

## USE OF PLATELET-RICH FIBRIN FOR JAW OSTEONECROSIS: A CASE REPORT

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### Summary

We present tooth extraction in a patient treated with bisphosphonates (BPs) for cancer and at risk of osteonecrosis of the jaw. The administration of platelet-rich fibrin (PRF) is an innovative method of promoting wound healing that allows hermetic closure at the surgical site after extraction without mucoperiosteal flaps or periosteal release sections. Here, we describe the case of a 60-year-old man who had osteonecrosis of the upper jaw and underwent surgery for prostate cancer in 2012. In 2014, bone metastases were detected, and the patient was treated with Xgeva and Zometa: a two-year therapy with Xgeva, followed by treatment with Zometa. In 2018, after extraction of a tooth in the upper right jaw, a healing wound of extraction and stripping of the maxillary bone occurred. The patient was admitted for hospital treatment and underwent surgery to remove the osteonecrotic lesion, sequester and administer PRF (platelet-rich fibrin), and sew tightly. As a result of the treatment, complete re-epithelialization of the wound without infection occurred. Generally, in more invasive surgical procedures, the use of PRF to close the wells after extraction in patients receiving BP appears to be a promising alternative. Additional clinical trials will be essential to clarify the effectiveness of PRF in preventing BP-related osteonecrosis after tooth extraction.

**Keywords:** bisphosphonates, osteonecrosis, platelet-rich fibrin, oral medicine

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### Introduction

High doses of bisphosphonates (BPs) are relatively effective in dealing with cancer metastases and other malignancies, including multiple myeloma. Low doses of BPs are also prescribed for the treatment of systemic conditions, such as osteoporosis. Bisphosphonates are bone antiresorptive agents that are commonly used in the treatment of disorders in bone metabolism. BPs operate at the osteoclast level. These drugs have a different mechanism of action in

reducing bone resorption by blocking osteoclast differentiation. In some clinical trials, a strong correlation has been found between using these drugs and the risk of osteonecrosis of the jaws, especially after surgical interventions like tooth extraction [5].

Complications are associated with signs of infection for a period of a minimum of 8 weeks. Intraoral oral mucosal lesion and bone exposure are observed [6].

The most effective approach in cancer-diagnosed patients is the prevention of MRONJ. Effective prevention or early identification of MRONJ in patients treated with denosumab or bisphosphonates depends on the patients' and practitioners' consciousness of the related adverse effects [7].

In dental practice, the number of patients with osteonecrosis of the jaws receiving BP is increasing. More than 85% of the cases reported in clinical trial reports relate to the intravenous use of zoledronic or pamidronic acid, usually prescribed for the treatment of cancer that affects bone tissue [9]. As a preventive measure, specialists often recommend avoiding tooth extraction and treatment of dental foci of infection, according to the generally-accepted protocol in patients receiving BP therapy. Osteonecrosis is rarely associated with local trauma due to bone exostosis, incompatible removable dentures, or implant placement [9].

The standard procedure, requiring the performance of atraumatic extraction procedures and surgical intervention to prevent medication-related osteonecrosis of the jaw (MRONJ), includes preparing mucoperiosteal flaps for intraoperative primary wound closure to reduce bone infection [7]. In addition to surgery, antibiotic treatment is prescribed. Several protocols for antibiotic therapy have been proposed - a broad-spectrum antibiotic in particular, such as amoxicillin (1 g, three times a day) with or without clavulanic acid, and in combination with metronidazole (500 mg, twice a day). In the case of a penicillin allergy, treatment with erythromycin (600 mg, three times a day), clindamycin (600 mg, three times a day) is administered. The therapy protocol that Lodi et al. have proposed is based on a combined antibiotic and antiseptic therapy. This therapy begins three days before surgery and continues for at least one week. However, it

could be extended, depending on the progress of wound healing [7].

Furthermore, several studies suggest a protocol for oral surgery in MRONJ patients and PRF administration. After removing the osteonecrotic (sequester) and granulation tissue, platelet-rich fibrin (PRF) is applied immediately in patients with osteonecrosis [1,6]. The set of rules consists of the following steps:

1. Anesthesia;
2. Reparation of the mucoperiosteal lump;
3. Excision of the osteonecrotic lesion;
4. Hemostasis;
5. Application of platelet-rich fibrin (PRF);
6. Sewing the surgical wound.

When closing a surgical site with minimum invasiveness, the use of biomaterial-based alternatives is crucial. That is why the use of platelet-rich fibrin (PRF) was examined. The results are outlined in this report.

## Description of the case

The case of a 60-year-old man with MRONJ of the upper jaw on the right in the region of 14, 15, and 16 is reported. From the patient's clinical background, it was found that in 2012 he underwent surgery for prostate cancer. In 2014, the patient started treatment with BP (Xgeva and later Zometa) after the detection of bone metastases. The patient was admitted for hospital treatment with complaints of severe pain in the upper right premolar. The intraoral examination revealed a fractured tooth 15 and lesion of the mucosa in the root area.

