ATATÜRK ÜNİVERSİTESİ YAYINLARI
ATATURK UNIVERSITY PUBLICATIONS

Case Report *Olgu Sunumu* DOI: 10.17567/ataunidfd.1039378

# Treatment of Apical Periodontitis Induced BRONJ with Endodontic Treatment

## Apikal Periodontitis Kaynaklı BRONJ'un Endodontik Tedavi ile Tedavisi

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**ABSTRACT**

Bisphosphonate related osteonecrosis of the jaw (BRONJ), which is one of the serious side effects of bisphosphonates, has an increasing clinical importance due to the widespread use of bisphosphonates in the treatment of many diseases such as osteoporosis, osteopenia, Paget's disease, osteogenesis imperfecta, and multiple myeloma. BRONJ can spontaneously develop in the jawbones. In addition, many factors such as tooth extraction, periodontal diseases, and local trauma can trigger BRONJ. In our case, it was detected that the lesion appearing like BRONJ in the left lower jaw of the 65 years old female patient with a history of oral bisphosphonate use developed due to apical periodontitis resulting from the tooth numbered 34. Root canal treatment was administered to the relevant tooth of the patient, the fistula tract was closed after this treatment, and as a result of the CBCT examination, it was observed that the enlargement in the necrotic bone area stopped. In addition, the patient's complaints about the relevant tooth disappeared. As a result, endodontic treatment is an effective treatment approach in the treatment of BRONJ developing due to apical periodontitis. In order to avoid the risk of BRONJ, a detailed oral examination should be performed before starting the bisphosphonate treatment, and necessary endodontic, restorative and periodontal treatments should be followed.
**Key words:** Apical Periodontitis; BRONJ; Endodontics; Osteoporosis.

**ÖZ**

Bifosfonatların ciddi yan etkilerinden biri olan bifosfonatla ilişkili çene kemiği osteonekrozu (BRONJ), osteoporoz, osteopeni, Paget hastalığı, Osteogenezis imperfekta, Multipl Myelom gibi birçok hastalığın tedavisinde, bifosfonatların yaygın kullanımı nedeniyle giderek artan klinik önem taşımaktadır. Çene kemiklerinde BRONJ spontan gelişebildiği gibi diş çekimi, periodontal hastalıklar, lokal travma gibi pek çok faktör BRONJ'u tetikleyebilmektedir. Bizim vakamızda oral bifosfonat kullanım hikayesi olan 65 yaşında kadın hastanın sol alt çenesinde BRONJ görüntüsü veren lezyonun #34 nolu diş kaynaklı irreversibl pulpitis sebebiyle gelişen apikal periodontitis kaynaklı olduğu tespit edilmiştir. Hastanın ilgili dişine kök kanal tedavisi uygulanmış, bu tedavi sonrası fistül yolu kapanmış ayrıca CBCT incelemesi sonucu nekroze kemik alanında genişlemenin durduğu görülmüştür. Ayrıca hastanın ilgili dişten şikayetleri ortadan kalkmıştır. Sonuç olarak apikal periodontitise bağlı gelişen BRONJ'un tedavisinde endodontik tedavi efektif bir tedavi yaklaşımıdır. BRONJ gelişme riskinden kaçınmak için bifosfonat tedavisine başlanmadan önce detaylı ağız içi muayene yapılıp, gerekli görülen endodontik, restoratif ve periodontal tedaviler yapılmalıdır.
**Anahtar Kelimeler:** Apikal Periodontitis; BRONJ; Endodonti; Osteoporoz

Geliş Tarihi/Received 07.09.2021
Kabul Tarihi/Accepted 21.12.2022
Yayın Tarihi/Publication Date 28.07.2024

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Cite this article: Sancar B, Akıncı L, Talay GA. Treatment of Apical Periodontitis Induced BRONJ with Endodontic Treatment. *Curr Res Dent Sci.* 2024;34(3): 238-241.

