Mod Rheumatol (2011) 21:101–105
DOI 10.1007/s10165-010-0352-0

CASE REPORT

# A case of disseminated DLE complicated by atopic dermatitis and Sjögren's syndrome: link between hypohidrosis and skin manifestations

**Saki Matsui · Shun Kitaba · Saori Itoi · Akiko Kijima · Hiroyuki Murota · Mamori Tani · Ichiro Katayama**

Received: 1 June 2010 / Accepted: 11 August 2010 / Published online: 8 September 2010


**Abstract** We report an unusual case of disseminated discoid lupus erythematosus (DLE) complicated by pre-existing atopic dermatitis (AD) and late-onset Sjögren's syndrome (SS). Disseminated DLE lesions were sparse on the expected sites for AD, such as the medial region of the extremities or v-neck area. The patient fulfilled the diagnostic criteria for AD and SS but not for systemic lupus erythematosus. Histopathological analysis of the crusted erythematous lesions revealed typical DLE with few $FoxP3^+$ cells and a moderate number of $IL\text{-}17^+$ cells. A quantitative sweating test showed impaired sweating of both lesional and non-lesional skin due to underlying hypohidrosis that was related to AD and SS. This finding suggests that dissemination of DLE was triggered by scratching and a Köbner phenomenon-like effect related to hypohidrotic and xerotic skin. To the best of our knowledge, this is the first reported case of disseminated DLE complicated by AD and SS.

**Keywords** Discoid lupus erythematosus · Atopic dermatitis · Sjögren's syndrome · Hypohidrosis

## Introduction

We present the first report of an unusual case of disseminated (widespread) discoid lupus erythematosus (DLE) complicated by pre-existing atopic dermatitis (AD) and late-onset Sjögren's syndrome (SS). Overlapping cases of collagen diseases are not uncommon in clinical practice; however, AD is very rarely complicated by collagen diseases, possibly due to the predominance of a Th2 response in AD. Dissemination of DLE also is thought to be affected by SS via a Th1-dominant immune-privileged state. Furthermore, dissemination may be due to a Kobner phenomenon-like effect related to xerosis of the skin that is induced by impaired sweating characteristic of AD and SS.

S. Matsui · S. Kitaba · S. Itoi · A. Kijima · H. Murota · M. Tani · I. Katayama (✉)
Department of Dermatology Integrated Medicine, Graduate School of Medicine Osaka University, 2-2 Yamada-Oka, Suita, Osaka 565-0871, Japan
e-mail: katayama@derma.med.osaka-u.ac.jp

## Case report

A 31-year-old female with disseminated itchy, scaly erythematosus lesions presented to our outpatient clinic. She had been treated with topical glucocorticoids and antihistamines following the diagnosis of refractory AD 10 years earlier. The lesions were restricted to the face, neck, inter-scapular region, and interstitial aspect of extremities. She had no previous history of allergic asthma or pollenosis. Three years before the first consultation, she developed itchy, scaly lesions on the extensor sites of the trunk and extremities. She had not noticed photosensitivity, alopecia, or systemic symptoms such as fever or joint pain except xerostomia with decreased salivary flow. Family and past histories did not reveal any genetic association.

Upon physical examination, pea-sized brownish-violaceous erythematous lesions with a white lamellar scale/crust were observed to be distributed symmetrically over the whole body with extensor predominance (Fig. 1a). Reticular slate-colored mottled pigmentation and slight lichenified eczematous lesions were present on her neck and interstitial aspects of extremities (Fig. 1b, c) where violaceous erythemas were nearly absent. Diffuse erythematous scaly patches with crusted and papular eruptions

