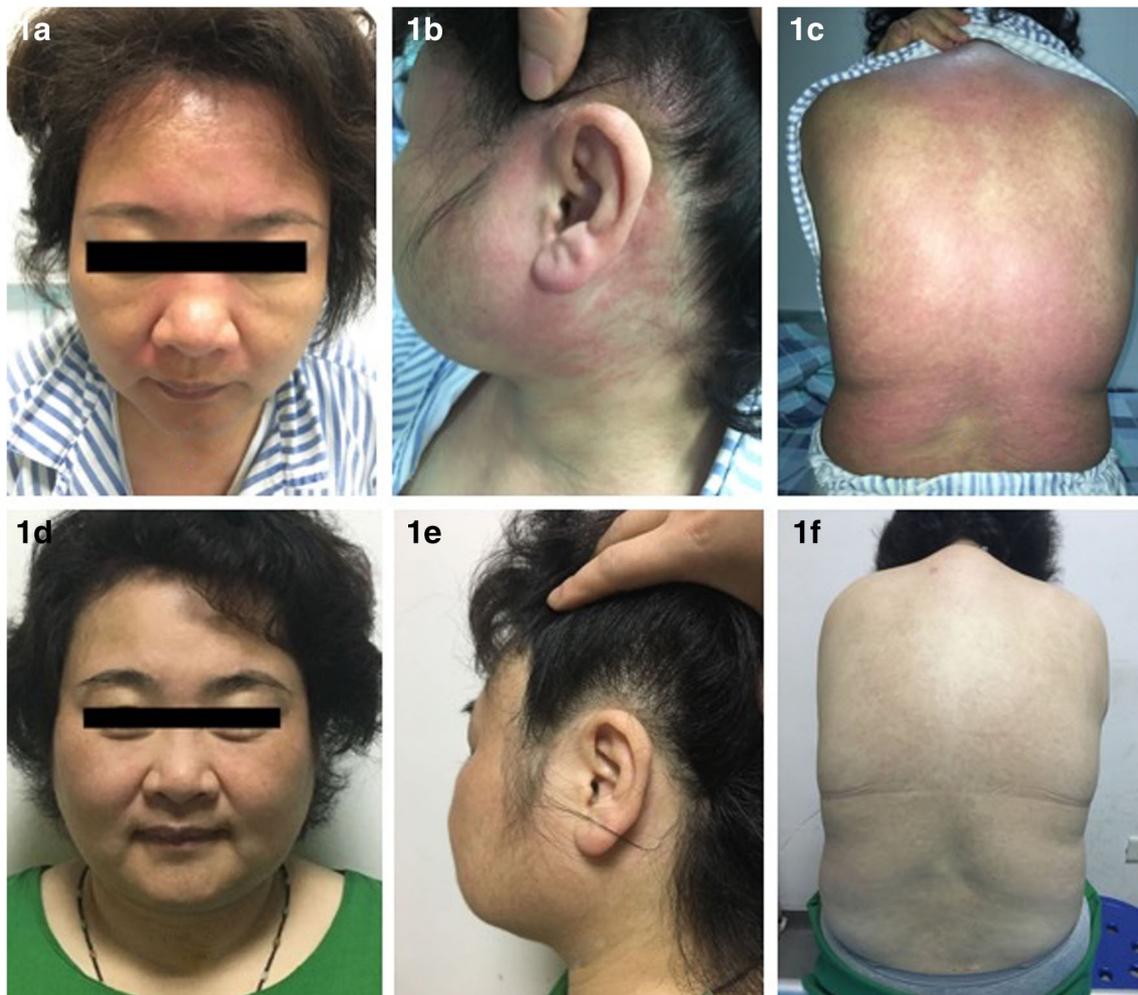
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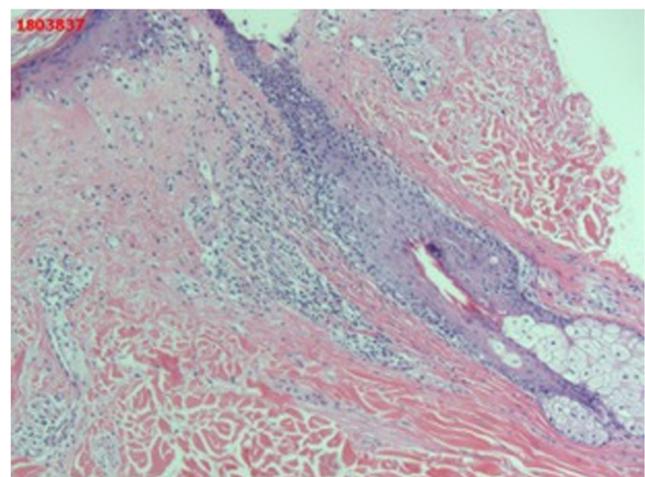
## Case presentation