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## INTRODUCTION

Bisphosphonates are used in the treatment of diseases such as osteoporosis, osteopenia, Paget's disease, Osteogenesis imperfecta as well as malignancies such as breast, prostate, lung cancer, and multiple myeloma with bone metastases.[1]

Bisphosphonates are divided into 3 main groups according to the classification made in the early 1990s. The first generation consists of the group represented by etidronate with alkyl derivatives, while the second generation is composed of the group represented by aminobiphosphonates with terminal group such as alendronate, ibandronate, and pamidronate. The third generation consists of nitrogen-containing bisphosphonates such as zoledronic acid and risedronate. [2]

One of the most important side effects of bisphosphonates is the osteonecrosis of the mandible and maxilla. This pathology was named as Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) according to the report published by Marx et al. in 2003.[3] The diagnostic criteria of BRONJ are reported as the presence of an intraoral/extraoral fistula tract in the maxillofacial area that reaches the exposed bone or bone and exists for more than 8 weeks in individuals who use or used antiresorptive and antiangiogenic drugs and

who have not received radiotherapy from the jaw area or have a disease with metastasis to the jaws.[4] Duration of the treatment and dose of bisphosphonates are important risk factors for osteonecrosis.[5]

In the literature, it has been reported that surgical interventions such as tooth extraction are an important factor in terms of inducing BRONJ.[6] However, in more recent data, periodontal and periapical diseases have also been reported to cause BRONJ at an important rate in addition to tooth extraction.[7]

In clinical studies, a potential relationship between periodontitis and BRONJ has been revealed.[8] In apical periodontitis, bacteria reach the deeper part of the alveolar bone through root canal systems. This suggests that apical periodontitis is an important etiological factor in the formation of BRONJ.

In the literature, there is not any osteonecrosis case developing due to apical periodontitis following the use of oral bisphosphonates as in our case. In this article, the endodontic treatment of an osteonecrosis case developing following apical periodontitis in the patient who used oral bisphosphonate

## CASE PRESENTATION

A 67-year-old female patient presented to our Oral and Maxillofacial Surgery clinic for pain in the teeth under her fixed prosthesis and to treat her missing teeth with dental implant application. In the anamnesis obtained from the patient, it was learned that she had osteoporosis and hypertension. The patient received Verapamil HCl+Trandolapril (Tarka® 180/2 mg) treatment due to hypertension and 1 tablet oral Alendronic Acid (Fosavance® 70 mg) once a week for 4 months until one year ago due to osteoporosis.

In the clinical examination, after the metal-supported porcelain restorations of the patient were removed, a deep caries reaching the pulp and sensitivity to percussion were observed in teeth numbered #34 and #43. In addition, fistula tract was observed in the buccal mucosa adjacent to the mucogingival border of the teeth numbered #33 and #34 (Fig: 1A). The mucosa in the fistula area was sensitive to palpation. Radiographic examination revealed an enlargement in the periodontal space at the apical of the tooth #34 (Fig 2A). In addition, the patient had missing teeth in both jaw posterior areas.

Considering the medical condition of the patient, the indications for tooth extraction and implant treatment were avoided. In order to eliminate the risk of BRONJ and relieve the patient's pain symptoms, the patient was directed to the Endodontics department for the treatment of the relevant teeth.

In this department, the teeth #31, #32, #33, #41 and #42 gave a vital response, while the teeth #34 and #43 gave a devital response in the vitalometric evaluation of the patient's teeth. The teeth #34 and #43 of the patient were diagnosed with acute apical periodontitis, and an appointment was arranged for 3 months later. Informed consent was obtained from the patient. After the removal of the metal-supported porcelain restoration on the day of the appointment, non-surgical root canal treatment was initiated for these two teeth. The initial film was not obtained from the patient, and the diagnostic radiography performed 3 months ago was taken as a reference. After cleaning the carious dentin, the entry to the pulp chamber was provided, and the canal mouths were detected. The working lenght was determined with an apex finder device (VDW Gold, VDW, Munich, Germany) by using #15 type K-file (VDW, Anteos, Munich, Germany). Root canals were shaped with rotary file (OneCurve, MicroMega, Brascon, France). At the end of the shaping, #25 apical diameter and 0.06 canal taper were obtained. Irrigation was performed with 2.5% sodium hypochlorite (NaOCl) between each file. The final irrigation was completed with 2 mL of 2.5% NaOCl followed by 2 mL of 17% ethylenediaminetetraacetic acid (EDTA), and 2 mL of normal saline. The root canals were filled with a resin-based root canal paste and a single gutta-percha having a taper of 25/.06. Endodontic treatment was completed in both teeth in one session on the same day.

