



## Case Report

# An Alendronate-Induced Oral Lichenoid Reaction

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### ABSTRACT

**A sixty-seven-year old female patient presented with an oral lichenoid reaction, which appeared two months after she started to take alendronate to treat osteoporosis. After withdrawal of the offending drug, the lesions subsided within three months, and at the follow-up visit one and a half years later, the patient was free of any oral lesions. Patient refused taking of oral biopsy specimen and re-challenge test. It might be that oral lichenoid reaction was caused by alendronate.**

**Keywords:** Lichenoid reaction, Alendronate, Osteoporosis

## INTRODUCTION

Many systemic medications can cause oral lichenoid reactions although the pathogenesis is still unclear. No standardized criteria for the diagnosis of lichenoid reaction due to the drug intake exist. Similar to oral lichen planus, lichenoid reactions can present clinically with either reticular or erosive patterns, however often present as a single lesion unlike oral lichen planus. Commonly reported medications that can cause oral lichenoid drug reactions (OLDR) include antihypertensives, nonsteroidal inflammatory drugs, antimalarials, and antiretrovirals used in the treatment of human immunodeficiency virus (HIV) infection. The microscopic features of drug-related lichenoid lesions share many similarities to oral lichen planus, however these microscopic features are not specific and rely on clinical information including a temporal association with any systemic medications (Müller S, 2011). There are no clear or distinct clinical or histological features that reliably distinguish OLDR from oral lichen planus or other lichenoid lesions. Drug reactions may occur anytime, even years after the introduction of the drug (Al-Hashimi et al., 2007).

The bisphosphonates are essential to the treatment of osteoporosis, Paget's disease, and a variety of malignant bone diseases. Adverse effects occur primarily in the upper gastrointestinal tract and are followed by renal toxicity, ocular adverse events, acute phase response, hypocalcaemia and secondary hyperparathyroidism, musculoskeletal pain, osteonecrosis of the jaw, atrial

fibrillation and atypical fractures of the femoral diaphysis (Papapetrou PD, 2009).

Cutaneous adverse effects due to alendronate have already been reported in the literature in the form of pruritus, fixed drug eruption, hypersensitivity, rash and allergic reaction (Phillips et al., 1998).

However, literature data on the oral adverse side effects of alendronate are scarce, and apart from osteonecrosis, other such side effects are rare. Moreover, a lichenoid drug reaction to alendronate has not been reported.

The exact pathogenic mechanism through which drugs may cause lichenoid reactions is not known, and those now most commonly implicated in these reactions are the non-steroidal anti-inflammatory drugs (NSAIDs) and the angiotensin-converting enzyme inhibitors. However, lichenoid reactions may also follow the use of thiazide diuretics, sulphonamides, phenothiazines, antimalarials, tetracyclines, HIV protease inhibitors and many others. Although the most reliable way to diagnose a lichenoid reaction is its disappearance after withdrawal of the offending drug and recurrence of the lesions upon re-challenge, our patient rejected this type of diagnostic procedure.

In most cases, clinical identification of lichenoid drug reactions has been based largely on subjective criteria, and although histology may help, there are no specific features (Scully C and Bagan JV, 2004).



**Figure1.** Patient's right buccal mucosa upon admission



**Figure2.** The same patient – right buccal mucosa after one and a half years

## CASE REPORT

A sixty-seven-year old woman was referred to our Department on account of oral lesions, which developed two months after she started to take alendronate for osteoporosis. The patient was otherwise healthy and was

not taking any other medication. Oral examination revealed a lichenoid reaction on her right buccal mucosa. The lesion displayed a reticular-like pattern, i.e., hyperkeratotic striae extending from the 45-47, while a discrete inflammation manifesting as a redness around this striae was visible. The patient refused to allow an

oral biopsy specimen to be taken. Withdrawal of the alendronate resulted in complete resolution of the lesions within three months. At the follow-up visit after eighteen months, no lesions could be seen on her right buccal mucosa. Obviously, a lichenoid reaction was not due to the bridges on that side nor to the presence of plaque, as she had good oral hygiene. The patient refused a re-challenge test.

## DISCUSSION

The incidence of side effects from commonly and new prescribed drugs is increasing, and dentists and other physicians must be aware of this fact. Obviously, the gold standard is a re-challenge of the offending drug, which is ethically questionable, unless the drug cannot be replaced by other one or the offending drug is vital to the patient's life. Re-challenge carries a risk of anaphylactic reactions that can be life threatening. Skin reactions to alendronate have been reported in the published literature, as has urticaria due to alendronate. Rare cases of rash/pruritus have also been reported as well as lichen planus, superficial gyrate erythema, papulo-petichial skin eruption and superficial spongiotic dermatitis. Some cases were confirmed by a positive re-challenge test (Lazarov et al., 2002; High et al., 2003; Kimura et al., 2003 and Brinkmeier et al., 2007).

Biphosphonates are used in the treatment of osteoporosis and malignant diseases such as malignant myeloma, breast, renal and prostate cancer. In most cases adverse reactions to biphosphonates include biphosphonate related osteonecrosis of the jaws (BRONJ) and less frequently oral ulcerations.

Assaf et al. (Assaf et al., 2013) reported that 8.9% of patients treated for breast, prostate and renal carcinoma developed BRONJ. The average time between diagnosis of malignancy and BRONJ was 80 months. The majority of patients with BRONJ (60%) received a bisphosphonate therapy including zoledronate. Statistical analysis did show a significant correlation concerning monocytostatic and triple-cytostatic therapy. The same authors (Assaf et al., 2013) confirmed a drug- and dose-dependent occurrence of BRONJ.

Habitual immediate contact of alendronate tablets with oral mucosa, i.e., sucking instead of swallowing them, was shown to cause of contact stomatitis with oral ulcerations in several cases (Demerjian et al., 2000; Krasagakis et al., 2004; Schmut et al., 2005; Rubegni P and Fimiani M, 200; and Gonzales-Morales MA and Bagan-Sebastian JV, 2000). Recently, there was a case of lichenoid dermatosis induced by alendronate in a patient, as reported by Husein-EIAhmed et al. (Husein-EIAhmed et al., 2010). Oral lichenoid reactions might develop due to the presence of different dental materials in the mouth, drug intake and some lesions with this appearance might prove to be plaque-induced lichenoid

reactions. In this patient, no plaque was present and the fixed partial denture prosthesis on the lower and upper jaw remained in place all the time, for which reason these possible causes were excluded (Carbone et al., 2009).

With regard to a possible differential diagnosis, it might be assumed that this could also be a case of oral lichen planus. This condition is usually seen bilaterally, i.e., lesions would have been present also on the left buccal mucosa, but this was not the case. On the other hand, spontaneous remission of oral lichen planus is seen in seven percent of patients, and usually several years after the oral lichen appeared. Furthermore, one double-blind study showed that even oral pathologists are not sure whether the diagnosis is one of an oral lichen/oral lichenoid reaction (Silverman et al., 1985).

## CONCLUSION

Regarding oral adverse reactions, biphosphonates usually cause osteonecrosis of the jaws. Rarely, oral ulcerations develop on the oral mucosa where patients dissolve tablet. One has to bear in mind that other possible adverse reactions might develop on the oral mucosa as a side effect of biphosphonate intake such as one seen in this case as lichenoid reaction.

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