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Atopic eczema complicated by systemic lupus erythematosus

We report two patients with atopic eczema (AE), who developed systemic lupus erythematosus (SLE). Case 1 was a 25-year-old man who developed SLE during treatment of AE in our department. He had a positive antinuclear antibody (ANA) (1:640), anti-ssDNA, anti-SSA and anti-RNP. Case 2 was a 27-year-old man who had a past history of AE. He developed SLE and had a positive ANA (1:320), anti-ssDNA, anti-dsDNA and anti-SSA. Among 33 patients with SLE in our department, four had suffered from AE (12%). There have been a few reports of AE complicated by SLE. Even if it is very rare, like case 1, that two morbid conditions, AE and SLE simultaneously exist in an individual, our findings suggest that it is necessary to measure various autoantibodies in ANA (+) patients with AE and to carefully monitor those patients for long-term development of SLE symptoms if other autoantibodies are positive.

Key words: allergy, antinuclear antibodies, atopic dermatitis, atopic eczema, autoimmunity, systemic lupus erythematosus

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Atopic diseases entail a hyperreactivity towards environmental antigens [1], whereas autoimmune diseases show hyperreactivity towards endogenous antigens. Therefore the two conditions could be mutually exclusive. So far there have only been a few case reports of patients displaying both atopic eczema (AE) and systemic lupus erythematosus (SLE). Both diseases express an enhanced Th2 cytokine profile [2]. Also, several autoantibodies have been detected in patients with AE [3, 4]. And 20 to 30% of AE patients show positive antinuclear antibodies (ANA) [5], but their significance is unclear. Recent reports have indicated that the incidence of AE in SLE is comparable to persons without SLE [6, 7]. Here, we present two patients with AE who developed SLE.

Case reports

Case 1

A 25-year-old man was admitted complaining of fever (37.5°C) and butterfly erythema (*figure 1A*). He had no active symptoms of AE at admission, but had suffered from mild to moderate AE since 5 years of age. His elder sister had also suffered from AE. He had been treated with topical steroids, moisturizing cream and oral anti-histamine in our outpatient clinic 3 years previously. Poikiloderma-like changes in his neck were observed as a clinical appearance of chronic AE. In addition he had Raynaud's phenomenon. Five years before admission he was found to have increased anti-RNP antibodies (> 500 U/ml), but was not diagnosed as having mixed connective tissue disease (MCTD). Three years before the present admission he was diagnosed with nephritic syndrome (membranous nephropathy, stage

II-III). On this admission, blood tests were normal except for increased lactate dehydrogenase (LDH) 648 IU/l (normal range 180-460 IU/l). Urinalysis revealed proteinuria (0.3 g/day). His immunological findings are summarized in *table 1*. A facial skin biopsy showed hyperkeratotic changes, follicular plugging, thinning of epidermis, slight degeneration of the basal layer, edema in upper dermis and a predominantly lymphocytic infiltration around hair follicles and appendages compatible with LE (*figure 1B*). The lupus band test revealed a moderate granular deposition of IgG, C3 in the dermis-epidermis junction. A new renal biopsy showed membranous nephropathy stage III. He was diagnosed as suffering from SLE, and steroid therapy (30 mg/day) [8] was effective in controlling his symptoms. His AE was treated with only moisturizing cream due to the treatment with systemic steroids.

Case 2

A 27-year-old man had suffered from mild AE since childhood. His elder brother had also AE. He was admitted complaining of facial edema and an acne-like eruption (*figure 2*) but without eczema. His past history besides AE was allergic rhinitis. Blood tests showed slight leukopenia, slightly elevated GOT, BUN and creatinine, increased total cholesterol and decreased total protein and albumin. Urinalysis revealed proteinuria (4.1 g/day), 50-99 erythrocytes, and 20-29 granular and hyaline casts per high-power field. The main immunological findings are summarized in *table 1*. A skin biopsy from a chilblain-like lesion showed changes compatible with LE. A renal biopsy showed lupus nephritis IV b. He was started on prednisolone 60 mg/day with much improvement.

