

## Resection of the Lower Jaw after a Pathological Fracture Caused By Medication-Related Osteonecrosis of the Jaw

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**ABSTRACT:** The aim of this paper is to present a case of a 65-year-old woman who was diagnosed with cancer of the right mammary gland in 2012 and two years later were found metastases in the bones and in the skin. She underwent chemotherapy with Xgeva and Zometa. Later after a tooth extraction, the patient was diagnosed with osteonecrosis on the right lower jaw. During the years the patient underwent several treatments, including antibiotic therapy, repeated treatment with bone cutters under local anesthesia of the exposed osteonecrosis area of the lower jaw. The patient was referred to the Clinic of the University Hospital "St. George" in Plovdiv with extra-oral fistula and leakage of purulent exudate and severe pain. A CT scan of the head and facial bones revealed a pathological fracture on the right side of the lower jaw in the osteonecrosis area. According to the characteristics of the case and adapting the best treatment for the patient's case was performed a resection of the necrotic area and the fracture area of the right jaw.

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### I. INTRODUCTION:

Medication-related osteonecrosis of the jaw (MRONJ) is defined as exposed bone in the oral cavity or extra-oral fistula in the maxillofacial region that does not heal within 8 weeks, in a patient who is currently receiving bisphosphonate medication and has no history of radiotherapy to the head-neck region or metastatic disease in the jaw. Risk factors for the disease are medication-related, local, demographic and systemic factors. MRONJ has a negative effect on quality of life, and can result in reduced social contact, pain and masticatory difficulties. A variety of medications pre-dispose patients to MRONJ. The disease is a common side effect of drug therapy applied to cancer patients for bone metastasis, multiple myeloma, and osteoporosis.

**Purpose:** The main purpose of the article is to present a case of surgical treatment of medication-related osteonecrosis of the jaw and to provoke awareness of MRONJ among dentists who should refer their patients to oral and maxillofacial surgeons, experienced in the treatment of patients with this disease.

**Case report:** Our article is based on the case of patient, diagnosed with the condition medication-related osteonecrosis of the jaw, who underwent surgical treatment in University Hospital "St. George", Plovdiv, Bulgaria. The patient responded well to the procedure, there were no postoperative complications or wound infections.

**Conclusion:** This case highlights the importance of lowering the risk of osteonecrosis of the jaw in cancer patients after drug therapy, the need of regular dental examinations because this will minimize the development of osteonecrosis of the jaw, and the accurate treatment of MRONJ. Even though complete prevention of MRONJ is not currently possible, the level of oral health is an important factor for the indication of intravenous bisphosphonates treatment. It is very important to improve the oral hygiene which combined with the regular dental examinations will allow local infection to be managed as early as possible and increases the quality of life in these group of patients.

**KEY WORDS:** *osteonecrosis, medication-related osteonecrosis of the jaw, bisphosphonates, pathological fracture, prevention, Gigli wire saw*

### I. INTRODUCTION

In 2003 Marx is the first who reports osteonecrosis of the jaw due to intravenous bisphosphonates and at the time, the disease was classified as bisphosphonate-related osteonecrosis of the jaw (BRONJ).<sup>1</sup> Later the development in diagnosing, treating and monitoring the disease revealed the correlation with drugs other than the bisphosphonates, so the American Association of Maxillofacial Surgeons standardized the diagnostic criteria for BRONJ in 2009, and updated the disease to Medication-related osteonecrosis of the jaw (MRONJ),

eventually merging both diseases in 2014.<sup>2,3</sup> Even though the most common clinical sign of MRONJ (up to 93.9%) is an exposed necrotic bone, it's important to underline that when diagnosing a patient with this disease, all of the following five criteria need to be satisfied: the patient has an exposed bone, or bone that can be probed through a fistula: either intra-orally, or extra-orally; the bone has been exposed for at least 8 weeks within the maxillofacial region; the patient has a history of using anti-resorptive or antiangiogenic drugs; there is no patient history of head and neck radiotherapy; there is no recognizable metastatic disease to the head and neck region.<sup>2,4,5</sup>The number of patients with MRONJ has grown recently. MRONJ has a negative effect on quality of life, and can result in reduced social contact, pain and masticatory difficulties.<sup>5</sup> A variety of medications predispose patients to MRONJ. The disease is a common side effect of drug therapy applied to cancer patients for bone metastasis, multiple myeloma, and osteoporosis. Common drugs implicated in MRONJ are bisphosphonates, receptor activator of nuclear factor- $\kappa$ B ligand (RANKL) inhibitors and anti-angiogenic drugs.<sup>5</sup>Bisphosphonates are some of the frequent used drugs for cancer-related conditions.<sup>6</sup>They have a significant positive effect for patients with advanced cancer, but on the other side, MRONJ is one of the main complications.They inhibit bone resorption and thus bone renewal by suppressing the recruitment and activity of osteoclasts thus shortening their life span.<sup>7</sup> The greater the duration of treatment with bisphosphonate medication, the higher is the risk of developing MRONJ.<sup>8</sup> In addition to the medication-related, there are also other risk factors, such as local ones - tooth extraction or other dentoalveolar procedures, as well as demographic and systemic ones - age, sex, corticosteroids, tobacco use, etc. Some of the main treatment goals for patients at risk of developing or who already have MRONJ, are prioritization and support of continued oncologic treatment in patients receiving antiresorptive and antiangiogenic therapy.<sup>4</sup> As the infection is one of the major factors in the development of medication-related osteonecrosis of the jaw to minimize the development of MRONJ in patients at risk regular dental examinations are encouraged, oral hygiene should be improved so local infection is managed as early as possible due to the fact that bacteria stimulate bone resorption and contribute to bone necrosis.<sup>4</sup>

