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DOI: 10.4274/tod.galenos.2022.90912
Turk J Osteoporos 2023;29:124-6

Oral Mucosal Ulcer Associated with Improper Usage of Bisphosphonate: A Case Report

Yanlış Bifosfonat Kullanımına Bağlı Oral Mukozal Ülser: Olgu Sunumu

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Abstract

Bisphosphonates are widely used agents for osteoporosis. Although bisphosphonates are generally well-tolerated drugs, especially oral forms may have gastrointestinal system side effects. Oral bisphosphonate-induced oral mucosal injury, oral ulcers, vesicles, and gingivitis are rarely reported in the literature. Lesions related to improper usage of bisphosphonates are atypical and need to be differentiated from other mucosal erosions. In this report, a case of painful, hemorragic oral ulcer in the soft palate in a patient with osteoporosis is discussed in light of the relevant literature.

Keywords: Biphosphonate, alendronate, mucosal ulcer, improper usage

Öz

Bifosfonatlar osteoporoz tedavisinde yaygın olarak kullanılan ajanlardır. Bifosfonatlar genellikle iyi tolere edilen ilaçlar olmakla birlikte özellikle oral formları gastrointestinal sistem yan etkilerine neden olabilir. Oral bifosfonat kaynaklı oral mukozal lezyonlar, oral ülserler, veziküller ve diş eti iltihabı nadiren literatürde bildirilmiştir. Bifosfonatların yanlış kullanımına bağlı lezyonlar atipiktir ve diğer mukozal erozyonlardan ayırt edilmesi gerekir. Bu yazıda osteoporotik bir hastada yumuşak damakta ağrılı hemorajik oral ülser olgusu ilgili literatür ışığında tartışılmıştır.

Anahtar kelimeler: Bifosfonat, alendronat, mukozal ülser, yanlış kullanım

Introduction

Bisphosphonates are pyrophosphate analogue drugs act as an inhibitors of osteoclasts apoptosis by binding hydroxyapatite cristals in bone (1). They are widely used agent for treatment postmenauposal osteoporosis,men osteoporosis and steroid related osteoporosis. Their clinical profile of bone-specific efficacy, rapid response, protection from both spine and hip fractures in patients with osteoporosis, and excellent tolerability is all that can be expected of an anti-remodeling drug (1). Although bisphosphonates are generally well tolerated drugs, especially oral forms may cause gastrointestinal system side effects like mucosal irritation and ulceration in esophageal and gastric mucosa and necrosis in bone structures such as maxilofacial bone and jaw (2). Bisphosphonate-related osteonecrosis of jaw (BRONJ) is the most commonly known oral side effect associated with bisphosphonates (3).

Oral bisphosphonate induced oral mucosal injury, oral ulcers, vesicles and gingivitis are rarely reported cases seen in elderly patient with physical and mental comorbidities. The regressed lesions by withdrawal or proper taking of oral bisphosphonates describes that oral mucosal lesions associated with inappropriate usage of bisphosphanates such as chewing and allowing to melt in the mouth (4,5).

Lesions related to improper usage of bisphosphonates are atypical and need to be differentiated from other mucosal erosions. In this report, a case of painful, hemorragic oral ulcer in a patient with osteoporosis is discussed in the light of the relevant literature.

Case Report

Seventy-year-male patient with osteoporosis under the treatment with weekly alendronate for nine months admitted to physical

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Received/Geliş Tarihi: 08.05.2022 **Accepted/Kabul Tarihi:** 04.10.2022

medicine and rehabilitation outpatient clinic with a complaint of oral ulcer on his soft palate. Oral ulcer was 1 cm in size, and had a hemorrhagic red appearance and not presented with pain, cough, bleeding and dysphagia or other symptoms (Figure 1).

He had a history of hypertension, familial mediterranean fever, coronary artery bypass graft and osteoporosis. Medications included acetilsalicylic acid, clopidogrel, colchicine, metoprolol,alendronate, vitamin D and calcium.

Patient referred to otorhinolaryngology clinic, diagnosed with gastroesophageal reflux and proton-pump inhibitor treatment was started. Follow-up evaluation showed enlargement of the lesion and an increase in the number of leukoplakia lesions with accompanying bleeding and severe pain complaints and incisional biopsy was taken. The biopsy result was reported as ulcer, inflamation with lymphocytes and plasma cells, compatible with dysplasia. Then he referred to skin and venereal disease clinic for further investigations had differential diagnosis squamous cell carcinoma, leukoplasia, paraneoplastic pemphigus. The second biopsy was reported that erosion, ulcer without dysplasia.

When patient was asked to describe the use of medications especially alendronate, it was noticed that he used the drug by chewing. Thereupon, the current alendronate treatment was stopped immediately, and in the follow-up, the patient's lesions were completely healed within two weeks. The lesions never had recur during follow-up of the patient.

Informed consent was obtained from the patient regarding this report.

Figure 1. Ulcer with well-defined borders on the soft palate

Discussion

Biphoshonates are mostly preferred drugs for the treatment of osteoporosis (1). Alendronate is widely used biphosphanates and has oral and iv forms. The side effects of weekly used oral alendronate on gastrointestinal system especially gastric mucosal ulcers, osteonecrosis (2). Oral ulcers with alendronate usage is underreported and rarely seen. Although the pathophsiology of cytotoxic effect on epithelium of oral alendronate is unclear, improper use of the drug, sucking, chewing and keeping the pill in the mouth until it dissolves, results in inflammation, erosion and ulcerations by a prolonged mucosal exposure (6). In this case report, the patient took the medication by chewing and made prolonged exposure of oral mucosa for alendronate and then swallowed it. After the cessation of the drug, the lesions are dissappeared and healed.

In literature review, the onset of oral ulcers occurs an average of 2 weeks-13 months after initiation of bisphosphonate therapy (7). In this case, the patient has complaints after 6 months from his first dose of oral alendronate and the lesions become evident on the day of taking the drug and subside at the end of the week. The lesions are most commonly identified in hard palate and tongue however the soft palate, larynx and buccal mucosa may also be affected. The soft palate lesion seen in this report is a very rare location not reported previously in the literature.

In this case report, it is emphasized that the physicians should be precisely sure that the patient had understand correctly the usage form and procedure of oral bisphosphonates and even should examine patients oral, buccal mucosa and gingiva during their follow-up. Weekly oral bipshophanates should be taken by swallowing with minimum one glass water in an upright position and staying upright for at least 45 minutes to prevent reflux, oesophageal irritation and ulceration. For patients having mental problems, cognitive impairments, difficulties for swallowing, other forms of biphosphanates should be considered as an alternative treatment.

Ethics

Informed Consent: Written informed consent was obtained from the patient prior to the drafting of the manuscript.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ş.N.B., B.D.K., A.İ., Concept: Ş.N.B., B.D.K., A.İ., Design: Ş.N.B., B.D.K., A.İ., Data Collection or Processing: Ş.N.B., B.D.K., A.İ., Analysis or Interpretation: Ş.N.B., B.D.K., A.İ., Literature Search: Ş.N.B., B.D.K., A.İ., Writing: Ş.N.B., B.D.K., A.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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