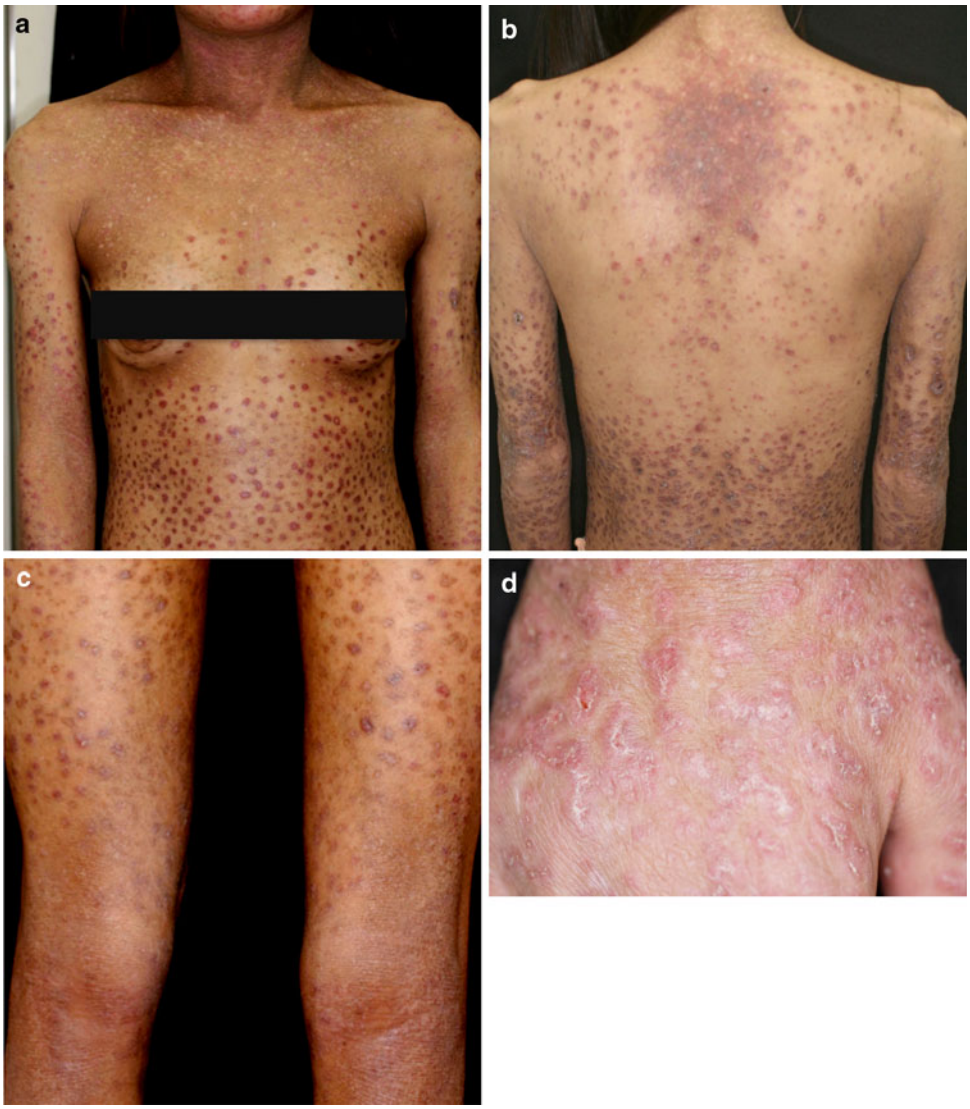


**Fig. 1** Clinical appearance of the patient. **a** Pea-sized brownish-violaceous erythema with white lamellar scale/crust distributed symmetrically over the whole body with extensor predominance. **b**, **c** Reticular slate-colored mottled pigmentation and slight lichenified eczematous lesions were present on her neck and interstitial aspects of the extremities where violaceous erythemas were nearly absent. **d** Diffuse erythematous scaly patches with crusted and papular eruptions were observed on her face, scalp, and dorsal aspect of the hands

were observed on the face, scalp, and dorsal aspect of the hands (Fig. 1d). Oral mucosa and the genital regions were devoid of any lesions.

Laboratory findings were as follows: white blood cells: 4.91 × $10^3$/μL; neutrophils: 54.5%; lymphocytes: 38.0%; monocytes: 1.1%; eosinophils: 6.1%; basophils: 0.3%; red blood cells: 4.09 × $10^6$/μL; platelets: 22.2 × $10^5$/μL; hemoglobin: 12.1 g/dL; hematocrit: 35.9%; blood urea nitrogen: 11 mg/dL; creatinine: 0.42 mg/dL; aspartate transaminase: 29 U/L; alanine transaminase: 27 U/L; γ-glutamyl transpeptidase: 16 U/L; LDH: 248 U/L; C-reactive protein: 0.05 mg/dL; immunoglobulin (Ig) G: 3795 mg/dL; IgA: 446 mg/dL; IgM: 169 mg/dL; serum interleukin-2R: 2103 U/ml; IgE: 24,800 IU/mL; Dog-dander-IgE-RAST: >100 IU/mL; dermatophagoides-IgE-RAST: >100 IU/mL; TARC: 1,532 pg/mL; ANAx80 anti-SSA (Ro): 62; anti-SS-B: 11.2; anti-Sm(−), anti-Gal(−)-IgG: 304: logC/mL; anti-CCP: >100 U/mL; anti-dsDNA: 3.9 IU/mL; CH50 (total hemolytic complement): 40.1 U/mL; MMP3: 45.7 ng/mL; rheumatoid factor: 628 IU/ml; urine protein (−).

