Dermatology Practical & Conceptual

Tocilizumab-Induced Sweet Syndrome in a Familial Mediterranean Fever Patient: A Case Report

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Introduction

Sweet syndrome is a rare neutrophilic dermatosis characterized by painful, edematous, and erythematous papules, plaques, or nodules. The disease can be categorized into three main groups: classical Sweet syndrome, malignancy-related Sweet syndrome, and drug-related Sweet syndrome. Although the cause of the disease is not fully known in most cases, infections, malignancies, drugs, and inflammatory diseases can be triggering factors. Drug-related Sweet syndrome is a rare subtype of Sweet syndrome and was first described in the literature after the use of trimethoprim/sulfamethoxazole. Over time, drug-related Sweet syndrome cases induced by antibiotics, antivirals, antineoplastics, retinoids, and granulocyte colony-stimulating factor (G-CSF) have been reported. Drug-related Sweet syndrome usually develops within two weeks after initial exposure, and recurrence may be observed with repeated exposure [1].

In this case report, we present a male patient who was followed up with familial Mediterranean fever (FMF) and developed Sweet syndrome secondary to the use of tocilizumab.

Case Presentation

A 33-year-old male patient presented at our clinic due to painful lesions and fever. His past medical history revealed FMF, renal amyloidosis, and hypertension, and he was taking tocilizumab, anakinra, colchicine, and nifedipine treatments. He described that tocilizumab was started three months prior for FMF. Three days after tocilizumab administration, painful lesions had developed on the legs accompanied by a fever exceeding 38° C, and his complaints recurred with the following drug administrations. On dermatological examination, erythematous papules and nodules on the legs were observed (Figure 1). Laboratory evaluation revealed

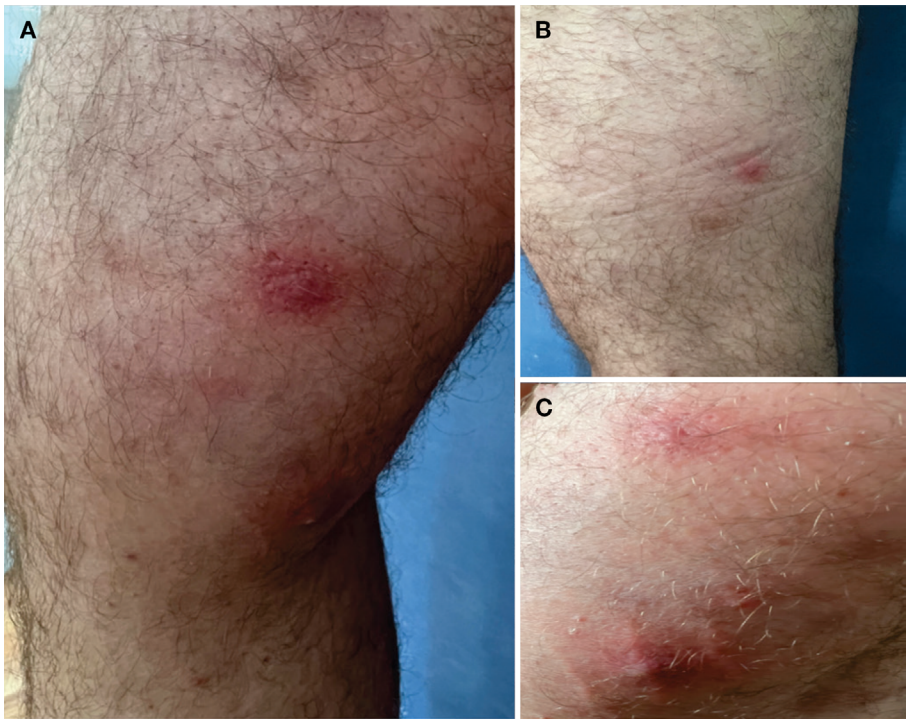

Figure 1. (A, B, C) Erythematous papules and nodules on the legs.

