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SHORT COMMUNICATION

Photoallergic Drug Eruption Caused by Certolizumab Pegol

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Certolizumab pegol is a novel tumour necrosis factor (TNF) inhibitor, comprising a humanized Fab antigen-binding fragment fused to a 40-kDa polyethylene glycol (PEG) moiety (1). This unique structure avoids the potential Fc-mediated effects seen *in vitro*, such as complement-dependent or antibody-dependent cell-mediated cytotoxicity or apoptosis (2). Certolizumab pegol is used to treat autoimmune diseases, such as Crohn's disease and rheumatoid arthritis, and exhibits strong anti-inflammatory effects. Although diarrhoea and vomiting have been reported as adverse events of treatment with certolizumab pegol, there have been few case reports of cutaneous side-effects, such as psoriasiform drug eruption (3). We report here the first case of photoallergy caused by certolizumab pegol.

CASE REPORT

A 58-year-old woman, who had had rheumatoid arthritis for 5 years, was referred to our department for evaluation of her eruption. Physical examination revealed erythematous eruption on her V-neck zone (Fig. 1A), face and forearm, sparing submental and post-auricular areas, which had developed one day after the first intravenous injection of certolizumab pegol (400 mg) for her rheumatoid arthritis. Small serous papules, 2–5 mm in diameter, scattered on her neck and face was also observed. She was not taking any other medication; however, she had been treated with other TNF inhibitor, inflixiamb 230 mg,c for several months.

Laboratory and biochemical examinations were within normal ranges. At the first visit, a skin biopsy specimen taken from an erythematous lesion on her neck revealed a lymphocytic infiltrate in the upper dermis and around small vessels (Fig. 1B). Spongiosis was also observed in the epidermis.

Based on the clinical course, we suspected her skin eruption to be a photoallergic drug eruption caused by certolizumab pegol. To examine this possibility, we performed a photo-lymphocyte stimulation test (LST) with certolizumab pegol, as described previously with some modification (4–6). To examine the photohaptenic ability of this TNF inhibitor, peripheral blood mononuclear cells (PBMCs) were incubated with certolizumab pegol for 1 h and subsequently irradiated with ultraviolet A (UVA), 1 J/cm^2, as described previously. Cells were then cultured for 72 h. To examine the prohaptenic ability, which is converted to the complete hapten by

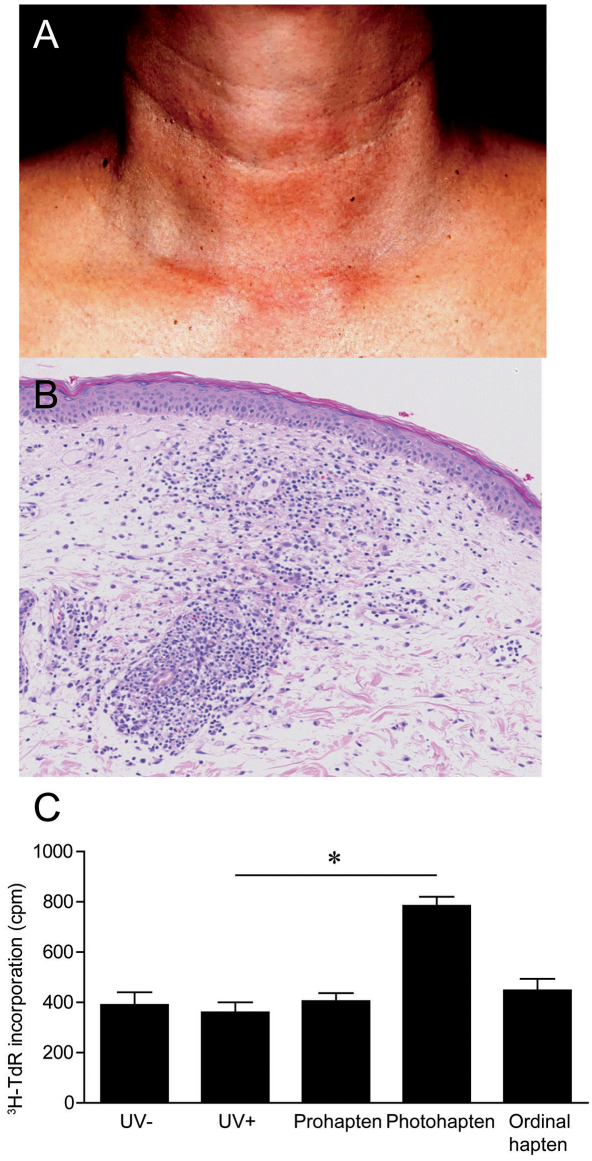

Fig. 1. (A) Clinical manifestation showing erythema on the patient's neck. (B) Histopathology of the skin showing lymphocyte infiltration in the upper dermis and around vessels. (C) Photo lymphocyte transformation test showing an elevation of ^{3}H-thymidine (TdR) incorporation in response to photohapten (certolizumab pegol) added to the 72-h culture of the patient's peripheral blood mononuclear cells. Results are presented as the mean ± standard error of the mean. *p*-value was obtained by Student's *t*-test. *$p < 0.05$.

UV irradiation, of certolizumab pegol, the certolizumab pegol was pre-irradiated with UVA, 1 J/cm^2, and then added to PBMCs, and the culture maintained for 72 h. To examine the ordinary haptenic ability, which means the hapten without UV irradiation, non-irradiated certolizumab pegol was added to PBMCs and the culture maintained for 72 h without UVA exposure. Among these groups, ^{3}H-thymidine incorporation was significantly increased only by photohaptenic stimulation of 5.1×10^{-7} M certolizumab pegol (corresponding to Cmax) to the peripheral lymphocyte culture with stimulation index of 2.2 (compared with UV-stimulated PBMC without certolizumab pegol) (Fig. 1C), whereas prohaptenic stimulation showed no effect. Because it has been reported that other TNF inhibitors have no influence on UV response in patients with rheumatoid arthritis (7), it is assumed that a photohaptenic response might have exacerbated the drug eruption in this patient.

Based on the clinical course and laboratory examination, the rash was diagnosed as a photo-allergic dermatitis due to certolizumab pegol. The patient was treated with topical betamethasone butyrate propionate ointment with discontinuation of certolizumab pegol. Her eruption improved remarkably within a week after the treatment.

DISCUSSION

Although photoallergic drug eruption is caused by various drugs, especially quinolone (8, 9), this is the first reported case of photoallergic drug eruption caused by certolizumab pegol. In the pathogenesis of photohaptenic drug eruption, epidermal cells are irradiated with UVA in the presence of photoallergic drugs, and then the photoadducts are formed in the treated cells. This photomodification is thought to be an initial step for sensitization and elicitation of this photoallergy (10). Although photoallergic drug eruption caused by other biologics, such as vemuvafenib, has been reported (11), to our knowledge this is the first case report of photoallergic drug eruption due to any anti-TNF inhibitors. It should therefore be kept in mind that cutaneous adverse events can occur after TNF inhibitor treatment.

The authors declare no conflicts of interest.

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