Histopathological findings of biopsied specimens from the scaled erythematous lesions on the extensor aspect of the forearm revealed hyperkeratotic erythematous change with liquefactive degeneration, follicular plugging, pigment incontinence, and peri-appendageal lymphocytic infiltration compatible with DLE (Fig. 2a). Lymphocytic infiltration around the salivary gland (grade 2) (Fig. 2b) was found in the specimen obtained from a minor salivary gland, with positive salivary scintigraphy findings consistent with SS. Salivary (gum test; 9 ml/10 min) and lacrymal flow [Schirmer test; 5 mm (right)/5 mm (left)] were decreased; however, keratoconjunctivitis was not demonstrated. According to the proposed diagnostic criteria of SS in Japan [1], our patient satisfied two criteria: positive anti-SSA antibody and impaired salivary functions. Immunohistochemical analysis revealed marked infiltration of

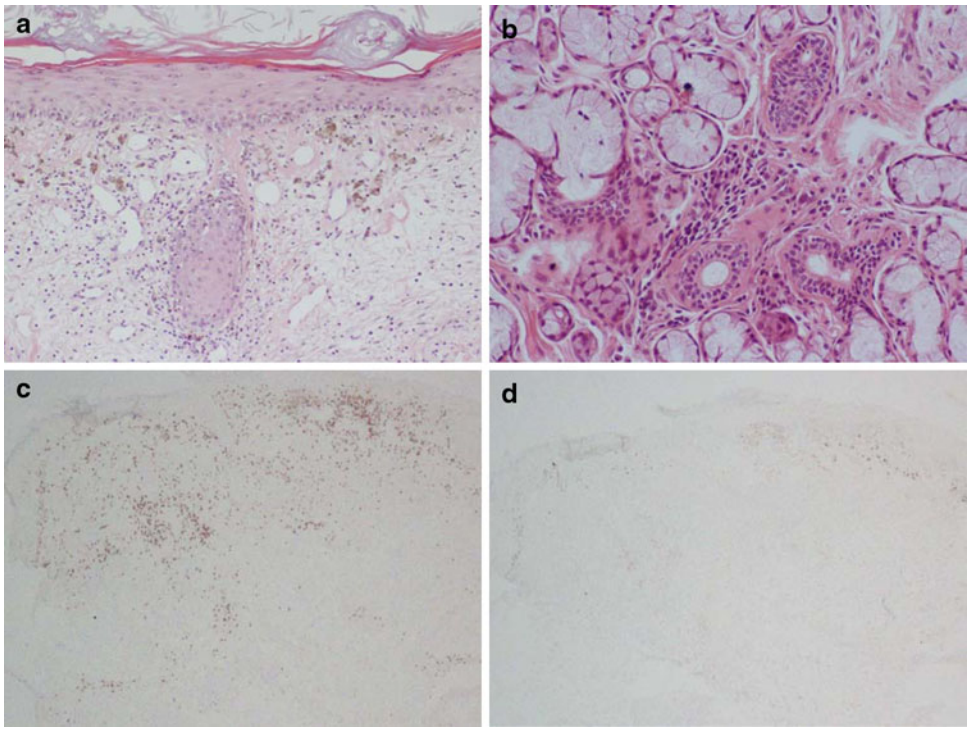


**Fig. 2** Histopathological findings. **a** Histopathological findings revealed hyperkeratotic erythematous change with liquefactive degeneration, follicular plugging, pigment incontinence, and peri-appendageal lymphocytic infiltration, all compatible with DLE. **b** Lymphocytic infiltration around the salivary gland was demonstrated in the specimen (obtained from a minor salivary gland), with positive salivary scintigraphy and decreased lacrymal flow, consistent with SS. **c** Immunohistochemical analysis for $CD8^+$ cells, **d** $CD4^+$ cells

