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Surgical management of medication-related osteonecrosis of the jaw: a retrospective study of Mronj patients

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Treatment for patients with Mronj vary according to stage. Purpose of this study is to inform the effectiveness of surgical treatment on Mronj stage 2 and 3 patients. We investigated the success rates and treatment outcomes of two stages of Mronj patients who received surgical treatment from March 2019 to May 2021 at Oral and Maxillofacial Surgery Department, Ewha Womans University Seoul Hospital. Total of 55 patients who underwent surgical treatment were studied. Data was collected by analyzing clinical and radiological findings. Of the 54 patients observed, 36 stage 2 patients ended treatment within six months of surgery and 4 out of 18 stage 3 patients went through another surgery. From the study, we could conclude that treating Mronj patients with aggressive surgical intervention properly enables reconstruction of settled oral environment. **(THE JOURNAL OF KOREAN ACADEMY OF OSSEOINTEGRATION 2021;13(1):36-41)**

Key words: Mronj, Surgical treatment, Bone morphogenic protein

INTRODUCTION

American Association of Oral and Maxillofacial Surgery (AAOMS) defines Medication - related osteonecrosis of the jaw (Mronj) as ischemic necrosis of the jaw caused by current or previous treatment with antiresorptive or antiangiogenic agents.

Mronj can be diagnosed from exposed bone or bone probed through an intraoral or extraoral fistula in the maxillofacial region that has persisted for more than 8 weeks, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.

Treatment for patients with Mronj vary according to stage. When treating patients in stage 1 and 2, conservative treatment—taking antibiotics and gargling with 0.12% chlorohexidine is recommended (Figure 1). However, many authors have recently supported the positive effect of resecting the affected area, expecting symptoms to relieve quickly.

Choi et al.[1] confirmed the success rate of surgical treatment of Medication - related osteonecrosis of the jaw (Mronj) by analyzing the outcomes of treatment. Of the 116 study subjects, 96 (83.0%) terminated treatment within 6 months of surgery, and 20 (17.0%) terminated treatment after 6 months or more. Treatment failure was observed in seven patients (6.0%). Purpose of this study was to inform the effectiveness of surgical treatment on Mronj stage 2 and 3 patients.

MATERIALS AND METHODS

We investigated the success rates and treatment outcomes of two stages of Mronj patients who received surgical treatment from March 2019 to May 2021 at Oral and Maxillofacial Surgery Department, Ewha Womans University Seoul Hospital.

Total of 55 patients who underwent surgical treatment were studied, 34 patients diagnosed as stage 2 and 21 patients as stage 3.

Data was collected by analyzing clinical and radiological findings. Items included in the analysis were as follows: (1) sex / age, (2) cause of necrosis (medication), (3) dental risk factor, (4) region of necrosis (5) stage of disease (6) number of surgery.

1. Surgical procedure

Surgical treatment of patients included removing the sequestrum and saucerization of adjacent cortical bones to achieve blood

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Figure 1. Clinical pictures of Stage 2 Mronj showing exposed, necrotic bone.

circulation. Then curettage of granulation tissues were done in conjunction with recombinant human bone morphogenic protein (rhBMP-2) using collagen sponges as carriers. Finally, Leukocyte-rich and platelet-rich fibrin (L-PRF) insertion was held before flap closure of the operation site (Figure 2).

2. Case I

The first patient, an 83-year-old woman, was a patient with systemic diseases such as high blood pressure, arteriosclerosis, and osteoporosis. She was diagnosed with Mronj in October 2019 and was admitted to Department of Oral and Maxillofacial Surgery, Ewha Womans Seoul Hospital. Sequestrectomy of necrotic bone was performed under sedation and bone morphogenic protein was transplanted. After antibiotic adjuvant therapy during the hospitalization period, symptoms improved and she was discharged from the hospital in November 2019. Afterwards, the patient started Forsteo injection from December 2019, and was injected until March 2020. No further bone necrosis was observed, and it remained without complaints of pain (Figure 3).

