CD30-positive Cutaneous Pseudolymphoma Caused by Tocilizumab in a Patient with Rheumatoid Arthritis: Case Report and Literature Review

Akiha Inoue, Yu Sawada*, Shun Ohmori, Daisuke Omoto, Sanehito Haruyama, Manabu Yoshioka, Daisuke Nishio and Moto-nobu Nakamura
Department of Dermatology, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan. *E-mail: long-ago@med.ueh-u.ac.jp
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Tocilizumab is a biological disease-modifying anti-rheumatic drug (DMARD) that targets interleukin 6 (IL-6) receptor, blocking IL-6 signalling (1). Tocilizumab has shown efficacy in the treatment of rheumatoid arthritis (2); however, it sometimes induces cutaneous adverse reactions. We report here a case of pseudolymphoma caused by tocilizumab, manifesting as an unusual cutaneous eruption. We also review the literature concerning drug eruption caused by tocilizumab, and pseudolymphoma caused by biologics in general.

CASE REPORT

A 68-year-old woman was referred to our department for evaluation of an eruption on her face and trunk. She had developed palpable papules and erythema 7 days after the fifth administration of tocilizumab for her rheumatoid arthritis. Physical examination revealed erythematous solid papules on her face (Fig. 1A) and trunk. Biochemical profiling revealed an elevated γ-GTP level (41 U/l; normal <32 U/l). At the first visit, a skin biopsy from a papular lesion revealed a massive infiltration of lymphocytes, some of which had large nuclei with prominent nucleoli in the upper and middle dermis (Fig. 1B). The infiltrates were intermingled with eosinophils. Immunohistochemical study of infiltrating cells showed that CD4+ cells were dominant and, notably, large atypical cells expressed CD30 (Fig. 1C). However, Southern blot analysis demonstrated no clonal T-cell receptor (TCR)-Cbβ1 gene rearrangement in a skin sample. The eruption was diagnosed as CD30+ pseudolymphoma, possibly due to tocilizumab. To clarify the causative drug, a lymphocyte stimulation test (LST) with tocilizumab was performed, as described previously (3). 3H-thymidine incorporation was significantly increased by the addition of 8.7×10−7 M tocilizumab (corresponding to Cmax) to the peripheral lymphocyte culture, with a stimulation index of 2.1 (Fig. 1D). Based on the clinical course and laboratory examination, the rash was diagnosed as CD30+ pseudolymphoma due to tocilizumab. The patient was treated with topical betamethasone butyrate propionate ointment and tocilizumab was discontinued. Her eruption gradually improved over a period of 2 months.

DISCUSSION

Several cases of drug eruptions due to tocilizumab have been reported previously. We reviewed the literature in English and in Japanese and found 7 case reports describing drug eruptions due to tocilizumab (4–10). Seven out of 8 patients were female. The mean interval between the last drug intake and the appearance of drug eruption is relatively short (3.6 days). Interestingly, 2 cases developed after the first administration of tocilizumab. Clinical manifestations were as follows; maculopapular (2 cases), skin ulcer (1 case), psoriasis-form eruption (1 case), pustules (1 case), toxicoderma (1 case), and pseudolymphoma (our patient). Furthermore, to our knowledge, this is the first report of pseu-
dolymphoma caused by tocilizumab. Pseudolymphoma can be caused by a variety of medicines. Although the detailed mechanism of pseudolymphoma remains unclear, disturbance of cytokine balance might contribute to the pathogenesis of pseudolymphomatous drug eruption. Indeed, other types of biologics, anti-tumour necrosis factor (TNF)-α drugs, have been reported to cause pseudolymphoma (11–13); there have been 4 reported cases including our case. The mean interval between first administration of TNF-α and appearance of pseudolymphoma is longer (mean 218.8 days) than that of non-biologic drugs (14).

In conclusion, it should be kept in mind that pseudolymphoma can occur after treatment with tocilizumab. Further investigation is necessary to clarify the exact pathogenesis of drug-induced pseudolymphoma.

REFERENCES