$CD8^+$ cells compared to $CD4^+$ cells (Fig. 2c, d), and the number of infiltrating $FoxP3^+$ T-regulatory cells was low (Fig. 3a), which is consistent with chronic LE lesions reported by Kuhn et al. [2, 3]. In contrast, the number of Th17 cells (Fig. 3b) was increased among the infiltrating cells, which is consistent with recent reports of SS [4, 5]. Unfortunately, we could not obtain biopsies of the eczematous lesion of AD. Thus, the patient fulfilled the diagnostic criteria for AD and SS but not for systemic lupus erythematosus (SLE) [1, 6]. From these findings, we made a diagnosis of widespread DLE complicated with AD and SS.

We measured the sweating function in this patient according to a previously described method [7], which revealed that both direct and indirect sweating, induced by iontophoretically applied acetylcholine, were reduced, which is consistent with the pattern seen in SS, as previously reported (Fig. 4) [7].

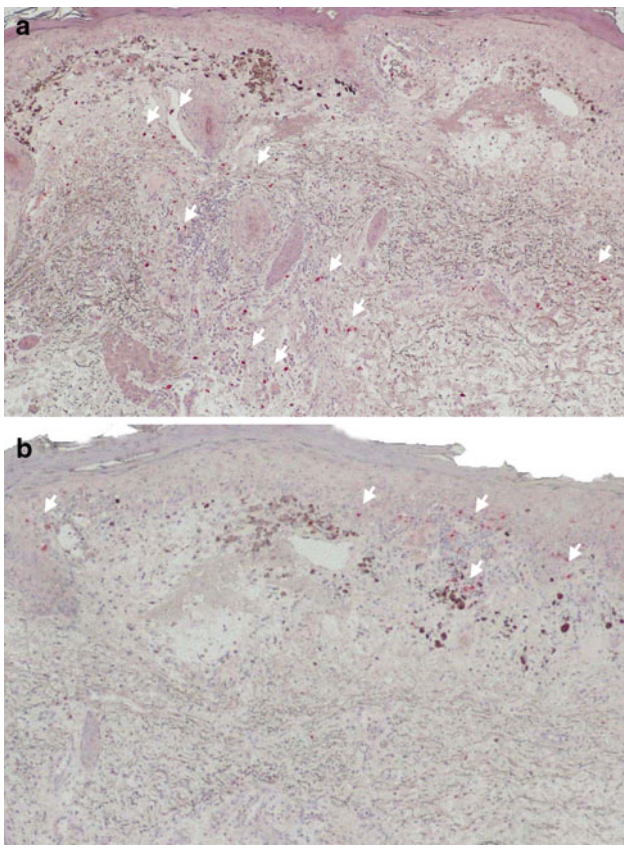


**Fig. 3** $FoxP3^+$ cells and interleukin (IL)-$17^+$ cells in the discoid lupus erythematosus (*DLE*) lesions. **a** Number of Th-17 cells was dominant among the infiltrating cells, **b** number of infiltrating $FoxP3^+$ regulatory cells were decreased

## Discussion

Discoid lupus erythematosus is usually classified as chronic cutaneous lupus erythematosus (CCLE) [8] and rarely complicated by other collagen diseases, with the exception of SLE [9, 10]. The case reported here may be the first documented case of disseminated DLE complicated with SS and AD.

Complications of AD and SLE are relatively, rare and very few case reports have been published [11, 12]