3. Case II

The second patient, a 70-year-old woman with osteoporosis, was admitted to Department of Oral and Maxillofacial Surgery,

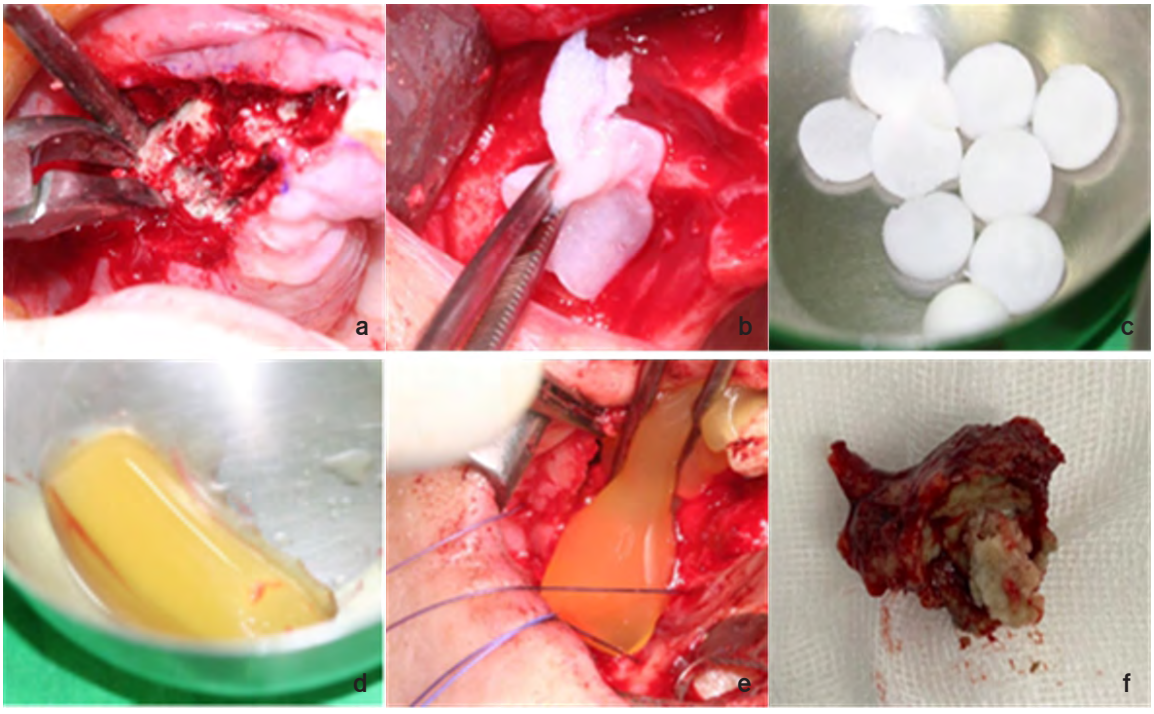

Figure 2. Surgical procedure of mronj stage 2 patients. (a) Removal of sequestrum. (b) Insertion of BMP. (c) BMP preparation. (d) PRF preparation. (e) Insertion of PRF before flap closure. (f) Removed sequestrum.