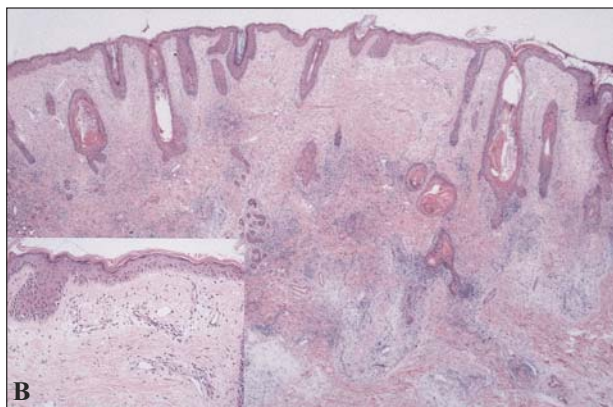


Figure 1. **A)** Clinical appearance of case 1, butterfly erythema on the face and poikiloderma-like changes in the neck were seen; **B)** representative histopathology of butterfly erythema from case 1 (H&E stain, original magnifications $\times 6.6$; $\times 40$).

Discussion

We present two patients with AE, who developed SLE. Case 1 fulfilled four of the revised American Rheumatism Association (ARA) criteria for SLE [8]. He had manifestations of MCTD, but did not strictly fulfill the criteria for a diagnosis of MCTD [9]. Case 2 satisfied five of the revised ARA criteria for SLE [8]. He was treated for AE in childhood. He had normal IgE, but a positive RAST to pollen.



Figure 2. Clinical appearance of case 2, acne-like malar erythema and facial edema were seen.

Histologically there was slight liquefaction degeneration of the basal layer of the epidermis and the lupus band test was positive in both cases. It is noteworthy that both were males, as 90% of patients with SLE are females. Interestingly, Case 1 developed SLE during treatment of mild AE in our department. Case 2 did not have any active symptoms of AE, but had a past history of AE.

Recently, Sekigawa *et al.* reported 2 cases of AE associated with MCTD-like immune abnormalities [10]. Although both cases had a high titer of anti-RNP Ab, they did not fulfill the criteria for a diagnosis of MCTD [9]. Only 4 patients with AE have been reported to develop SLE in conference abstracts in Japan. The 4 reported patients were female, unlike our cases. The reason why there are few case reports of AE with SLE is unknown. It is unlikely that two morbid conditions, AE and SLE, simultaneously exist in an individual. Another conceivable reason may be the difference of developmental age between AE and SLE. When a patient developed SLE, no symptom of AE was generally found, due to self-healing in AE, like our case 2. Thus we considered case 1 a very rare status.

Sekigawa reported that the incidence of AE was 6% in SLE patients, comparable to that in healthy control (15%) [7]. In accordance with this report, among 33 patients with SLE in our department, four had suffered from AE (12.1%). There was only 1 case who developed SLE during treatment of

active symptoms of AE. Thus we reconsidered case 1 as a very rare patient, because Morton and Sekigawa referred the past history of AE in SLE.

Several autoantibodies have been detected in patients with AE [3, 4]. Between 20 to 30 % of AE patients have ANA ranging in titer between 1:40 and 1:1280 [5]. Nineteen percent of patients with AE in our department had positive ANA (range 1:40 to 1:640). We do not know whether ANA (+) patients with AE will develop autoimmune disease or not. Case 1 had a high titer of anti-RNP Ab before development of SLE. Thus it is necessary to measure various autoantibodies in ANA (+) patients with AE and to carefully monitor those AE patients for a long period for development of SLE symptoms, if other autoantibodies are positive in ANA (+) patients with AE.

Becker described a relationship between AE and other autoimmune disease such as SLE, Crohn's disease and rheumatoid arthritis, as there is an overlap of autoimmune/inflammatory loci on 1p22.3-p22.1 (TGF- β RIII), on 3q21-q22.2 (CD80, CD86) and on 19p13 suggesting that underlying genetic components may not be disease or tissue specific, but may share basic mechanisms of immune regulation [11].

Further investigations should clarify the relationship between AE and SLE and thus contribute to reveal pathophysiological features of AE and SLE. ■

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