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CORRESPONDENCE

A case of pregabalin-induced drug eruptions accompanied by extremely high serum thymus and activation-regulated chemokine levels

Thymus and activation-regulated chemokine (TARC/CCL17) is produced by monocyte-derived dendritic cells and vascular endothelial cells and functions as a selective chemoattractant of type 2 helper T (Th2) cells. Serum TARC levels are elevated in patients with atopic dermatitis[1] and drug-induced hypersensitivity syndrome (DIHS)[2] and reflect disease activity. However, patients with these diseases rarely exhibit serum TARC levels of >100,000 pg/mL.[1,3] We report a case of non-DIHS drug eruption caused by pregabalin, in which the peak serum TARC level was >100,000 pg/mL.

A 78-year-old Japanese female had severely itchy eruptions on her back in May 2017 and soon developed eruptions on her trunk and extremities without any systemic involvement. She had suffered from eosinophilic granulomatosis with polyangiitis (EGPA) for

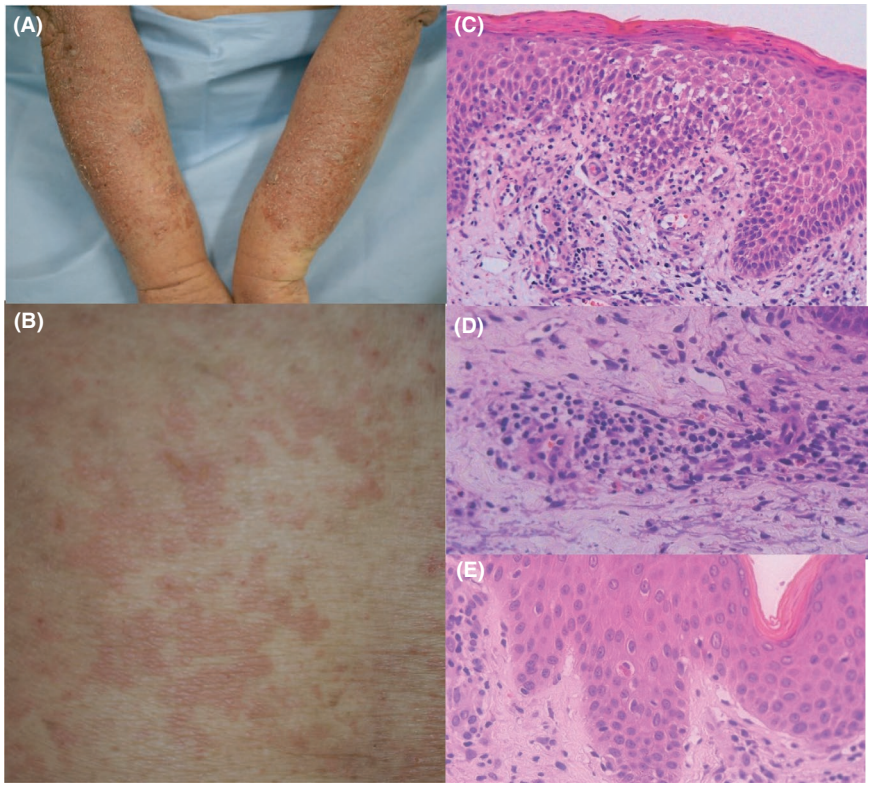

FIGURE 1 Clinical and histopathological manifestations. The clinical findings of (A) an eczematous lesion on the patient's forearm and (B) an erythema multiforme-like lesion on her back are shown. A histopathological examination of a sample taken from her forearm revealed acanthosis, hyperkeratosis, parakeratosis, and spongiosis in the epidermis (C), and perivascular lymphocytic and eosinophilic infiltration in the upper dermis (D). A specimen from her back contained necrotic keratinocytes (E)

9 years and was taking 10 oral medicines, including 5 mg prednisolone and 75 mg pregabalin for the neuralgia on her legs, daily. She did not have atopic dermatitis or other allergies. A physical examination performed at her first visit in August revealed infiltrative eczematous lesions on her chest and extremities and erythema multiforme (EM)-like lesions on her abdomen and back (Figure 1A,B). Her laboratory data were as follows: WBC: 10,360/μL (eosinophil count: 1388.2/μL), platelet: 40.3 × 10^4/μL, AST: 31 U/L, ALT: 28 U/L, LDH: 592 U/L, CRP: 0.63 mg/dL, serum IgE level: 8390 IU/mL, serum TARC level: 94,040 pg/mL, MPO-ANCA level: <1.0 EU. Neither test for anti-human herpesvirus 6 antibody nor lymphocyte stimulation tests (LST) for drugs were performed. A skin biopsy examination of an eczematous lesion on her forearm revealed acanthosis, hyperkeratosis, parakeratosis, and spongiosis, and a specimen taken from an EM-like lesion on her back contained necrotic keratinocytes in the epidermis. Both specimens showed perivascular lymphocytic and eosinophilic infiltration in the upper dermis (Figure 1C, D, and E).

Treatment began with a very-strong-class steroid ointment; however, the patient's skin rash worsened, and her serum TARC level increased to 105,200 pg/mL. The prednisolone dose was then increased to 30 mg/day, and other medicines were discontinued, which was markedly effective against her lesions and reduced her serum TARC level to 46,430 pg/mL. The prednisolone dose was slowly tapered to 7 mg/day over 2 years, which resulted in the following findings: serum IgE level: 1400 IU/mL, TARC level: 2561 pg/mL, and LST for pregabalin: 265%. We finally diagnosed the patient with pregabalin-induced drug eruptions. She had taken pregabalin for 4 years, and eosinophil count before taking the medicine was 160.4/μL.

Drug eruptions induced by pregabalin are rare, and we only found 5 other cases reported in English,[4,5] one of which only showed eosinophilia. The patient's serum TARC and IgE levels were extremely high during her condition and did not normalize even after she was successfully treated. This might have been because her underlying disease, EGPA, is considered to involve activation of the Th2 pathway.[6,7] DIHS was ruled out because she only met one of the seven diagnostic criteria established by a Japanese consensus group.[8] Clinicians should be aware non-DIHS drug eruptions can produce peak serum TARC levels of >100,000 pg/mL.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed Consent: The written informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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