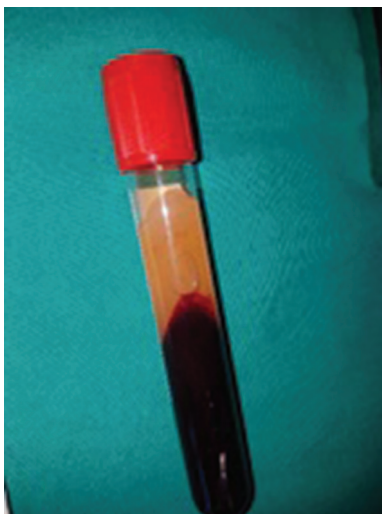
The patient underwent a professional oral-



**Figure 1.** Initial intra-oral clinical presentation of the lesion in area 15

hygiene session one week before the extraction, and also local antiseptic therapy with 0.2% chlorhexidine in the mouth twice daily. Antibiotic treatment was administered before the intervention for three days: amoxicillin, 1 g (tablets) 1 tablet every 8 hours), and continued for one week after the extraction.

The PRF membrane was made immediately before the intervention. In two sterile tubes of 20 ml, blood samples were collected on the intervention day without any anticoagulant. The samples were centrifuged once at 3000 rpm for 10 minutes. At the end of the centrifugation, separate fractions were expected: the formation of a so-called platelet-poor plasma in the upper part, and the concentrated red cells in the lower part of the tube. The dense PRF clot was visible, as shown in Figure 2.



**Figure 2.** A test tube with platelet-rich fibrin (PRF) obtained from the patient's blood



**Figure 3.** Intra-oral clinical view after 24 hours after the intervention

After the administration of intraoral local anesthesia by tissue infiltration (2% mepivacaine mg/ml + 1:100,000 adrenaline), the mucoperiosteal flap was repaired and after that atraumatic extraction of teeth 14, 15 and 16 was performed. The next step was to excise the osteonecrotic tissue and application of two layers of PRF. The final stage was adapting and sewing of the mucoperiosteal flap (Figure 3). The healing process was without complications.

Six months after the surgery, a complete restoration of continuity of the area had occurred. There were no signs of new inflammatory foci (Figure 4).



**Figure 4.** Intraoral view, six months after treatment - without complications, completely relaxed upper jaw

## Discussion

Data from many studies have confirmed that 60% of MRONJ cases result from dental extraction and other surgical interventions, made under a routine protocol. As the mechanism of BP makes it difficult for bone wounds to heal, the risks associated with causing injury after oral surgery, such as dental extraction, have increased [1,2,4].

In clinical practice, mainly conservative treatment methods for osteonecrosis are used: necrectomy, debridement, antibiotic treatment, local antiseptics, and physiotherapy [11]. However, in recent years, surgical treatment has taken precedence over conservative treatment, based on the experience already gained by some authors [12]. In 2005, Marx and colleagues reported the failure of conservative treatment



in 119 of 119 cases [8]. Data from 97 studies involving 4867 patients showed that surgical treatment is more successful than conservative [9]. The problem with surgical treatment is the inability to make an objective clinical assessment of the extent of osteonecrosis of the jaw.

Tsolov et al. [13] have conducted a study to monitor the healing process in patients with MRONJ after the conservative and surgical treatment of patients in Bulgaria in 2018. The study included 237 MRONJ patients, divided into two groups – one treated surgically, using platelet-rich fibrin membranes, in addition to the standard surgical protocol, and another group that received conservative treatment. The results showed that healing after surgical treatment for osteonecrosis was faster and more favorable compared to that after conservative treatment. In Bulgaria, MRONJ incidence is continuously increasing in cancer patients treated with intravenous bisphosphonates [14]. In 2017, Chisini, L. et al. concluded that the PRF method could improve clinical translational therapies, based on the use of PRF cultured cells and has significant regenerative potential in dentistry [10]. Concerning its contribution to bone regeneration and limiting osteonecrosis after extraction, including soft tissue regeneration, treatment with PRF might be a key factor. Platelet-rich fibrin could stimulate the healing process by promoting re-epithelialization. Besides, to minimize bacterial contamination, it is recommended that the extraction is sutured well in tooth extraction in patients treated with BP. In this way, complete wound closure is achieved [1,6].

In the literature, authors aiming to prevent osteonecrosis describe some clinical and pharmacological valves or the release of periosteum. In this manner, the invasiveness of the surgical procedure can be reduced, and atraumatic tooth extraction could be performed, if using the PRF minimizes the invasiveness of the surgical procedure [1,4].

The reported case showed that autologous PRF used in surgical treatment allows for acceleration of bone healing, as shown by a thicker buccal bone wall, higher bone density, and lower bone resorption.

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