A case report of erythrodermic amyopathic dermatomyositis

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ABSTRACT:

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Patient with amyopathic dermatomyositis accounts for 10-20% of the cases of dermatomyositis. In this report we describe a case of adult-onset amyopathic dermatomyositis presenting with an unusual cutaneous presentation of erythroderma. Histopathology and other laboratory investigations supported the diagnosis and revealed no concurrent internal malignancy.

Key words: Amyopathic dermatomyositis, erythroderma, erythrodermic dermatomyositis

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Introduction

Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by varying degrees of skin manifestation with or without muscle involvement. Amyopathic dermatomyositis (ADM) is a subset of DM, accounting for 20% of all DM patients, characterized by biopsy-confirmed hallmark cutaneous manifestation of classic DM with no clinical evidence of proximal muscle weakness and no serum muscle enzyme abnormalities[1]. In 1991, the criteria for qualifying for ADM was initially proposed by Euwer and Sontheimer[2]. They proposed that ADM include one to two of the pathognomonic skin features, which are Gottron's papules and Gottron's sign, with one or more characteristic signs of heliotrope, periungual telangiectasia with associated dystrophic cuticles and macular violaceous erythema on particular areas[1]. Moreover, a skin biopsy compatible with a diagnosis of DM and an absence of clinical muscle disease for 2 years are needed[2]. Sontheimer revised the criteria in 2002 to shorten the duration of absence of muscle involvement to 6 months to allow for earlier management (table 1)[1].

Diagnosis of ADM can be very difficult especially in the patients without typical skin features. Awareness of the disease together with history taking, physical examination and lab investigation are essential to make a diagnosis. We report a Thai female patient who presented with generalized erythroderma without muscle involvement.

Table 1 Diagnostic criteria for clinically amyopathic dermatomyositis[3]

Characteristic of ADM:
1. Biopsy-confirmed
2. Hallmark cutaneous manifestations of classic DM occurring for 6 months or longer
3. No clinical evidence of proximal muscle weakness and no serum muscle enzyme abnormalities for 6 months or longer
4. If more extensive muscle testing is carried out, the results should be within normal limits
Exclusion criteria:
1. Treatment with systemic immunosuppressive therapy for consecutive months or longer within the first 6 months after skin disease onset
2. Use of drugs known to be capable of producing DM-like skin changes (e.g. hydroxyrurea, statin cholesterol-lowering agents) at the onset of cutaneous DM changes.

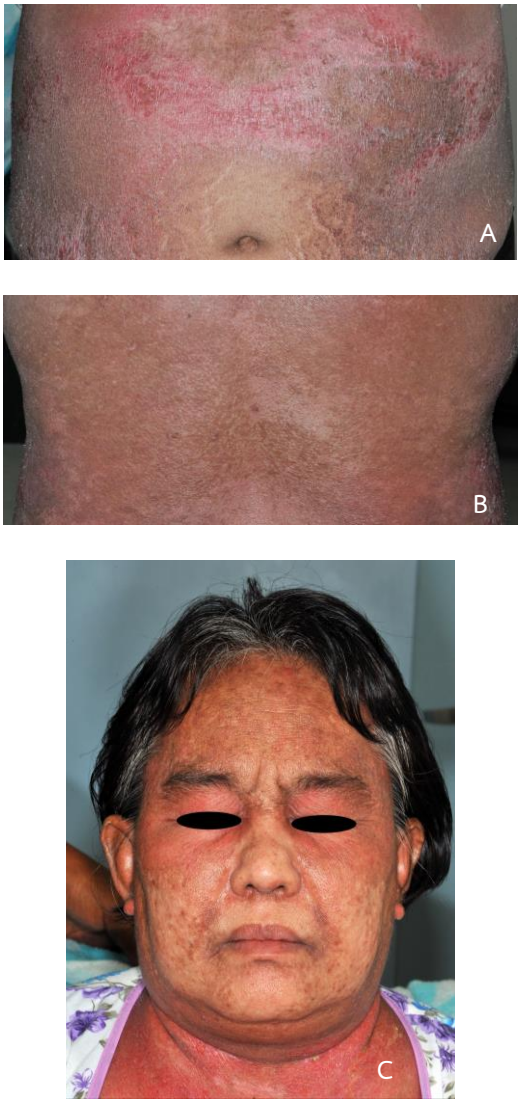

Figure 1 Erythematous scaly patches involving the abdominal wall (A) and back (B); Periorbital violaceous erythema with associated edema of the eyelids (C)