A 48-year-old female presented diffuse pruritic erythema for 5 months. The erythema was distributed on her scalp, face, neck, chest, and back (Fig. 1a–c). Other skin manifestations included heliotrope rash, Gottron's signs, V-neck sign, shawl

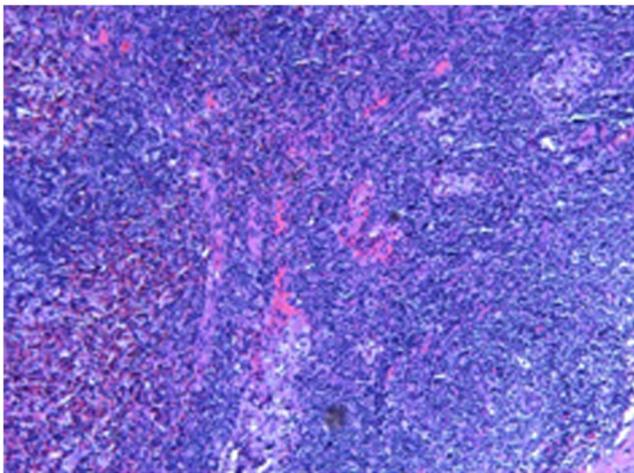


**Fig. 1** The diffuse erythema distributed in face (a), scalp (b), and back (c) before treatment. The diffuse erythema was improved in face (d), scalp (e), and back (f) after treatment

sign, periungual lesions, and Mechanic's hands. Muscular weakness, dysphagia, or interstitial lung disease (ILD) was not found. A swollen lymph node was observed on the left occipital. According to the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), the total activity score was 33, and total damage score was 4. ANA (1:320), anti-SAE, and anti-SSA/Ro52 were positive, while other myositis-specific antibodies were normal. Creatine kinase (CK), lactate dehydrogenase, aspartate aminotransferase, aspartate aminotransferase, and electromyography were normal. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tumor markers, anti-HBV, anti-hepatitis C virus (anti-HCV), anti-human immunodeficiency virus (anti-HIV), syphilis antibody, thyroid function, and serum potassium were normal. There was a palpable 2 cm × 2 cm swollen lymph node on the left occipital bone. Histopathological examination of the skin revealed mild hyperkeratosis, localized atrophy and thinning of the epidermis, denatured collagen fibers of the superficial dermis, and deposition of a small quantity of pigment-like particles, as well as perivascular edema with



**Fig. 2** Pathology of skin tissue biopsy: the epidermis of the skin tissue was slightly hyperkeratotic, the local epidermis atrophied and thinned, the collagen fibers in the superficial dermis were degenerated, and a few pigment-like particles were deposited



**Fig. 3** Pathology of lymph nodes: it was reactive hyperplasia with lymphocytic infiltration

lymphocytic infiltration (Fig. 2). Reactive hyperplasia was confirmed by lymph node pathology (Fig. 3). The patient had been misdiagnosed as eczema and given anti-histamine treatment, while it was not efficient. The pruritic erythema improved after taken 30 mg of prednisolone daily and 10 mg of methotrexate weekly. However, after 6 months, the patient developed hair loss, and then the daily treatment plan

changed to 100 mg of cyclosporine and 10 mg of prednisolone. However, the pruritic erythema relapsed. The pruritic erythema improved after adding 50 mg of thalidomide daily for 6 months (Fig. 1d–f). The total activity score was 4, and total damage score was 0.

### Discussion

The anti-SAE antibodies are classified into two subtypes, SAE1 and SAE2, with molecular weights of 40 and 90 kDa, respectively. A large-scale study on Chinese DM patients found that the frequency of anti-SAE antibody-positive DM was 3% [3]. The frequency of anti-SAE antibodies in Japanese DM patients was 1.8% [4], and 8% in British Caucasian adult DM patients [5]. A research conducted in Italy reported that 5 of 75 patients with DM had anti-SAE antibodies [6]. A Greek research reported the similar frequency (3/44) of anti-SAE in DM [7]. The autoantibody was strongly associated with the HLA-DQB1\*03, HLA-DRB1\*04, and HLA-DQA1\*03 haplotypes [5].

Here, 75 cases of anti-SAE antibody-positive DM have been reported, including the presented case (Table 1). The races have been differentiated based on the literatures. Asian