## II. CASE REPORT

The patient in our case report is a 65-year-old woman who was diagnosed with cancer of the right mammary gland in 2012. In 2014 metastases were found in the bones and skin of the body. After that, she underwent chemotherapy with Xgeva and Zometa. In 2015, after a tooth extraction, the patient was diagnosed with osteonecrosis on the right lower jaw (Fig. 1).

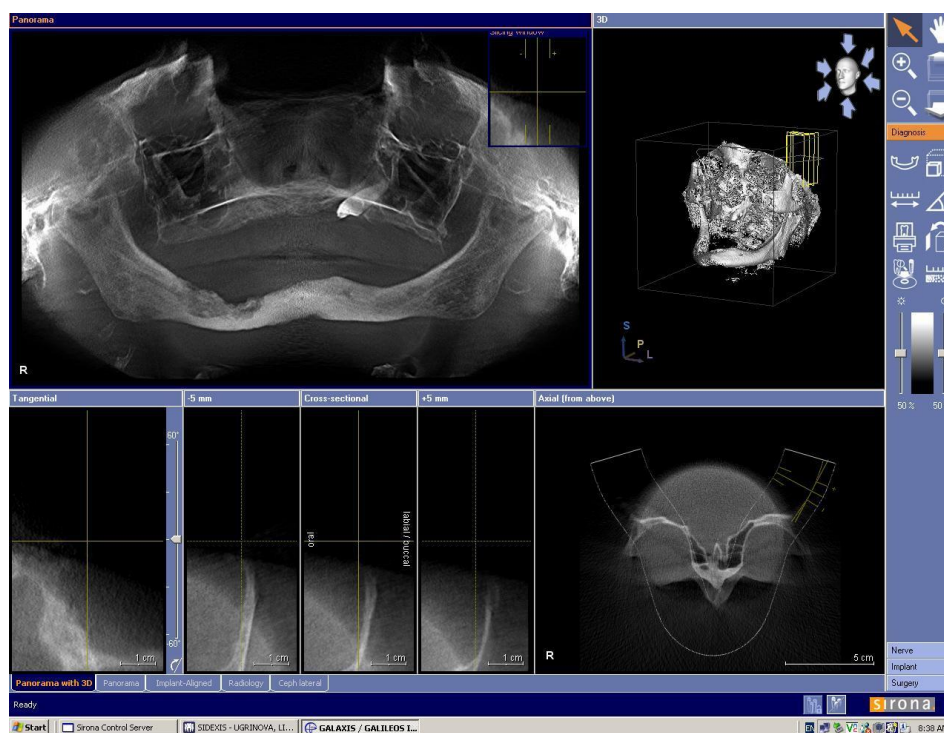


Fig. 1. Scan proving osteonecrosis of the lower jaw

There is a high risk a dental extraction to result in MRONJ especially in case of patients who were medically treated with bisphosphonates and RANKL inhibitors as it is in our case – with Xgeva and Zometa.<sup>5</sup> During the years the patient underwent several treatments, including antibiotic therapy, repeated treatment with bone cutters under local anesthesia of the exposed osteonecrosis area of the lower jaw.