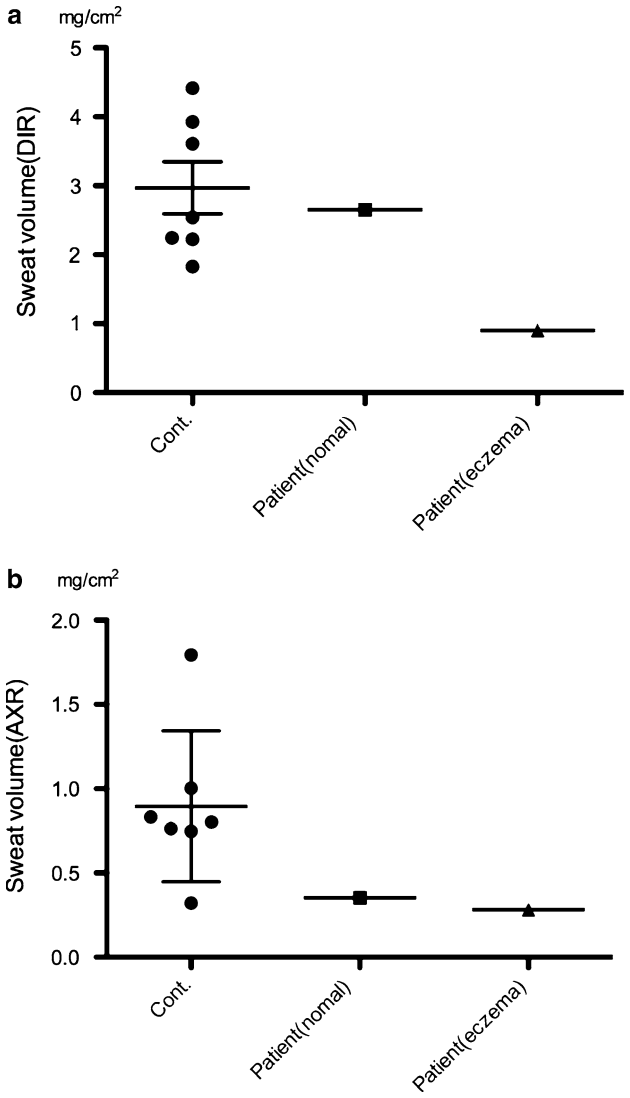


**Fig. 4** Quantitative sweating test. The quantitative sweating test was performed according to a previously described method [7]. Both direct and indirect sweating induced by iontophoretically applied acetylcholine were reduced, which is consistent with the pattern seen in Sjögren's syndrome, as previously reported. *DIR* Direct sweat volume, *AXR* axon reflex-mediated indirect sweat volume

although the prevalence of adult AD in Japan is 6.9% [13]. The Th1 and Th2 balance theory or the use of immunosuppressive drugs for SLE has been thought to be responsible for the rare complications of these allergic and systemic autoimmune diseases. Reports of AD and SS as co-morbidities are uncommon in the literature, although SLE is known to occasionally overlap with secondary SS [14].

We previously reported that the sweating function is impaired in patients with AD compared to normal controls as well as in patients with primary SS [7, 15]. In SS, sweating induced by both the direct action of acetylcholine and the axon reflex is impaired, possibly due to eccrine gland dysfunction resulting from autoimmune mechanisms mediated by CD8 T cells [16] or M3 receptor-specific autoantibodies [17], as previously described. In contrast to SS, the reduced sweating function seen in AD is restricted to axon reflex-induced indirect sweating only, which usually is restored to normal levels following improvement of the dermatitis [7]. Therefore, the xerotic skin lesions seen in our patient may have been evoked by AD and SS related-hypohidrosis, which is responsible for the dissemination of DLE.

Interestingly, disseminated DLE lesions were sparse in the areas predisposed to AD, such as antecubital and popliteal fossa or around the neck. The reason for this unique site-specific distribution pattern of DLE is not known at the present time. One possible explanation is the Th1/Th2 balance theory; i.e., AD is known as a typical Th2 cell-mediated allergic skin disease, while SS is considered to be a Th1 or Th17 cell-mediated autoimmune disease [4, 5]. It has been shown that $CD8^+$ T cells are the predominant infiltrating cell type in DLE, as also demonstrated in our case [18]. In support of this explanation is our observation that the number of infiltrating $FoxP3^+$ T cells, which are the counterpart of Th17 cells [2, 4], was reduced in the DLE lesions of our patient (Fig. 3a) compared to AD, respectively (manuscript in preparation).

The patient was treated with topical glucocorticoids and antihistamines after the diagnosis of AD and was subsequently diagnosed with acute dissemination of DLE. Therefore, we may conclude that the patient initially developed AD and underlying SS, which may have aggravated the xerotic eczematous skin lesions due to the sweating dysfunction. Dissemination of DLE is also thought to be affected by SS via a Th1-dominant immunoprivileged state.

**Conflict of interest** None.

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