**Table 1** Clinical characteristics and treatment of SAE antibody-positive patients

	Number (%)	Asian cohort (n = 34)	Western cohort (n = 41)	$\chi^2$	P
<b>Clinical characteristics</b>					
Skin involvement	75 (100)	NA	NA	NA	NA
Heliotrope rash	38 (50.7)	23	15	7.174	0.007*
Gottron's signs	46 (61.3)	28	18	11.587	0.001*
V-neck sign	28 (37.3)	17	11	4.265	0.039*
Shawl sign	23 (30.7)	18	5	14.513	0.000*
Mechanic's hands	11 (14.7)	11	0	15.545	0.000*
Periungual lesions	23 (30.7)	NA	NA	NA	NA
Diffuse erythema	20 (26.6)	17	3	17.316	0.000*
Alopecia	1 (1.3)	NA	NA	NA	NA
Calcinosis	2 (2.7)	NA	NA	NA	NA
Myopathy	58 (77.3)	22	36	5.658	0.170
Dysphagia	26 (34.7)	16	10	4.417	0.040*
Elevation of CK	35 (46.7)	18	17	0.984	0.321
Lung involvement	26 (34.7)	21	5	20.164	0.000*
Arthritis	4 (5.3)	NA	NA	NA	NA
Malignancy	14 (18.7)	10	4	4.730	0.030*
<b>Treatment</b>					
GC (21–39 mg)	2	NA	NA	NA	NA
GC (≥ 40 mg)	4	NA	NA	NA	NA
GC + MTX	1	NA	NA	NA	NA
GC + tacrolimus	2	NA	NA	NA	NA
GC + immunoglobulins	1	NA	NA	NA	NA
GC + CYS	2	NA	NA	NA	NA
GC + AZA	1	NA	NA	NA	NA
GC + CYC + MTX + CYS	1	NA	NA	NA	NA
GC + CYS + MTX + AZA	1	NA	NA	NA	NA
GC + CYS + thalidomide	1	1	NA	NA	NA

Five patients were not illustrated gender. NA not available, CK creatine kinase, GC glucocorticoid, MTX methotrexate, CYC cyclophosphamide, CYS cyclosporine, AZA azathioprine

\*P < 0.05 between Asian cohort and Western cohort

cohort was major Chinese and Japanese patients, and Western cohort was major Caucasian patients. Except for one case of a male with DM for 5 years, all were adult onset. The female/male ratio was 1.8:1; however, 5 patients did not describe their gender [6], and there was no significant difference in female/male ratio between in the Asian (22/12) and the Western (23/18) cohorts.

The frequency of Heliotrope rash, Gottron's signs, V-neck sign, Shawl sign and Mechanic's hands was higher in the Asian cohort than the Western cohort. Especially, the frequency of diffuse erythema was substantially higher in the Asian (50.0%) cohort than the Western (7.3%) cohort, which may reflect differences in ethnicity. Only the patient in our case report suffered from diffuse pruritic erythema. Thus, diffuse erythema should be taken as one kind of cutaneous manifestations of DM into account with anti-SAE antibodies. Skin manifestations preceded muscle involvement (77.3%) in all cases. There was no difference in myopathy and CK level between the Asian and Western cohorts ( $P = 0.321$ ). The frequency of dysphagia in the Asian cohort was higher than that in the Western cohort. ILD was mainly systemic manifestation (34.7%). The frequency of ILD in the Asian cohort (61.8%) was also higher than that in the Western cohort (12.2%). The frequency of arthritis in all cases was low (5.3%). In addition, a significantly higher frequency of anti-melanoma differentiation-associated gene 5 (MDA5) antibodies was observed in Chinese patients with polymyositis (PM)/DM than in Japanese patients [8]. These findings suggest that distinct genetic and/or local environmental factors affect Chinese and Japanese patients with PM/DM, who have been considered a homogeneous population in previous studies.

A previous study found that the incidence of cancer in SAE-positive patients was significantly higher than that in anti-SAE-negative patients, 57% and 12% [9]. We here found that the incidence of malignancy was 18.7% (14/75). The frequency of malignancy in the Asian cohort [3, 9–11] was remarkably higher than that in the Western cohort (10/34 vs. 4/41) [5, 6, 12]. The difference in malignancy may be associated with ethnicity as well. Tumors in the Asian cohort were various, including esophageal cancer (1/10), colon cancer (3/10), rectal cancer (2/10), lung cancer (1/10), renal cell carcinoma (1/10), uterine cancer (1/10), and other tumors (1/10), in which the incidence of digestive system malignancy was the highest (6/10). Ovarian cancer (1/4), colon cancer (1/4), and other tumors (2/4) were reported in the Western cohort. In addition, at least 50% of patients had tumors within 3 years after the diagnosis of DM. These results indicate that anti-SAE antibody in DM patients is a risk factor for malignancy, especially in the Asian cohort.

Glucocorticoid (GC) had been preferred for the treatment of DM. High dose of GC is always combined with immunosuppressive agents (methotrexate, cyclophosphamide, cyclosporine, or cyclosporine) for clinical application. In the presented case, the pruritic erythema improved after adding thalidomide. Thus, we considered that thalidomide may be used to improve diffuse erythema. The majority of anti-SAE antibody-positive patients (78%) improved after receiving GC and/or immunosuppressive agents.

In this study, diffuse erythema was one kind of cutaneous manifestations of DM with anti-SAE antibodies. The Asian patients may be more susceptible to diffuse erythema, dysphagia, ILD, and malignancy compared with the Western patients.

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## Compliance with ethical standards

**Disclosure** None.

**Patient consent and confidentiality** The patient signed a written informed consent form for the purpose of publication of results of this case study.

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