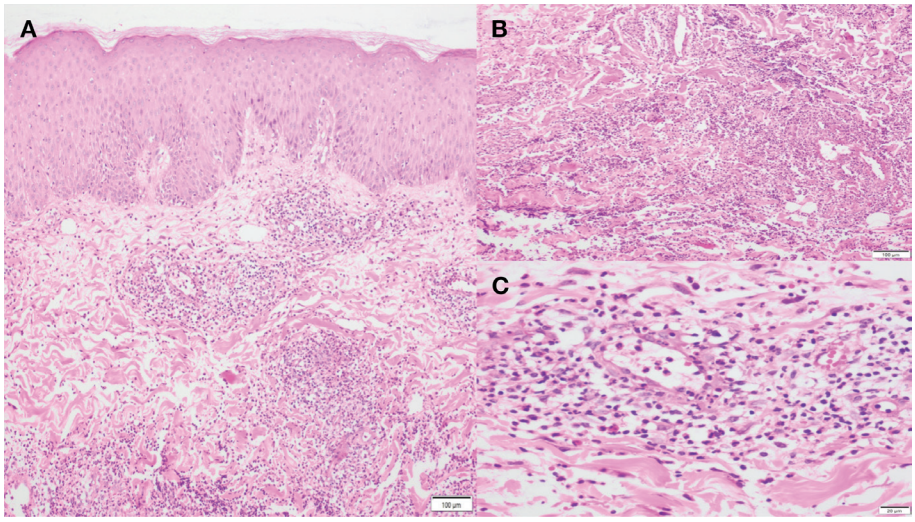

Figure 2. (A, B, C) Spongiosis, and neutrophil accumulation in the epidermis, perivascular-periadnexal neutrophil-dominated mixed-type inflammation in the dermis (H&E, x40, x100, x100).

leukocytosis, neutrophilia, and elevated acute phase reactants. Histopathological examination of the punch biopsy from the erythematous nodule showed spongiosis and neutrophil accumulation in the epidermis, perivascular-periadnexal mixed-type inflammation dominated with neutrophils in the dermis (Figure 2). Based on clinical examination and histopathological findings, the patient was diagnosed with Sweet syndrome. Following the discontinuation of tocilizumab and topical steroid treatment, regression of the lesions was observed. When the Naranjo Adverse Reaction Probability Scale calculated for tocilizumab was 7 (5–8: possible), and the patient met all diagnostic criteria for drug-related Sweet syndrome, it was accepted Sweet syndrome had developed secondary to tocilizumab.

Conclusion

Increased cytokines such as IL-1, IL-6, IL-8, and G-CSF have a role in the pathogenesis of Sweet syndrome, and successful treatment of cases with the inhibition of cytokines supports

Table 1. Diagnostic criteria for the diagnosis of drug-related Sweet syndrome

Drug Induced Sweet Syndrome	Our Case
Sudden onset of painful erythematous plaque or nodule	+
Dense neutrophilic infiltration without signs of leukocytoclastic vasculitis in the histopathological examination	+
Fever above 38 °C	+
Temporal relationship between drug intake and clinical findings	+
Regression of lesions with discontinuation of the drug or systemic steroid treatment	+

this role [1-4]. However, in the literature, paradoxically developed Sweet syndrome cases have been reported with treatment agents that inhibit these cytokines [5]. The development of Sweet syndrome in our patient after the use of tocilizumab, an inhibitor of IL-6, which is involved in the pathogenesis of Sweet syndrome, brings to mind the idea that this may be a paradoxical reaction.

Tocilizumab is a recombinant human monoclonal antibody developed against the IL-6 receptor and is used to treat various diseases such as rheumatoid arthritis, polymyalgia rheumatica, and temporal arteritis. Filippi et al. observed a Sweet syndrome in a polymyalgia rheumatica patient after tocilizumab treatment [6].

Our aim in presenting this case is to raise awareness about the cutaneous side effects of tocilizumab and to emphasize the clinical features of drug-related Sweet syndrome.

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