Following the endodontic treatment, the patient's old restoration was cemented. Final periapical radiographs were obtained from both teeth after the root canal treatment was completed. The radiography revealed that the root canal treatment of the teeth #34 and #43 was performed in the optimal limits. However, in the apical of the tooth #34, radiolucent areas with unclear borders compatible with BRONJ were observed (Fig:2B). The lesion seen in the last radiography suggested that BRONJ appearance developed as a result of apical periodontitis within 3 months.

The patient was referred to our Oral and Maxillofacial Surgery clinic to evaluate this appearance. In the examination performed in our clinic, it was seen that the presence of fistula in the relevant tooth continued, and the patient was prescribed antibiotics (Augmentin®BID 1000 mg, Flagyl® 500mg) and chlorhexidine-containing mouthwash (Cloroben®), and routine control was recommended.

In the control examination 1 month later, Cone Beam Computed Tomography (CBCT) was performed, and the radiographic image compatible with BRONJ was confirmed (Fig:3A). Serum-Ctx (C-terminal telopeptide) measurement was demanded from the patient, and the Beta-Ctx result was obtained as 0.15 µg/L (reference range; postmenopausal 0-0.556). This value is within the reference range.

In the 2nd control examination performed 1 month later, the fistula tract was closed and replaced by keratinized gingiva (Fig:2A). The patient could not continue her controls due to the Covid-19 pandemic. However, in the 3rd examination performed 1 year later, it was found that there was no change in the lesion borders. The patient did not have any complaints regarding the relevant area.

As a result of the developing BRONJ, we recommended the patient to restore the missing teeth with a removable prosthesis compatible with the mucosa instead of implant application. Follow-up of the patient continues in our clinic.


**Figure 1.** (A) Fistula mouth seen between the teeth #33 and #34 (B) Fistula mouth recovering as a result of canal treatment between the teeth #33 and #34

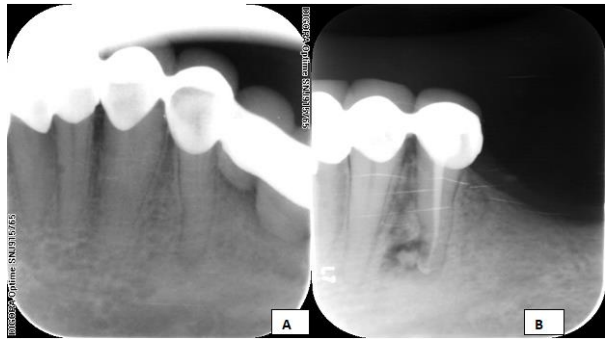


**Figure 2. (**A) Diagnostic radiography obtained from the tooth #34 before the development of BRONJ (B) Radiolucent areas with unclear borders compatible with BRONJ

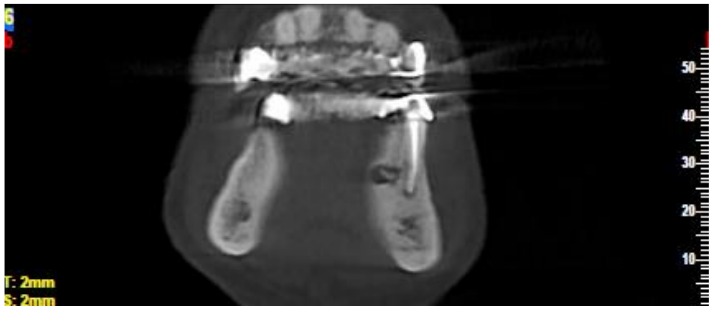


**Figure 3.** CBCT coronal section; radiolucent areas without border prominence compatible with BRONJ in the lingual of the tooth #34

## DISCUSSION

Despite some potential complications, bisphosphonates are used to improve the quality of life of cancer patients and reduce the risk of femoral and vertebral fractures in osteoporosis patients(9)(10). The effect mechanism of bisphosphonates in osteoporosis patients can be summarized as "the reduction of bone resorption by affecting osteoclasts". When administered in physiological doses, bisphosphonates readily bind to the bone matrix due to their high affinity for bone, and bisphosphonates are also potential inhibitors of osteoclastic activity. It affects bone metabolism by reducing both activity and the number of osteoclasts.[11]

