

# Retrospective study of patients with medication-related osteonecrosis of the jaw treated conservatively



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## Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is often difficult to treat once it occurs. MRONJ causes pain and other adverse events, markedly impairing quality of life for patients. Furthermore, because the number of affected cases is rising annually, diversification of treatment options is also necessary.

## Objectives

In Japan, with respect to treatment strategies for MRONJ, cases with malignant tumors and osteoporosis (injectable and oral medications) are regarded as the same. Because aggressive surgical therapy allows early coverage of exposed bone, many studies recommend surgical therapy. However, when only patients with malignant tumors are considered, numerous cases are inevitably managed mainly with conservative therapy for the following reasons: patients do not want to change their treatment schedules because continuous administration of antitumor agents is effective; surgical therapy is not feasible because of poor general conditions; and patients refuse surgical therapy. We herein report a retrospective study of cases in which MRONJ that occurred during treatment of malignant tumors was conservatively managed.

## Methods

This retrospective study was conducted on 79 patients with malignant tumors who visited our department between 2010 and 2016, were diagnosed as having MRONJ, and received conservative therapy.

## Results

male	38	( 49%)
female	41	( 51%)
Median of age	68 ( 45 - 86 )	
Primary Site of disease	n=79	
breast cancer	25	32%
Prostate Cancer	22	28%
Lung Cancer	15	19%
multiple myeloma	6	7%
kidney cancer	4	5%
the others	7	9%

Time to onset	
Median	22months ( 3 – 112 months)

medicine	
denosumab	39
Zoledronic acid	35
denosumab	4
Zoledronic acid	
Bevacizumab	1

Affected jaw		
maxilla	27	34%
mandible	51	65%
maxilla	1	1%
mandible		


Pathogenesis		
tooth extraction	23	29.1%
marginal or apical periodontitis	29	36.7%
ill-fitting dentures	13	16.4%
unknown	13	16.4%

	Stage 0	stage1	stage2	stage3	Total
n	17	3	59	0	79
better	2	1	24	0	27
stable	10	2	36	0	48
worse	4	0	0	0	4

	Stage 0	stage1	stage2	
antimicrobial agents				
AMPC	3	0	21	24
AMPC→CLDM	1	0	4	5
CLDM	7	0	25	32
CLDM→AMPC	3	0	5	8
SBTPC	0	0	2	2
AMPC+ (AMPC+ CVA)	0	0	1	2
The others	0	0	3	3
none	0	3	0	3


### Case 1

A 55-year-old woman had been treated with denosumab as part of a palliative care regimen for breast cancer and multiple bone metastases at a local hospital. She underwent tooth extraction at its dental department. After the procedure, jaw pain and bone exposure persisted. Because no resolution was achieved despite continuous treatment with disinfection, oral administration of sitafloxacin hydrate, etc., she visited the dental department of our hospital. The gingiva around the exposed bone was swollen, and compression of the swelling resulted in purulent discharge and jaw pain. After discussion with the patient, conservative therapy was initiated. Continuous oral care and proper use of an antibiotic agent (clindamycin 900 mg 3×) reduced the exudate and pain, although extensive bone exposure persisted. Her symptoms were well controlled until her death.



### Case 2

A 57-year-old woman visited our dental department for mandibular pain and bone exposure, which had developed while she was receiving chemotherapy (Perjeta, Herceptin, and gemcitabine) in combination with zoledronic acid for breast cancer, multiple bone metastases, brain metastasis, and lung metastasis. Compression of the lesion resulted in purulent discharge and severe jaw pain. Because surgery was considered to involve extensive tooth loss, conservative antibiotic therapy (clindamycin 900 mg 3× for 5 months, amoxicillin 1500 mg 3× for 5 months) was administered after discussion with the patient. This long-term antibiotic regimen reduced the exudate and prevented progression of bone exposure. The dental prosthesis was retained, while she was able to eat a general diet, until her death.



• Patients with an increase in the number or size of bone exposure sites, despite the MRONJ stage not progressing during long-term antibiotic therapy

increase in the number or size of bone exposure sites	n=6			
Primary Site	Prostate Cancer(2)	multiple myeloma (2)	Lung Cancer(1)	Ureteral Cancer(1)
Pathogenesis	marginal or apical periodontitis(3)	unknown (2)	ill-fitting dentures (1)	
Affected jaw	maxilla(3)	mandible( 3)		
antimicrobial agents	AMPC(2)	CLDM (4)		
Factors favoring exacerbation	impaired renal function (4)	prolonged poor oral hygiene (2)		

## Conclusions

In patients treated with bone-modifying agents (BMAs), osteonecrosis of the jaw can occur even without invasive dental procedures. We advocate, for the prevention of periodontal disease and denture ulcer, continuous oral hygiene interventions and cooperation between physicians and dentists before administration of BMAs. When surgery is not feasible (difficulties related to changing treatment schedules, poor general conditions due to primary diseases, and refusal of over-invasive or surgical procedures), many patients can be managed with conservative therapy. At our hospital, treatment of primary diseases is prioritized in principle. Even if MRONJ occurs, BMAs will not be discontinued or suspended. However, in our view, consideration should be given to discontinuation of BMAs followed by conservative management, as well as addition of surgical therapy, in cases including but not limited to the following: contamination persists despite repeated explanation of oral care because a patient poorly understands the care procedures, and types and doses of applicable antibiotics are limited because of impaired renal function. In patients with malignant tumors who develop MRONJ, surgical therapy should not be the first choice to aggressively achieve cure. Instead, sufficient consideration should also be given to conservative management for pain relief, control of symptoms, etc. It seems that appropriate long-term antibiotic therapy can be as effective a treatment option as surgical therapy.