Case report

A 49-year old Thai female from Saraburi province presented with itchy generalized erythematous rash for 5 months. She had no fever, photosensitivity, joint pain or muscle weakness. She had lost 6 kg in the past 5 months. The rash had been worsening and she started to develop scattered localized erosions with minimal serum oozing in flexural areas. She denied taking any medication and had no underlying disease.

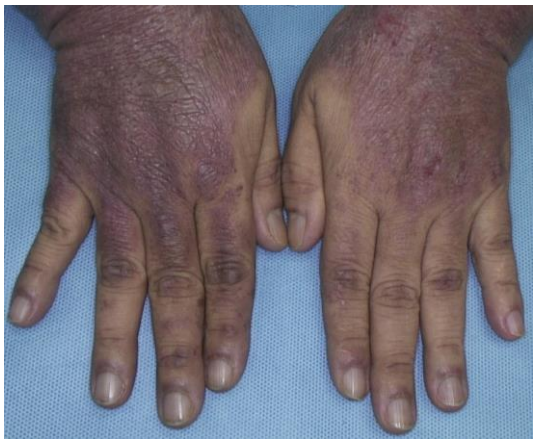

Figure 2 Dorsal aspect of the hands showing Gottron's papules and erythematous to violaceous scaly plaques; note the nailfold erythema

The skin lesions were observed as confluent, mild scaly, violaceous to erythematous patches involving more than 90% of the total body area (Figure 1). Scattered erosions with minimal serum oozing in nape of neck and both popliteal fossae were noted. Periorbital, edematous, well-defined violaceous erythema and a few scaly erythematous to violaceous flat-topped thin

papules affecting the extensor aspects of the metacarpophalangeal and interphalangeal joints of the hands were seen (Figure 2). In addition, ragged cuticles and periungual telangiectasias were also observed in some fingers (Figure 3). A total of 4 punch skin biopsies were performed in different hospital visits. One of the skin biopsies was obtained from the erythematous to violaceous thin papule on extensor surface overlying the 3rd right metacarpophalangeal joint. The rest of the tissue specimens were collected from erythematous scaly patches on right forearm (2 specimens) and left mid back. Histopathology of all biopsy specimens showed old lichenoid dermatitis with multiple melanophages, papillary dermal edema and mild dermal perivascular lymphocytic infiltration with mucin deposition (Figure 4). Direct immunofluorescence staining showed positive IgM and C3 at colloid bodies.

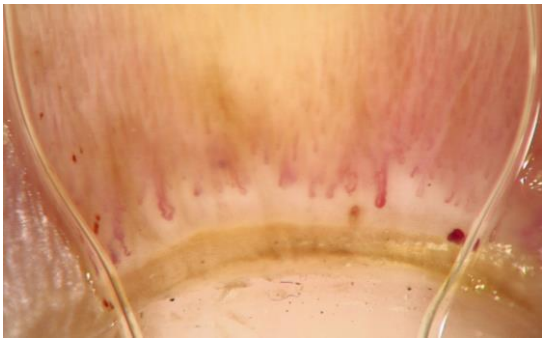

Figure 3 Dermoscopic examination of the proximal nailfold showing dilated capillary loops alternating with vessel dropout

Laboratory investigations demonstrated positive ANA 1:1280 with speckled pattern, negative anti-dsDNA, anti Jo-1 IgG, anti-Ro, anti-La, U1RNP and anti-Smith antibodies. Normal level of C3 and C4 complement. Serum autoantibodies, namely anti-Mi-2, anti-Ku, anti-PM-Scl 100, anti-PM-Scl 75, anti-PL-7, anti-SRP, anti-PL-12, anti-EJ, anti-OJ, anti-TIF1-Υ, anti-MDA5 and anti-NXP-2 were negative, but anti-SAE 1 was positive. The electromyography revealed no evidence of neuropathy or myopathic pattern. Serial CPK levels were performed at 6 and 15 months after the onset of the skin manifestation and the results were normal. Additional laboratory tests for screening of complications and malignancy were investigated including gynecologic examination, pap smear, chest X-ray, electrocardiography, mammography, AFP, CA19-9, stool occult blood and ultrasound of ovary and whole abdomen. All of the results were unremarkable.

