

## CLINICAL SCIENCE LETTERS

# Mouth Sores Caused by Alendronate

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To the Editor:

Alendronate sodium is a primary aminobisphosphonate, widely used in the treatment of postmenopausal osteoporosis and Paget disease. Most of the adverse effects reported involve the esophageal and gastric mucosa. Lesions in the oral mucosa are less well known, although some cases have been reported. We present 2 cases of ulceration of the oral mucosa caused by incorrect administration of alendronate sodium tablets.

The first case involved a 68-year-old man, whose only relevant history was hypertension treated with verapamil for the last 3 years and collapsed vertebra treated with 10

mg/d alendronate sodium with calcium salts for 1 year. The patient consulted 3 days after the presentation of extremely painful ulcers on the oral mucosa, palate, tongue, and lower lip. Following careful questioning, the patient reported having allowed the alendronate tablet to dissolve in his mouth on one occasion several days previously because he was traveling.

The second case was a 57-year-old woman, postmenopausal for 10 years, who had received treatment for osteoporosis with alendronate 10 mg/d for 2 weeks prior to consultation. She presented painful ulcers on the tongue, palate, and oral mucosa that had been present for 2 days (Figures 1 and 2). On questioning she stated that she had experienced difficulty in swallowing a tablet that had dissolved in her mouth some days before the lesions appeared. Neither patient had a previous history of gastric problems, mouth ulcers, or herpes. Other mucosae were not affected and no related skin lesions were present in either case. Both patients had taken the drug (alendronate sodium) incorrectly and the erosions appeared shortly after the tablet had dissolved in the mouth.

The lesions were diagnosed as oral ulcerations caused by alendronate sodium and treatment with the drug was suspended. The lesions were treated and healed completely within 2 weeks.

Bisphosphonates are synthetic pyrophosphate analogs that bind to hydroxylapatite in bone inhibiting osteoclastic activity. Alendronate sodium is a primary aminobisphosphonate used in the treatment of postmenopausal osteoporosis (10 mg/d) and Paget disease (40 mg/d), which acts by inhibiting osteoclastic resorption. It has also been used in the treatment of bone metastasis and tumor-related hypercalcemia. Secondary skin conditions are rare, with reports of lichenoid eruptions, superficial erythema annulare,<sup>1</sup> urticaria, angioedema, erythema multiforme, fixed pigmented erythema, eczema eruptions, and pruritus. Exceptional cases of mouth ulcers restricted to the oral mucosa have been reported before.<sup>2-4</sup> Erosive esophagitis,<sup>5</sup> esophageal ulcers, dysphagia, and retrosternal pain have been associated with the ingestion of alendronate sodium.

As the drug is administered orally, the patient must be instructed well, and be provided with the following advice in order to allow adequate absorption and to reduce adverse effects to a minimum<sup>6</sup>:



Figure 1. Mouth sores (second patient).



Figure 2. Detail of lesions on the tongue (second patient).

1. Take the tablet with a glass of water (200 mL) first thing in the morning.
2. Not to chew the tablet or allow it to dissolve in his or her mouth.
3. Not to eat, drink, or lie down for at least 30 minutes after taking the tablet.
4. Suspend the medication at the least symptom of dysphagia, pyrosis, or retrosternal pain.

Findings from endoscopic studies in patients with esophagitis caused by alendronate are associated with chemical esophagitis, similar to that caused by acetylsalicylic acid.<sup>7</sup> The pathophysiological mechanism involved in these cases was direct irritation of the mucosa due to prolonged exposure to the drug. The same mechanism could apply to our patients who allowed tablets to dissolve in their mouths, causing erosion due to prolonged contact of the drug with the oral mucosa.

In view of the increasing use of alendronate sodium we presume this must be quite a common complication despite the paucity of cases cited in the literature. As we are aware that alendronate sodium can cause erosions or ulcerations of the oral mucosa if not ingested properly, we must consider the drug as a possible causal agent in such cases and must question the patient carefully on how they ingested the tablets.<sup>8,9</sup>

### Conflicts of Interest

The authors declare no conflicts of interest..

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## Primary Cutaneous Cryptococcosis Presenting With a Sporotrichoid Pattern in a Cancer Patient

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To the Editor:

Cutaneous cryptococcosis is the outcome of infection by *Cryptococcus neoformans*, an opportunistic encapsulated yeast principally found in soil contaminated by bird droppings (mainly pigeons), wood debris, fruit and vegetable waste, and dust.<sup>1-3</sup> It usually presents in immunocompromised patients as a secondary disseminated infection, as occurs in 10-15 % of cases.<sup>1-5</sup> Cutaneous cryptococcosis remains a controversial entity despite

articles on presumed instances of the condition being published since the 1950s. The infection can also occur in immunocompetent patients, in which case prognosis is better.<sup>1</sup> The causal agent in both types of infection is almost always serotype D organisms, as a result of their greater epidermotropism.<sup>1-4,6</sup>

We present the case of a 66-year-old man referred to us by the oncology department with dermatosis that had been present for 1 month. The patient had received treatment