Factors associated with treatment outcomes for medication-related osteonecrosis of the jaw

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Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is refractory osteonecrosis caused by side effects of antiresorptive agents (ARAs). Conservative therapy was previously recommended as the first-line treatment, but recently there have been many reports showing the efficacy of surgical therapy. We have also made surgical therapy the standard treatment for MRONJ, but there are cases in which complete healing cannot be obtained even after surgery. In this study, we investigated factors associated with poor treatment outcome in cases of mandibular MRONJ surgery.

Materials and methods

Subjects are 66 surgeries out of 55 patients of mandibular MRONJ who underwent surgery from 2016 to 2022. Age, sex, primary disease, type of ARA, diabetes, steroids, CT findings (separation of sequestrum, osteolysis, periosteal reaction (Fig. 1), surgical method, and treatment outcome were investigated from medical records. Patients where all symptoms including bone exposure disappeared were defined as healing, and the others were defined as non-healing.

Results

Patient characteristics were shown in Table 1.
Resection of sequestrum was performed in 3 patients, marginal mandibulectomy in 43, and segmental mandibulectomy in 20. The cumulative healing rate was 95.8% for patients with osteoporosis and 79.0% for patients with malignant tumors (Fig. 2).

In univariate Cox regression analysis, factors associated with poor outcome were malignant tumor, DMB, no separation of sequestrum, and no osteolysis (Fig, 3). Multivariate analysis showed that malignant tumor was significantly correlated with poor outcome (Table 2).
In some patients treated with DMB, no osteolysis was observed on CT, and it was difficult to determine the extent of bone resection, which may have affected the poor treatment outcome (Fig. 4).

Fig. 1 CT findings

Osteolysis | Periosteal reaction | Mixed-type osteosclerosis

Fig. 2 Treatment outcome

Primary disease

Table 1 Patient characteristics

Variable		Number of patients / mean ± SD
Sex	male	18
	female	37
Age (years)	mean ± SD	74.7 ± 9.69
Stage	stage 0	3
	stage 1	3
	stage 2	35
	stage 3	14
Primary disease	osteoporosis	24
	malignant tumor	31
Sort of ARA	BP	21
	DMB	26
	BP→DMB	8
Duration of ARA admistration (months)	mean ± SD	44.8 ± 36.5
Drug holiday > 3 months	(-)	37
	(+)	17
Corticosteroid	(-)	38
	(+)	17
Diabetes	(-)	43
	(+)	12
Separation of sequestrum	(-)	38
	(+)	17
Osteolysis	(-)	8
	above mandibular canal	25
	including mandibular canal	8
	including lower edge	14
Periosteal reaction	(-)	38
	attached type	7
	gap type	6
	irregular type	4
Osteosclerosis	(-)	29
	uniform type	13
	mixed type	13
Number of teeth		17.2 ± 8.81
Leukocytes (/μL)		6496 ± 2383
Albumin (g/dL)		3.75 ± 0.518
Creatinie (mg/dL)		1.03 ± 0.949
Total		55

Table 2 Factors related to treatment outcome

Variable		p-value	HR	95% CI
i) Univariate analysis				
Sex	female / male	0.093	1.757	0.909-3.397
Age	year	0.053	1.040	1.000-1.083
Stage	stage 3/2/1/0	0.411	1.233	0.749-2.028
Primary disease	malignant tumor / osteoporosis	<0.001	0.316	0.172-0.581
Dabetes	(+) / (-)	0.164	1.645	0.815-3.318
Corticosteroid	(+) / (-)	0.646	0.858	0.447-1.649
Sort of ARA	DMB or both / BP	0.016	0.666	0.260-0.872
Duration of ARA administration	months	0.003	1.012	1.004-1.020
Separation of sequestrum	(+) / (-)	0.007	2.415	1.280-4.557
Osteolysis	(+) / (-)	0.024	9.820	1.345-71.704
Periosteal reaction	(+) / (-)	0.888	1.047	0.553-1.983
Mixed type osteosclerosis	(+) / (-)	0.057	0.491	0.235-1.022
Number of teeth		0.082	0.968	0.932-1.004
Leukocytes	/μL	0.481	1.044	0.927-1.176
Albumin	g/dL	0.350	1.327	0.733-2.400
Creatinie	mg/dL	0.849	1.037	0.716-1.501
Drug holiday > 3 months	(+) / (-)	0.791	1.089	0.580-2.044
ii) Multivariate analysis				
Primary disease	malignant tumor / osteoporosis	0.032	0.400	0.173-0.926
Sort of ARA	DMB or both / BP	0.430	1.408	0.602-3.292
Duration of ARA administration	months	0.158	1.007	0.971-3.737
Separation of sequestrum	(+) / (-)	0.061	1.905	0.971-3.737
Osteolysis	(+) / (-)	0.082	6.058	0.797-46.015

