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CORRESPONDENCE

Urticarial drug eruption following tocilizumab administration

Interleukin 6 (IL-6) plays a vital role in the pathogenesis of various inflammatory diseases, especially rheumatoid arthritis.[1] Tocilizumab is a humanized anti-IL-6 receptor antibody that exerts its immunosuppressive effect by blocking IL-6 receptor-mediated signal transduction[23] and shows therapeutic anti-inflammatory action in autoimmune diseases. On the contrary, several cutaneous adverse reactions have been reported in patients treated with tocilizumab administration.[4] Herein, we report a case of urticarial drug eruption following tocilizumab administration.

A 50-year-old woman had developed rheumatoid arthritis 5 years ago and was treated with methotrexate and certolizumab. She had no history of urticaria. Because her arthritis was intractable by these treatments, tocilizumab was administrated. One month after the repeated tocilizumab administration, she recognized urticarial eruption in trunk and extremities after the second-time administration of tocilizumab (Figure 1). Her eruption occurred in several hours and disappeared within 24 h after the tocilizumab administration. Her eruption continued to repeat the occurrence of urticaria following repeated tocilizumab administration. Blood examination showed that eosinophil frequency in peripheral blood (11.9%) and IgE-RAST (443 U/ml) were elevated, while the white blood cell count (6,000/μl) and CRP (0.04 mg/dl) were within normal ranges. Although an anti-histamine agent showed less response to her eruption, her urticaria completely diminished after switching into certolizumab without the recurrence of her eruption. Tocilizumab was administrated in total 12 times before switching into certolizumab. Because her urticaria was reproducible following every tocilizumab administration recognized as a positive reaction to challenge test, we diagnosed her skin eruption as urticaria following tocilizumab administration.

Tocilizumab shows various cutaneous adverse reactions, and the majority of these cases are type IV delayed hypersensitivity reactions. However, this case showed an unusual clinical manifestation of type I allergic reaction. As a reason to cause urticarial eruption, we thought there were several possibilities. The first one is an immune response to additives in this drug. Tocilizumab contains polysorbate 80, which is a synthetic nonionic surfactant and is used in various medications. Polysorbate 80 is also known as one of the representative agents to cause type I allergic reactions.[5] Indeed, polysorbate 80 containing medication induces urticaria.[6] Although allergic skin test could be conducted in our case, it should be kept in mind a possibility to cause the same skin eruption following polysorbate 80 containing biologic agents.

The second one is a pharmacological effect of tocilizumab mediated by the IL-6 blocking pathway. However, IL-6 increases in various types of urticaria,[7] suggesting that a pharmacological effect of tocilizumab mediated by the IL-6 blocking pathway might not contribute to the development of urticaria. As another possibility, tocilizumab might become a trigger to produce tocilizumab-specific anti-IgE production and contribute to the development of urticaria. Since there is no case report of urticaria responding to biologics itself, a further case study is expected to conclude the possibility.

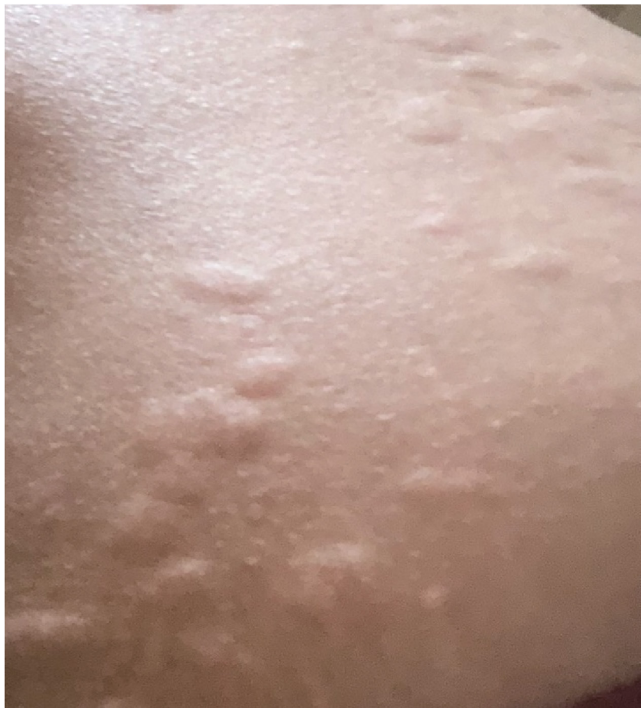

FIGURE 1 Clinical manifestation showed itchy wheals on her trunk

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DECLARATION SECTION

Approval of the research protocol: No.
Informed Consent: N/A.
Registry and the Registration: N/A.
Animal Studies: N/A.

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