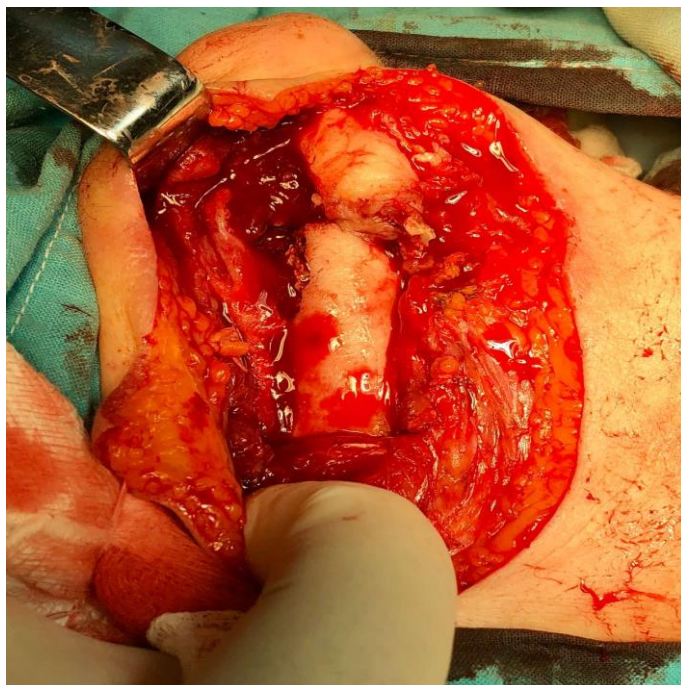
The patient was admitted to the Clinic of the University Hospital "St. George" in Plovdiv with extra-oral fistula (Fig. 2) and leakage of purulent exudate and severe pain. A CT scan of the head and facial bones was performed, which revealed a pathological fracture (Fig. 3) on the right side of the lower jaw in the area of the osteonecrosis area. Pathological fracture with extra-oral access is described in Fig. 4.



**Fig. 2.** Extra-oral fistula of the lower jaw



**Fig. 3.** Scanner proving a pathological fracture

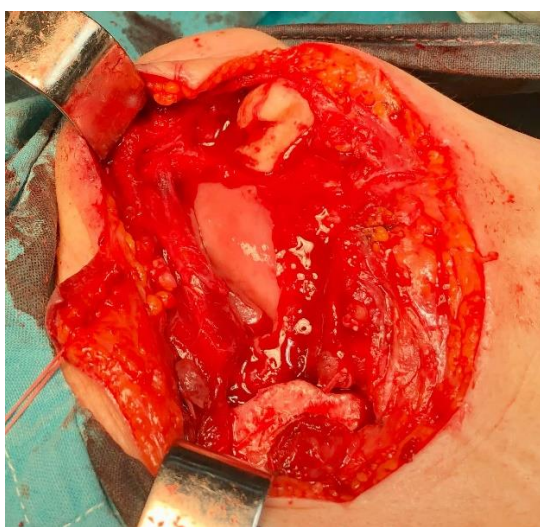


**Fig. 4.** Pathological fracture with extra-oral access

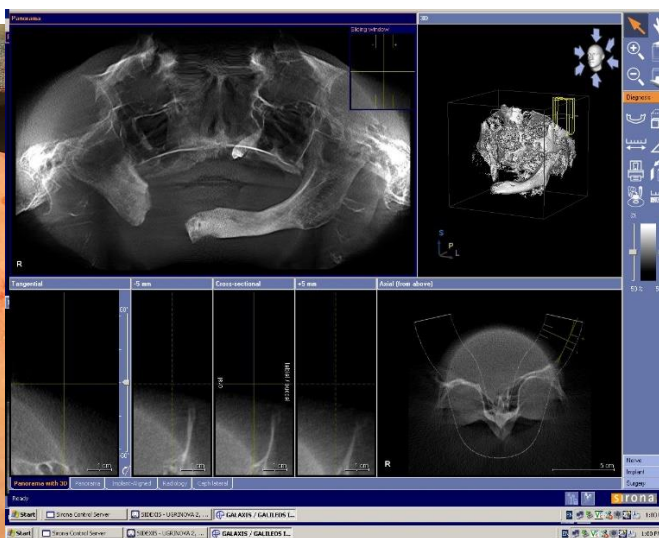
After one week of preparation, during which the patient was treated with antibiotic therapy, two bags erythrocyte concentrate transfusion and TOT'HEMA ampoules (due to patient's low hemoglobin and iron



levels), a resection of the necrotic area and the fracture area of the right jaw was performed (Fig. 5). Fig. 6 describes a CT scan of the lower jaw after resection.