The lack of characteristic clinical findings of osteonecrosis in the jawbones developing due to bisphosphonates, especially the absence of clinically exposed necrotic bone, delay in diagnosis and prolongation of the disease duration may make treatment protocol more difficulty and lead to the failure of the treatment.[12]

Apical periodontitis is a group of inflammatory diseases. It is a continuation of endodontic infection and manifests as the host's defense response against microbial infection originating from the root canal system. This process is comprised of pulp necrosis caused by the invasion and colonization of the root canal system by bacteria through tooth decay, trauma or iatrogenic processes. The bacteria that colonize in the necrotic root canal trigger the damage to periradicular tissues and increase the inflammatory changes.[13] Local inflammation at the interface of the infected radicular pulp and periodontal ligament is observed as an active battle between host defenses and microbial factors resulting in destruction of hard tissues and eventually apical periodontitis in various histopathology categories called periapical lesions[14]

BRONJ and osteoradionecrosis are the most important types of osteonecrosis seen in the jaws(15). In our case, since the patient did not receive radiotherapy before, the possibility of osteoradionecrosis was excluded. The diagnosis of BRONJ was established in our patient, who received oral bisphosphonate treatment, due to the irregular bone margins and the appearance of the fistula tract in the oral mucosa in the radiography of the present lesion. Since there was a risk of triggering BRONJ, biopsy was not performed in this patient, and this was a limitation of our study.

Applying root canal treatment instead of tooth extraction in patients using bisphosphonates is a more conservative approach in terms of reducing the risk of BRONJ.[16]

In the literature, there are BRONJ cases that developed as a result of root canal treatment(16)(17)(18). In these cases, the causes of BRONJ resulting from root canal treatment include soft tissue trauma caused by the rubber-dam clamp, improper irrigation procedure, perforation and ending of the canal treatment beyond the optimal margins.

In our case, it is understood that the lesion seen in the final periapical radiography obtained at the end of a single-session root canal treatment did not develop as a result of root canal treatment. Spread of the pulpal inflammation through the root canal to the apical within 3 months between the diagnosis and treatment confirms that BRONJ was caused by apical periodontitis. In addition, in the CBCT obtained after canal treatment, it was determined that the enlargement in the necrotic bone margins stopped

## CONCLUSION

Protective and preventive interventions should be prioritized to avoid BRONJ in patients who has a potential of developing BRONJ. In order to reduce the risk of BRONJ, all invasive procedures including tooth extraction, periodontal, and endodontic treatment should be completed prior to bisphosphonate use, and protective applications such as oral hygiene training, fluoride administration, etc. should be performed. If BRONJ develops due to apical periodontitis, the first treatment alternative should be the endodontic treatment.

**Hasta Onamı:** Hastadan bilgilendirilmiş onam alındı
**Hakem Değerlendirmesi:** Dış bağımsız.
**Yazar Katkıları:** Fikir – B.S., L.A., G.A.T.; Tasarım – B.S., L.A., G.A.T.; Denetleme – B.S., L.A., G.A.T.; Kaynaklar – B.S., L.A., G.A.T.; Veri Toplanması ve/veya İşlemesi – B.S., L.A., G.A.T.; Analiz ve/veya Yorum – B.S., L.A., G.A.T.; Literatür Taraması – B.S., L.A., G.A.T.; Makaleyi Yazan – B.S., L.A., G.A.T.; Eleştirel İnceleme – B.S., L.A., G.A.T.;
**Çıkar Çatışması:** Yazarlar, çıkar çatışması olmadığını beyan etmiştir.
**Finansal Destek:** Yazarlar, bu çalışma için finansal destek almadığını beyan etmiştir.

**Informed Consent:** Informed consent was obtained from the patient**.**
**Peer-review**: Externally peer-reviewed.
**Author Contributions:** Concept – B.S., L.A., G.A.T.;; Design – B.S., L.A., G.A.T.; Supervision – B.S., L.A., G.A.T.; Resources B.S., L.A., G.A.T.; Data Collection and/or Processing – B.S., L.A., G.A.T.; Analysis and/or Interpretation – B.S., L.A., G.A.T.; Literature Search –Ö.G.; Writing Manuscript – B.S., L.A., G.A.T.; Critical Review – B.S., L.A., G.A.T.
**Conflict of Interest:** The authors have no conflicts of interest to declare.
**Financial Disclosure:** The authors declared that this study has received no financial support.

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