A case of toxic epidermal necrolysis-like dermatitis evolving from contact dermatitis of the hands associated with exposure to dendrimers

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Erythema multiforme-like contact dermatitis is rare but could occur because of various allergens (1). Here, we describe a case of erythema multiforme-like contact dermatitis speculatively because of dendrimers, which are novel materials for drug delivery system or nanotechnology. Notably, the lesions converted to toxic epidermal necrolysis (TEN)-like dermatitis.

Case Report

A 22-year-male student was well and took no medications. In June 2006, the student started experiments handling various chemicals such as acrylonitrile, triethylamine, tetrahydrofuran, thionyl chloride, carbonic acids, amines, and some catalytic metals including cobalt and palladium to synthesize very complex compounds called dendrimers whose molecular weight were more than 20 kDa with a number of surface functional groups.

On 7 July, he noticed a rash on his hands, predominantly on the right hand. He was treated with oral predonisolone and topical glucocorticoid ointment by a dermatologist. He stopped his experimental work, but the rash and blister worsened again after withdrawal of oral prednisolone.

He consulted our hospital on 14 July. He had erythematous lesions on his hands varying from 0.5–1 cm, predominantly on the right hand (data not shown). Most of the plaques had a target-like appearance. The skin biopsy sample showed mononuclear cell infiltration at perivascular and subepidermal areas and confluent epidermal necrosis with partial eosinophilic degeneration. He was diagnosed as having erythema multiforme-like contact dermatitis and topical steroids and anti-histamine agents were prescribed. But on 17 July, he developed fever up to 38° C. Oral predonisolone was restarted, but the lesions progressed.

He was admitted to hospital on 21 July. Diffuse exudative erythema and bullae were present on his forearms, together with a burning sensation and pain. The rash and erosive blisters were also observed over his entire body except the face (Fig. 1). The bullae fused and displayed Nikolsky sign. The inguinal area was also erythematous but he showed no sign of mucosal involvement. His eyes were not affected. Biochemical investigation indicated almost normal data, including no signs of inflammation, infection, or autoimmune diseases except that the

Fig. 1. Erythematous lesions and flaccid bullae on the dorsal trunk (a) and the magnified image of the bulla on the lumbar area (b) at hospitalization. The hands (c) and the close-up of the bulla (d) were also shown.

titre of serum complement and C3 were extremely low.

He was diagnosed as having a TEN-like dermatitis and immediately received 1000 mg/day of methylprednisolone intravenously for 3 days because his symptoms could not be controlled by oral predonisolone. The treatment was followed by oral administration with 40 mg/day of predonisolone, which was tapered gradually. His skin lesions improved after the medication, and he was finally discharged on 16 August with 15 mg/day of oral predonisolone.

However, he complained of frequent relapse of exudative erythema on his right hand each time he entered his office near the laboratory. Interestingly, the recurrences coincided with the cleaning of his laboratory, with possible contact with hazardous materials. The rash again showed target-like lesions, but the rash was successfully treated with a temporarily increased dose of prednisolone. We carried out drug lymphocyte stimulation test for candidate compounds including acrylonitrile, triethylamine, and tetrahydrofuran, but the results were negative for all chemicals. The patient has not yet had a patch test because of the potential risk of recurrence.

Discussion

Dendrimers belong to a class of polymers consisting of a central core, interior branches, and terminal groups with various functions (2). Recently, they have attracted considerable attention because of their unique features such as well-defined globular structures, uniformity, low polydispersity, and various potential functions due to their terminal groups. They are able to mimic biological molecules such as proteins and lipids because of their amphiphilic properties, hydrophibic cores and hydrophilic surface layer. The patient had been performing extremely complex reactions to synthesize such complex molecules, so the variety of intermediate and final products including gaseous materials is high. Identification of causative factor(s) would be quite difficult even if a patch test preparations were available.

Dendrimers may be novel drug-carrier alternatives to improve water solubility of drugs, permeability to cells, and site specificity, simultaneously decreasing toxicity and protecting the molecules from enzymatic degradation or hydrolysis. For example, covalent dendrimer–ibuprofen conjugates showed a significant inhibition of prostaglandin release after 30-min incubation of lung epithelial cells, while free ibuprofen did not inhibit until 1 hr (3). However, rapid distribution to tissues also might perturb the immune system more aggressively. Many efforts have focused on the development of dendrimers as drug-carrier systems, and several of these compounds have progressed into Phase I and Phase II clinical trials (4). In our case, dendrimers are one potential cause of many possible agents. The possibility of skin rashes to dendrimers should be considered in those exposed to them.

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