

Mandibular Osteoradionecrosis

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The presentation of osteoradionecrosis (ORN) after radiotherapy (RT) for head and neck cancer varies from small, asymptomatic bone exposures that may remain stable for months to years or heal with conservative management, to severe necroses necessitating surgical intervention and reconstruction. The risk of developing ORN depends on a number of factors, including primary site, T stage, proximity of the tumor to bone, dentition, type of treatment (external beam RT, brachytherapy, surgery, and chemotherapy), and RT dose. Other factors that probably influence the likelihood of developing ORN include the nutritional status of the patient and continued tobacco or alcohol abuse. The mandible is the most common site of ORN, probably because it is often necessary to deliver a high RT dose to tumors near the mandible and possibly also because the blood supply may be less abundant than that of the maxilla. The incidence of severe ORN, defined as necessitating either surgical intervention, hyperbaric oxygen (HBO) treatments, or both¹ in a series of 1,495 patients treated with definitive RT for head and neck squamous cell carcinomas at the University of Florida (Gainesville, FL) is depicted in Table 1. Minimum follow-up was 2 years; all but two patients (0.13%) had follow-up until death or within 1 year of data analysis. Twenty-seven patients (2%) experienced severe ORN, which occurred most often in those patients treated for oral cavity cancers. Although patients treated with definitive RT for oral cavity malignancies are more likely to experience minor or moderate bone complications compared with those treated with surgery and adjuvant RT, the likelihood of severe ORN is probably similar after either treatment strategy.^{2,3} Patients in whom the RT portals include only the angle or ramus of the mandible, such as those with laryngeal or hypopharyngeal cancers, have a very low likelihood of experiencing severe ORN. Edentulous patients probably have a lower risk of developing ORN than dentulous patients. Patients with poor dentition whose teeth will be in the high-dose fields should undergo extractions before RT and should be allowed to heal for 2 to 3 weeks before initiating treatment. Whether it

is advisable to extract healthy teeth that will receive high-dose RT is controversial. The use of ill-fitting dentures after RT increases the risk of ORN and should be avoided.

Patients who develop small, asymptomatic bone exposures are initially managed conservatively with penoxifylline and vitamin E. Conservative debridement may be necessary to remove spicules of devitalized bone, particularly if the adjacent tongue is abraded. Patients who have ORN that progresses are traditionally treated with HBO alone or combined with debridement. Segmental mandibulectomy and reconstruction are necessary in patients with severe ORN who do not improve with conservative treatment.

Theoretically, HBO increases blood oxygen levels and enhances healing of bone necrosis. However, as pointed out by Annane et al,¹¹ the efficacy of HBO is based almost exclusively on uncontrolled studies. The major disadvantages of HBO are that it is time consuming and expensive. In this issue of the *Journal of Clinical Oncology*, Annane et al¹¹ report on a prospective randomized trial comparing HBO to placebo in the treatment of patients with ORN. Surprisingly, those treated with HBO not only failed to benefit from the treatment, they actually had a more unfavorable outcome than the patients treated with placebo. Although it is not surprising that those treated with HBO did not benefit from the treatment, particularly given the small sample size, it is difficult to explain why they did not do as well.

The treatment of ORN is unsatisfactory. Although it has been tempting to employ HBO because it should theoretically work, the data supporting its use are solely from uncontrolled trials. The prospective randomized trial reported by Annane et al,¹¹ albeit underpowered, suggests that it is ineffective. Although it is unfortunate that the trial was terminated prematurely with only 68 patients entered, it seems unlikely that HBO would have proven beneficial even if the study had been completed with a total planned accrual of 222 patients. Thus, at the present time, the efficacy of HBO in the treatment of ORN is unclear and further investigation is warranted. As pointed out by Annane et al,

Table 1. Severe Bone Complications After Definitive Radiotherapy at the University of Florida

Primary Site	No. of Patients	Severe Bone Complications	
		No. of Patients	%
Floor of mouth ²	117	6	5
Oral tongue ³	105	6	6
Tonsillar region ⁴	400	11	3
Base of tongue ⁵	217	2	1
Soft palate ⁶	107	2	2
Pharyngeal wall ⁷	99	0	0
T1-T2 Piriform sinus ⁸	101	0	0
T3 Glottis ⁹	75	0	0
Supraglottic ¹⁰	274	0	0

NOTE. Two of 1,495 patients (.13%) lost to follow-up were disease-free at 9.6 years and 12.2 years, respectively.

it is possible that a subset of patients, such as those with more severe ORN, may benefit from HBO.

Author's Disclosures of Potential Conflicts of Interest

The author indicated no potential conflicts of interest.

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