The patient has been treated with hydroxychloroquine and topical steroid. Given that the patient had severe extensive erythrodermic skin involvement, oral prednisolone was also prescribed with the dose of 1 mg/kg/d. Because the clinical improvement could not be achieved in the following visit, azathioprine was then added. Later on, erythroderma gradually subsided and prednisolone was tapered successfully. Up until

now, 15 months after the onset of the rash, erythroderma has resolved and there has been no evidence of muscle involvement.

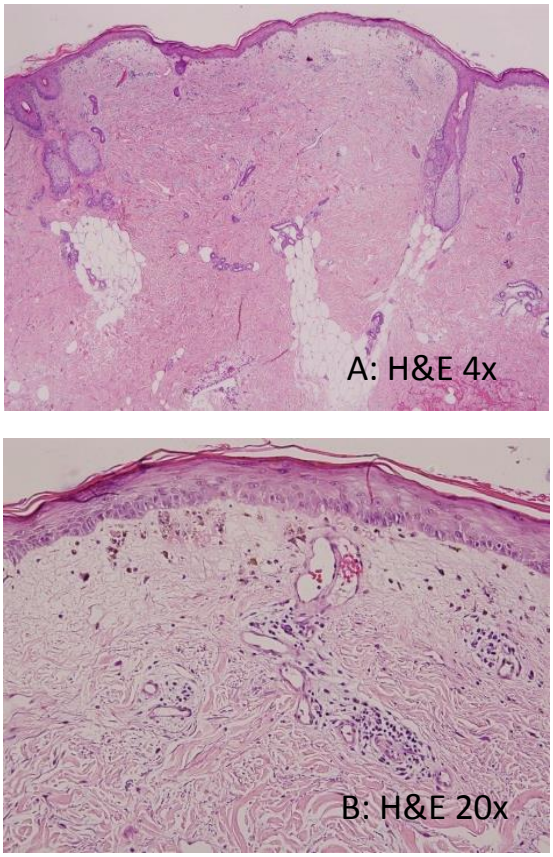

Figure 4 Histopathology of the skin lesion from right forearm showing multiple melanophages presenting in papillary dermis with lymphocytic infiltration around superficial vascular plexuses (H&E, A: x4, B: x20)

Discussion

The diagnosis of ADM in our patient was very challenging in the beginning as she presented with erythroderma. However, by using the diagnostic criteria of ADM proposed by Sontheimer, the final diagnosis could be made as our patient developed hallmark cutaneous manifestations of classic DM, all of her skin biopsies were compatible and there was no evidence of proximal muscle weakness for at least 6 months. The diagnosis was also confirmed by the detection of one of myositis-specific antibodies (MSA), anti-SAE 1. Erythroderma has been previously reported as an unusual cutaneous manifestation of DM[4]. More unusual cutaneous manifestations of the disease described in the literature are acquire ichthyosis, panniculitis, anasarca, facial swelling without erythema, lichen planus-like lesions, porcelain white atrophic scars, vesicle and bullae formation, follicular hyperkeratosis, hypertrichosis, malakoplakia, papular mucinosis, perforating skin ulcers, pityriasis rubra pilaris, pyoderma gangrenosum, urticaria, cutaneous vasculitis and centripetal flagellate erythema[4,5].

