

**POSTHERPETIC ORAL ULCERS MISDIAGNOSED AS PEMPHIGUS IN A PATIENT WITH RHEUMATOID ARTHRITIS UNDER BUCILLAMINE THERAPY**

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None

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**Abstract**

Autoimmune bullous disease is sometimes seen in patients with rheumatoid arthritis (RA). In addition, pemphigus can be induced by certain disease modifying anti-rheumatic drugs (DMARDs) for RA, such as thiol compounds. Antibodies against desmogleins are occasionally detected in the sera of drug-induced pemphigus patients. We herein describe a case which showed ulceration following herpes zoster in the oral cavity of a patient with RA under treatment with bucillamine. The patient was misdiagnosed with pemphigus in another clinic, because of mucous membrane lesions and positive circulating levels of anti-desmoglein-1 IgG. Clinicians should know that circulating antibodies against desmogleins can be detected, although at low titers, in the sera of patients under therapies with certain drugs.

**Key words:** rheumatoid arthritis; bucillamine; pemphigus; desmoglein-1**Cite this article:**

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**Introduction**

Drug-induced pemphigus is well known, with thiol compounds and amide containing drugs being the most common causative drugs. Circulating antibodies against desmoglein-1 are occasionally detected in the sera of patients with drug-induced pemphigus. On the other hand, thiol compounds induce the production of anti-desmoglein antibodies in the sera, even if the skin and mucous membrane lesions are absent. Herein, we report a case of rheumatoid arthritis (RA) under therapy with bucillamine, a thiol compound, which was misdiagnosed as pemphigus due to the presence of oral ulcers and serum anti-desmoglein-1 levels.

**Case Report**

A 66-year-old female was suffering from RA for 20 years. She had been treated with oral bucillamine (200mg per day) for 5 years. One month prior to the initial visit to our department, painful vesicles and erythematous lesions appeared on the right side of her face. She presented to a nearby dermatology clinic, where she was diagnosed with herpes zoster and prescribed oral anti-viral tablets (Valaciclovir 3000mg per day for 7 days). Thereafter, she visited the dental department complaining of painful ulcers in the upper hard palate. After examination, she was referred to our department under suspicion of pemphigus, because she was positive for anti-desmoglein-1. On physical

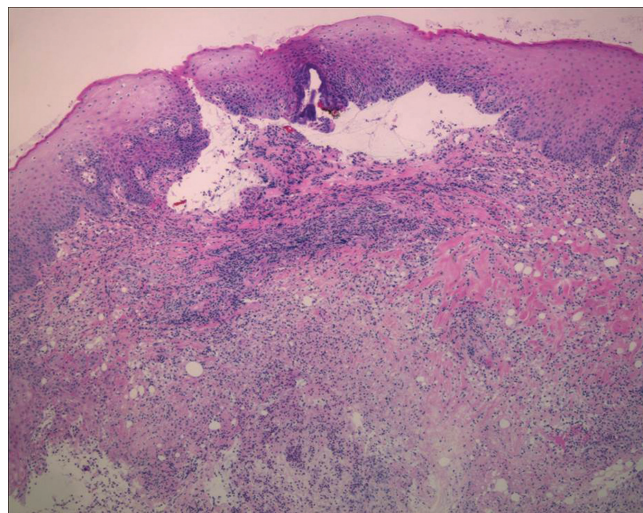
examination, there were a few ulcers in the upper hard palate in the oral cavity (Fig. 1). A biopsy specimen revealed subepidermal blisters with inflammatory cell infiltrates in the dermis (Fig. 2). Examination by direct immunofluorescence (DIF) staining was not carried out. Laboratory examination showed that titers of IgG antibodies to desmoglein-1 were 25 (normal index <14), whereas those to desmoglein-3 were within normal range. The ulcers on the hard palate healed spontaneously within one month.

**Discussion**

Drug-induced pemphigus is well known, and amongst disease modifying anti-rheumatic drugs (DMARDs), D-penicillamine is a representative drug that induces pemphigus [1-3]. Although the mechanism of D-penicillamine-induced pemphigus is still obscure, it has been suggested that epidermal cell surface proteins acquire new antigens reacting with a thiol group (-SH) contained in the drugs [4]. In addition, in vitro studies showed that those drugs have the potential to induce acantholysis of keratinocytes [5]. Other than D-penicillamine, captopril, enalapril, and bucillamine are also thiol drugs. Bucillamine is an analogue of D-penicillamine, and thus its mode of action is similar to that of D-penicillamine. So far, bucillamine-induced pemphigus is rare, and only several cases have been reported [6-8].



**Figure 1.** Ulceration in the hard palate (arrow).



**Figure 2.** Histological features showing subepidermal blisters and cellular infiltrates in the dermis.

Our patient developed herpes zoster at the V3 region, with mucous membrane lesions in the oral cavity. After treatment with anti-viral drugs, ulceration remained. Biopsy was carried out at another clinic, but direct immunofluorescence study was not examined. Laboratory examination showed low but positive titers of desmoglein-1 by ELISA. Desmoglein-1 is targeted in pemphigus foliaceus, while desmoglein-3 is targeted in pemphigus vulgaris. It has been shown that circulating desmoglein-specific antibodies are detected in patients with drug-induced pemphigus [9]. Withdrawal of the drugs resulted in rapid decline of anti-desmoglein titers by ELISA, suggesting that thiol-drugs are important in not only induction but also maintenance of the autoantibodies [10]. In addition, the thiol compounds contribute to gaining autoantibodies [11]. It is important to remind that serum levels of desmoglein-1 become positive in patients under bucillamine therapy, even without features of pemphigus.

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