Osteonecrosis of the jaw and dental extractions: A single-center experience

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Background

- Osteonecrosis of the jaw (ONJ) may develop spontaneously or secondary to local trauma or an infection.
- While extractions should be minimized in patients at risk of developing osteoradionecrosis (ORN) or medication-related osteonecrosis of the jaw (MRONJ), delay in extracting infected teeth- potential risk for ORN/MRONJ.
- No clear consensus regarding the choice, timing, and duration of antibiotic coverage to prevent ONJ.

Objectives

To investigate:

- The frequency of ORN/MRONJ after extraction in patients who received radiation therapy to head and neck (RT-HN) with post-extraction antibiotic coverage, but without prophylactic HBO or anti-resorptive medications;
- Factors associated with the development of ORN/MRONJ

Methods

Retrospective cohort study

Electronic medical records reviewed to identify patients who were "at risk" for the development of ORN/MRONJ and who received dental extractions in Oral Medicine and Dentistry Clinic at Brigham and Women's Hospital (BWH) between January 2003 to October 2019.

Inclusion criteria:

- History of RT-HN and/or exposure to anti-resorptive therapy (bisphosphonates, RANKL inhibitors), and anti-angiogenic agents.
- Underwent dental extractions from 2003 to 2019.

Exclusion criteria:

- Treatment with oral bisphosphonates only,
- Patients who did not receive post-extraction antibiotics for 14 days, and
- Lost to follow-up after extraction(s) (n = 18).

Clinical post-extraction protocol:

- Atraumatic dental extraction.
- Post-extraction prescription of amoxicillin 500 mg TID for at least 14 days (or an alternative broad-spectrum antibiotic for patients allergic to amoxicillin).
- CHX 0.12% rinses BID until complete healing of the extraction site.
- 2-week post-operative follow-up.
- Additional 2-week systemic antibiotic coverage with same antibiotic considered if signs of infection at follow-up.

Statistical analysis

- Descriptive statistics, such as median and range, were used for continuous variables, and frequency(%) was used for categorical variables.
- Differences between patients who developed ONJ vs. those who did not were calculated by using the Pearson's and Wilcoxon's tests.

Results

- Ninety patients underwent a total of 243 extractions.
- Fifty patients (55.5%) received a median of 54.1 Gray to the extraction site and 40 (44.4%) were on antiresorptives. None of the patients received both RT and antiresorptives.
- Of 40 patients, 3 (7.5%) developed MRONJ, and of 50 patients, 1 (2%) developed ORN.
- Among those at risk for MRONJ, male gender and concomitant immunosuppressant medications were associated with MRONJ development (P<.05)

Conclusion

- In our patient cohort, rate of postextraction ORN/MRONJ was lower and comparable with the rates reported in the literature.
- Larger prospective studies required to validate efficacy of postextraction antibiotics in reducing ONJ.

Table I. Primary outcome: development of osteoradionecrosis (ORN) among "at risk" patients

Variable n (%)	*ORN Yes (n = 1)*	*ORN No (n = 49)*	*P value*
Age (years)			
Median (range)	59 (59)	61 (29–90)	.96
Gender			
Male	1 (2)	36 (72)	.51
Female	0 (0)	13 (26)	
Immunosuppressive medications			
No	1 (2)	48 (960)	.97
Yes	0 (0)	1 (2)	
Diabetes Mellitus type II			
Yes	0 (0)	7 (14)	.68
No	1 (2)	42 (84)	
Smoking Status			
Never	0 (0)	21 (42)	.63
Former	1 (2)	25 (50)	
Current	0 (0)	3 (6)	
Radiation dose to primary tumor site (Gy)			
Median (range)	60 (60)	64 (44–71)	.49
Radiation dose to extraction site (Gy)			
Median (range)	54.1 (54.1)	50.4 (22–72)	.71
Months between completion of radiation therapy and extraction			
Median (range)	18 (18)	36 (3–264)	.56
No. of extractions			
Single extraction	0 (0)	24 (48)	.79
Multiple extractions*	1 (2)	25 (50)	
Site of extraction			
Maxillary posterior	1 (2)	12 (24)	.68
Maxillary anterior	0 (0)	3 (6)	
Mandibular posterior	0 (0)	23 (46)	
Mandibular anterior	0 (0)	6 (12)	
Maxillary and mandibular posterior	0 (0)	5 (10)	

*Multiple extractions were considered when 2 or more teeth were extracted.

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Table II. Primary outcome: development of medication-related osteonecrosis of the jaw (MRONJ) after dental extraction(s)

Variable n (%)	*MRONJ Yes (n = 3)*	*MRONJ No (n = 37)*	*P value*
Age (years)			
Median (range)	65 (61–75)	66 (41–78)	.55
Gender			
Male	3 (7.5)	17 (42.5)	< .05
Female	0 (0)	20 (50)	
Smoking status			
Never	1 (2.5)	19 (47.5)	.34
Former	2 (5)	11 (27.5)	
Current	0 (0)	7 (17.5)	
Diabetes mellitus type II			
Yes	1 (2.5)	4 (10)	.36
No	2 (5)	33 (82.5)	
Concomitant corticosteroids			
No	0 (0)	22 (55)	< .05
Yes	3 (7.5)	15 (37.5)	
Diagnosis			
Multiple myeloma	1 (2.5)	21 (52.5)	.52
Metastatic cancer	2 (5)	13 (32.5)	
Osteoporosis	0 (0)	3 (7.5)	
AR/AA medications			
Zoledronic acid (Zometa)*	2 (5)	21 (52.5)	.95
Zoledronic acid (Reclast)†	0 (0)	2 (5)	
Pamidronate	0 (0)	4 (10)	
Pamidronate/Zometa	0 (00)	1 (2.5)	
Denosumab (Xgeva)‡	1 (2.5)	3 (7.5)	
Denosumab (Prolia)§	0 (0)	1 (2.5)	
Bevacizumab	0 (0)	1 (2.5)	
Zometa/Xgeva	0 (0)	4 (10)	
Duration of AR/AA (months)			
3–12	1 (2.5)	13 (32.5)	.17
12–48	2 (5)	17 (42.5)	
48–72	0 (0)	7 (17.5)	
No. of doses of AR/ AA before extractions, median (range)			
Zoledronic acid	20 (16–24)	24 (3–72)	.82
Pamidronate	0 (0)	8 (4–13)	
Denosumab	5 (5)	12 (3–72)	
Bevacizumab	0 (0)	24 (24)	
No. of extractions			
Single extraction	2 (5)	24 (60)	.92
Multiple extractions‖	1 (2.5)	13 (32.5)	
Site of extraction			
Maxillary posterior	0 (0)	14 (35)	.06
Maxillary anterior	0 (0)	2 (5)	
Mandibular posterior	2 (5)	17 (42.5)	
Mandibular anterior	0 (0)	1 (2.5)	
Maxillary and mandibular posterior	1 (2.5)	3 (7.5)	

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