**Fig. 5.** Resected lower jaw

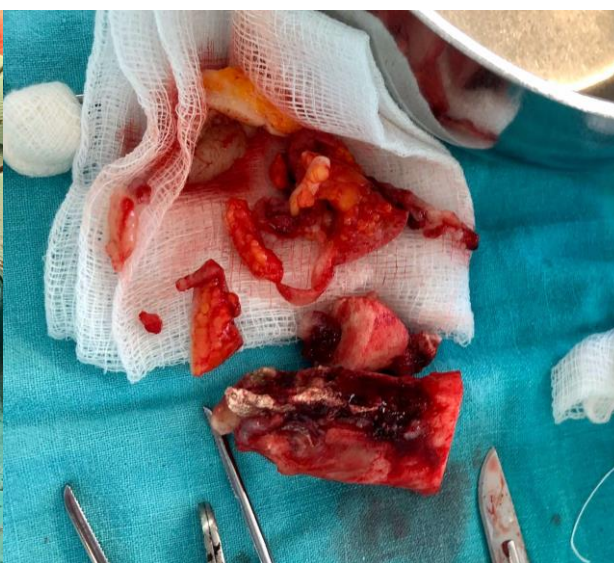


**Fig. 6.** A CT scan of the lower jaw after resection

The surgical procedure was performed under general anesthesia with extra-oral access. A Gigli wire saw was used for the resection of the lower jaw (Fig. 7). On Fig. 8 is described the surgical specimen sent for histopathological examination and on Fig. 9 – the suture of the wound.



**Fig. 7.** A Gigli wire saw was used for the resection



**Fig. 8.** The surgical specimen sent for histopathological examination



**Fig. 9.** Suture of the wound

### **III. DISCUSSION**

Usually the first who identify signs and symptoms of MRONJ are the dentists. In this case it is very important for the patient to be referred to oral and maxillofacial surgeon or an oral oncology center, experienced in the treatment of patients with MRONJ.<sup>6</sup>In the best case the patient should visit oral and maxillofacial surgeon or an oral oncologist who works at the same hospital to facilitate communication between care providers. So it is necessary to underline that a collaborative approach involving dentists, prescribing doctors and pharmacists is crucial to prevent the occurrence of consequences such as MRONJ or at least to start the right treatment of the disease before it becomes more complicated and there is need of resection of the bone. The important role of oral medicine physicians in prevention and treatment of osteochemonecrosis is inevitable as early prevention and accurate treatment increases quality of life in this group of patients. The risk of MRONJ is pronounced in oncological patients treated with bisphosphonates intravenously in relatively large doses and during a longer period of time, especially with highly potent nitrogen-containing bisphosphonates pamidronate and zoledronate.<sup>9</sup>The management of patients presenting with MRONJ depends on the severity and classification of MRONJ and the treatment options range from conservative management with observation, to surgical intervention.<sup>5</sup>

Our patient was in stage 3 of MRONJ, defined as exposed and necrotic bone or fistula that probes to bone with evidence of infection and at least one of the following: 1. Exposed necrotic bone extending beyond the region of alveolar bone to the inferior border and ramus in the mandible, maxillary sinus, and zygoma in the maxilla; 2. Pathologic fracture; 3. Extra-oral fistula; 4. Oral antral or oral nasal communication; 5. Osteolysis extending to the inferior border of the mandible or sinus floor.<sup>4</sup>Treatment of MRONJ varies with the stages of the disease. The American Association of Oral and Maxillofacial Surgeons recommends for stage 3 of MRONJ treatment with antibacterial mouthwashes, analgesics to control pain, and antibiotics to control infection, superficial debriding to relieve soft tissue irritation but surgical debridement/resection of the necrotic bone is also indicated. According to the characteristics of our case and adapting the best treatment to the patient's needs, we decided to apply at first antibiotic therapy and pain control and then surgical resection for longer-term palliation of infection and pain. The surgical intervention included resection of the necrotic bone with flexible Gigli wire saw, which was the preferred tool because it is minimally invasive and does not burden the healthy bone. During the surgery a tension-free primary closure has been achieved. The surgical wound healed successfully and the patient responded well to the procedure. There were no postoperative complications or wound infections, which are usually common in the postoperative period for people with MRONJ.

### **IV. CONCLUSION**

The benefits of prescribing bisphosphonates are significant, but they do come with well-documented oral risks so regular dental examinations should be encouraged for patients at risk because this will minimize the development of osteonecrosis of the jaw.<sup>5</sup> The prevention and management of osteoporosis is of extreme importance. Unfortunately, complete prevention of MRONJ is not currently possible but since there is a significant risk of jaw osteonecrosis in oncological patients, the level of oral health is an important factor for the

indication of intravenous bisphosphonates treatment.<sup>9</sup> It is very important to improve the oral hygiene which combined with the regular dental examinations will allow local infection to be managed as early as possible. In lowering the risk of osteonecrosis of the jaw helps the use of antibiotics before and after oral surgical procedures and daily use of antimicrobial mouth rinses.

**Author Contributions :** Dr. Rosen TSOLOV is responsible for the diagnostic procedures, clinical diagnosis, treatment decisions, performed the surgery and also wrote the manuscript. Assoc. Prof. Georgi YORDANOV has read and agreed to the published version of the manuscript.

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