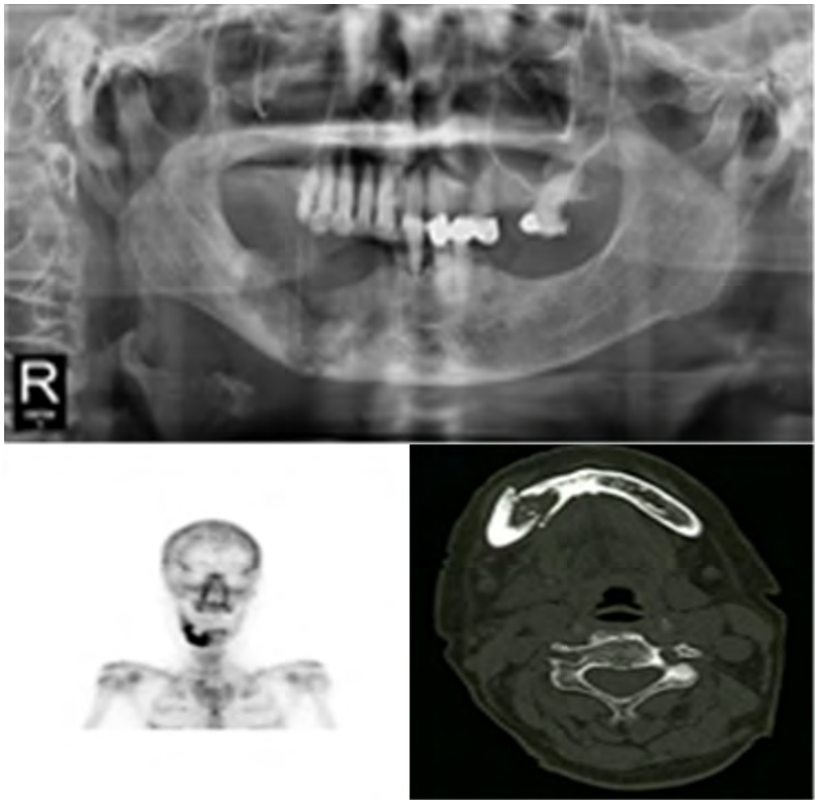

Figure 3. Panorama, CBCT, and bone scan of patient before operation (case 1).

Figure 4. Panorama, CBCT, and bone scan of patient before operation (case 2).

Ewha Womans Seoul Hospital for persistent pain after extraction of #34i and 35i implants. She was diagnosed with Mronj and hospitalized in August 2020. Sequestrectomy of necrotic bone was performed under general anesthesia and bone formation-inducing protein with platelet-rich fibrin were transplanted into the affected bone. Antibiotic adjuvant therapy was performed, symptoms improved, and the patient was discharged. Continuous follow-up was conducted and normal healing state was maintained (Figure 4).

RESULTS

In this retrospective study, 54 Mronj patients were enrolled to a surgical procedure. Patients' data were acquired analyzing clinical and radiological findings, including sex, age and medical records, any underlying primary diseases such as cancer and osteoporosis (Table 1). Overall, the mean age was 75.59 years old.

A total of 37 patients received Mronj related medication for the treatment of osteoporosis, and 17 patients administered medication including zoledronic acid from cancer and cardiovascular diseases. 33 out of 54 patients showed Mronj symptoms at their mandible region, which was 1.5 times the amount of maxilla symptoms. Characterization of the Medication - related osteonecrosis of the jaw (Mronj) is reported in Table 2.

Patients followed up at 7 to 10 days after surgery, and three to six months after then. Healing state of the bone were evaluated based on panoramic radiograph clinical examination (Figure 5). When symptoms worsened without healing during follow-up, another surgery was considered. Of the 54 patients observed, 36 stage 2 patients ended treatment within six months of surgery, and 4 out of 18 stage 3 patients went through another surgery.

DISCUSSION

Medication-related osteonecrosis of the jaw (Mronj) is primarily an adverse side effect of denosumab or bisphosphonates, or possibly anti - angiogenic cancer treatment. In general, the incidence of Mronj increases as the duration of drug administration increases[8], and is increased by antiresorptive agents like denosumab, which confer greater risk of Mronj than bisphosphonates. However, our data analysis shows that developed stages of Mronj does not correlate with the medical intake between osteoporosis and cancer patients.

In Min and Kang's study[4], use of rhBMP on bone defect sites after sequestrectomy increases the rate of new bone formation. Therefore, use of rhBMP on bone defect sites after sequestrec-

Table 1. Symptoms before surgery by patients with Mronj

Pus	Sinusitis	Bleeding	Bone exposure	Swelling	Pain	Bone fracture
20	5	2	3	17	17	1