Fig. 3 Factors related to outcome

Separation of sequestrum | Osteolysis | Sort of ARA
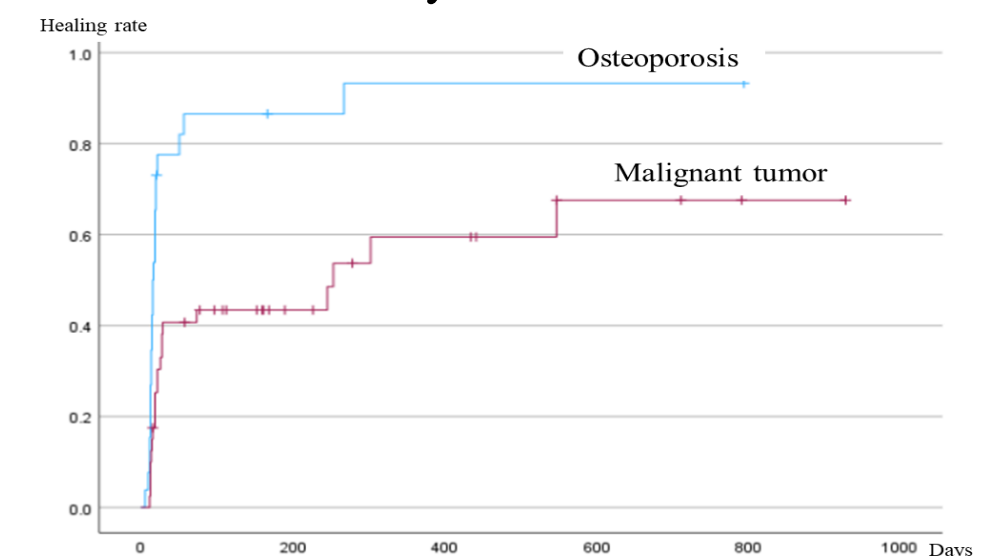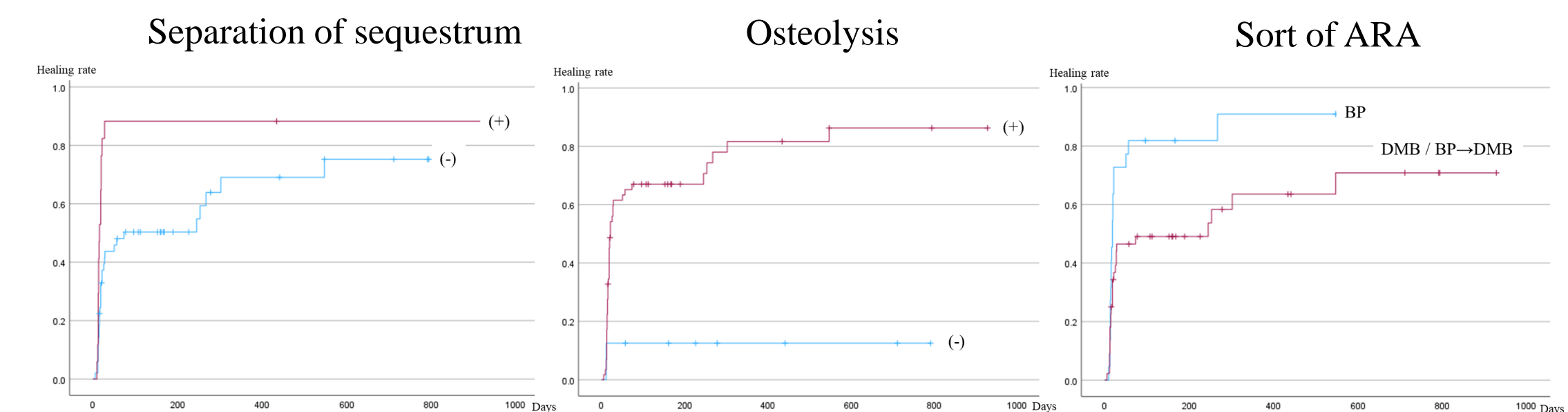
Fig. 4 Patient without osteolysis

Conclusion

Surgery is an effective treatment for mandibular MRONJ. Since no clear conclusions can be drawn due to a small number of cases in a single institution, it is necessary to carefully consider the extent of bone resection in patients with a primary disease of malignant tumor who received DMB.