DOI: 10.1002/cia2.12114

Journal of Cutaneous Immunology and Allergy
WILEY

LETTER TO THE EDITOR

Severe bisphosphonate-related mucosa ulcerations in the oral cavity and upper aerodigestive tract

Dear Editor,

Bisphosphonates are widely used to manage osteoporosis, osteopenia, Paget's disease, bone metastasis of cancer, and multiple myeloma.[1]

We report a patient with severe bisphosphonate-related oral/esophageal mucosal disorder.

The patient was a 71-year-old female. She noted mucosal disorder of the lips upon waking. She had taken an antiepileptic drug for paralysis of the left half body as a sequela of stroke. After a consultation at a local clinic, she was referred to our hospital under a tentative diagnosis of Stevens-Johnson syndrome. Ulcers of the lips/lingual mucosa/oral cavity with false membrane formation were observed (Figure 1A). There was no exanthema, congestion of the eyes, or fever. Blood testing on the initial consultation demonstrated a white blood cell (WBC) count, eosinophilic cell rate, segmented cell rate, lymphocyte rate, and C-reactive protein (CRP) level of 10 030 μL, 0.6%, 69.3%, 15.7%, and 15 mg/dL, respectively. Liver dysfunction was absent. Fungal examination of the lingual mucosa resulted in a Candida-negative reaction. Considering the presence of pharyngeal/esophageal lesions, we requested the Department of Oral Surgery and Department of Gastroenterology to examine the patient. An esophageal mucosal ulcer was found on endoscopy (Figure 1B). The examination results suggested bisphosphonate-related mucosal disorder. The patient stated that the oral mucosa had been affected upon waking up the day after taking a 50 mg tablet of minodronic acid hydrate. She was admitted, and fasting, fluid infusion, intravenous drip of an antibiotic, and administration of sodium alginate at 4.5 g per day were performed. The WBC count and CRP level were 9280/μL and 3.97 mg/dL, respectively, 12 days after admission, demonstrating hematological improvement. Liquid diet was started, and the patient was discharged 18 days after admission. She was negative for autoantibodies against desmoglein 1/3 and type 17 collagen.

Oral ulcers due to bisphosphonates often result from incorrect use of oral bisphosphonates such as chewing the tablet or dissolving it in the mouth.[1] Bauer et al investigated the upper gastrointestinal tract safety of alendronate. The incidence of serious gastroduodenal events (perforation, ulcers, and bleeding) was 1.6% in the alendronate group and 1.9% in the placebo group. The incidence of nonspecific upper GI complaints, such as abdominal pain, dyspepsia, nausea, and vomiting, was similar in the two groups.[2] Incorrect use of medications often occurs in elderly patients and especially in patients with dementia.[1]

This patient had taken the drug with jelly. Therefore, the drug may have remained in the oral cavity over many hours because of poor swallowing, and swallowing of saliva containing a high concentration of the drug may have led to an esophageal lesion. Prolonged mucosal exposure to bisphosphonates can damage the epithelial

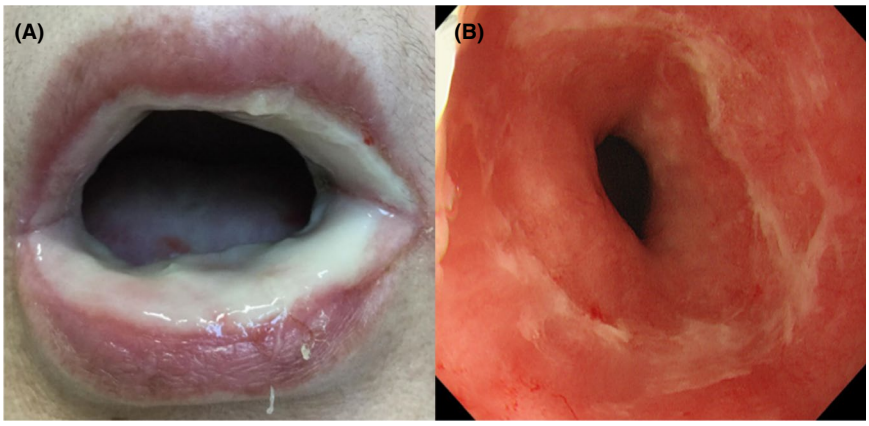

FIGURE 1 A, Ulcers of the lips/lingual mucosa with false membrane formation were present. B, White moss was adhered to the middle to inferior thoracic areas of the esophagus. Inflammation of the mucosa was observed

cells of the oral mucosa, probably because of alteration of the MAPK signaling pathway.[3]

Regarding monthly preparations of bisphosphonates, if patients consulting a medical institution with oral mucosal lesions present the prescriptions issued within 3 weeks as a recent prescription list, the drug name may not be included.

To avoid bisphosphonate-related mucosa ulcerations, sufficient guidance for oral administration is necessary.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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