It is known that both adult-onset classic DM and ADM are associated with internal malignancy that could have occurred before, after, or at the time of skin disease onset[6]. In ADM, the malignancy risk has been variable across series, with a prevalence of 8-28%[7] comparing to that of 20-25% in patients with adult onset classic DM[1]. In erythrodermic DM, some cases were associated with internal malignancies i.e. gastric

cancer[8,9], pancreatic carcinoma[6], and hepatocellular carcinoma[5]. Several features of cutaneous manifestation of DM have been suggested to correlate positively with increased risk of malignancy including corticosteroid resistance, a bright vascular flush of the skin of shoulders, neck, face, and scalp, cutaneous ulceration, advanced age, normal serum creatinine kinase level, increased erythrocyte sedimentation rate, presence of cutaneous vasculitis and cutaneous necrosis[6,8]. Additional evidence is needed to confirm that erythroderma is a predictive factor for a malignancy in patients with DM[5]. Because our patient had extensive skin involvement that was steroid-resistant, malignancy screening is very crucial. As for the risk of developing interstitial lung disease (ILD), there is no statistical difference in the prevalence of ILD between ADM and classic DM groups[10]. However, both groups have an increased risk of ILD relative to the general population[10]

Myositis-specific antibodies (MSA) are helpful diagnostic tools in idiopathic inflammatory myopathies, especially for confirming the diagnosis and determining the prognosis (table 2)[11]. In our patient, the anti-SAE antibodies were positive. The antibodies have been exclusively detected in patients with DM[12]. The antibodies target SUMO-1 activating enzyme heterodimer, SAE1 and SAE2, of 40 and 90 kD, respectively[11,13]. These anti-small ubiquitin-like modifier activating enzyme (SAE) antibodies are found in 6-8% of adult DM Caucasian patients and only 2% in Asian patients, presenting with severe skin disease, dysphagia, mild muscular manifestation with favorable prognosis.[11,14] Anti-SAE antibodies might occur in patients who present with clinically ADM first, and then progress to develop myositis with a high frequency of systemic features including dysphagia and weight loss, but a low frequency of ILD and cancer[13]. This supports the clinical manifestation of our patient with weight loss and severe cutaneous finding without muscle involvement. However, our patient has no dysphagia.

Conclusion

Herein we report a case of erythrodermic ADM. Recognition of this subset of DM, especially its unusual clinical presentations, is imperative in order to early diagnosis and appropriately screen for internal malignancy. In addition, population-based studies of the epidemiology, evidence-based optimal treatment of patients with ADM and efforts to identify risk factors associated with poor prognosis such as malignancy and ILD are needed. Further investigation is also required to confirm the unique clinical characteristics of patients with positive anti-SAE antibodies, including potential utility as a prognostic marker in ADM patients.

Table 2 Myositis-specific antibodies (MSA): target antigens and clinical associations in adult myositis patients [11]

Autoantibody	Immune target	Function of autoantigen	Clinical associations
Anti-ARS (Jo-1, PL-7, PL-12, EJ, OJ, KS, Ha, Zo)	tRNA synthetase	Aminoacylation of tRNAs	PM, anti-synthetase syndrome
Anti-MI-2	NuRD subunit	Gene transcription, nucleosome remodeling	Classic DM, mild disease
Anti-TIF1-Υ	Transcriptional intermediary factor 1Υ	Ubiquitination, gene transcription	Severe DM, cancer-associated DM
Anti-NXP-2	Nuclear matrix protein 2	Gene transcription	Severe DM, cancer-associated DM
Anti-MDA5	Melanoma differentiation-associated protein 5	Innate antiviral response	ADM, ILD, poor prognosis
Anti-SAE	SUMO-1 activating enzyme	Protein sumoylation, gene transcription	DM, initially ADM
Anti-SRP	Signal recognition particle	Protein translocation across the ER	Necrotizing myopathy
Anti-HMGCR	3-Hydroxy-3-methylglutaryl-CoA reductase	Cholesterol biosynthesis	Necrotizing myopathy, prior statin use

ARS Aminoacyl-tRNA synthetases, *tRNAs* transfer RNAs, *PM* polymyositis, *NuRD* nucleosome remodeling-histone deacetylase, *DM* dermatomyositis, *ILD* interstitial lung disease, *SUMO-1* small ubiquitin-like modifier 1, *ER* rough endoplasmic reticulum

Statement of ethics

The authors have no ethical conflicts to disclose.

Disclosure statement

The authors declare no conflict of interest.

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