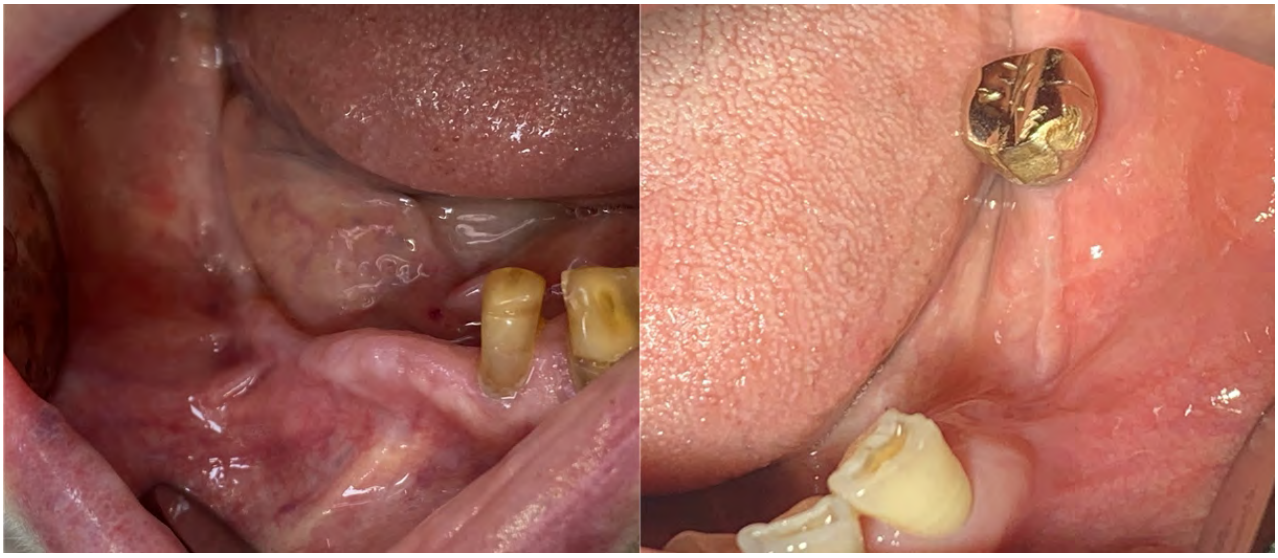

Figure 5. 6 months post-operative state (case 1, 2).

Table 2. Clinical characteristics of patients with Mronj

	Patients (n = 54)	Percentage (%)
Sex		
F	43	79.63
M	11	20.37
Age	75.59 (average)	
Osteoporosis	37	68.51
Non–osteoporosis	17	32.49
Cancer	9	17.68
Breast	2	
Prostate	1	
Multiple myeloma	1	
Stomach	4	
Cardiovascular disease	8	14.81
DM	14	25.95
Nervous system disease	4	7.4
Hypertension	31	57.4
Stage		
II	36	66.66
III	18	33.33
Region of necrosis		
Maxilla	21	38.89
Mandible	33	61.11
Dental risk factor		
Denture	13	24.07
Implant	21	38.89
Extraction	14	25.92
No dental factors	6	11.11
Inflammation findings including actinomycosis	12	22.22
Number of surgery		
Once	50	92.59
Twice	3	5.55
Third time	1	1.85

tomy could be a successful strategy in treatment of Mronj patients. Cicciù et al.[5] investigated the clinical effects of rhBMP in Mronj patients undergoing sequestrectomy and reported successful healing of the necrotic region. In their study, the experimental group identified an increase in radiographic index 6 months after surgery (Wilcoxon signed rank test, $P < 0.05$). In addition, there was a statistically significant difference in the radiographic index increase between experimental and control groups (Mann–Whitney U-test, $P < 0.05$), which may be the result rhBMP facilitating bone healing. This result suggests that rhBMP contributes to new bone formation.

PRF, containing white blood cells in combination with neutrophils and platelets, is able to enhance tissue wound healing, improve angiogenesis, and enhance tissue formation. In particular, the peculiarity of PRF consists in acting as a scaffolding material in which leukocytes, macrophages, neutrophils, and platelets present in supraphysiological doses release chemotactic factors and growth factors for wound healing[3]. So the use of PRF can improve the outcome of wound healing preventing osteonecrosis and leading to an early epithelization[6].

Marcianò et al.[2] also emphasized that surgical treatment of Mronj is a reliable approach to the disease, and they confirm that appropriate soft tissue management procedures represent an additional guarantee against wound dehiscence, favoring the release of endogenous growth factors and leading to the successful healing of Mronj disease.

CONCLUSION

This study was conveyed to determine the effectiveness of surgical treatment on stage II and III Mronj patients. 50 out of 54 Mronj patients (92.5%) in all stages achieved effective healing state after surgical treatments and failed in only 4 (7.4%) patients. Four patients in the failure group were initially diagnosed as

Mronj stage III before treatment and went through additional surgeries. From the study, we could conclude that treating Mronj patients with aggressive surgical intervention properly enables reconstruction of settled oral environment.

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