

Oncology

Management of refractory osteoradionecrosis of the jaws with surgery and adjunctive hyperbaric oxygen therapy

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Abstract. This retrospective study aimed to determine the effectiveness of surgery and hyperbaric oxygen (HBO) treatment in the management of refractory osteoradionecrosis (ORN) of the jaws. Of the 18 patients who had undergone this treatment, 14 patients had complete healing, 3 patients had improved and one patient did not show any improvement. Of the 14 patients who had complete healing, only 4 still had a discontinuity defect of the mandible but they declined additional reconstructive surgery. In conclusion, surgery/HBO therapy showed satisfactory results in the management of refractory ORN of the jaws.

Key words: osteoradionecrosis; hyperbaric oxygenation; jaws.

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The combination of surgery and radiation is the standard treatment for oral squamous cell carcinoma. Long-term effects of radiotherapy, however, are well known and osteoradionecrosis (ORN) is one of the most serious late complications^{1,11,12,20,21,24}. Radiation injuries include hard and soft tissues because of damage to tissue cells and the vascular system. These changes are progressive and may result in gradual devitalization of bone tissue, which may lead to bone and/or soft tissue necrosis in a small percentage of patients^{4,5,18}.

The pathogenesis of ORN is still not completely understood, but according to MARX's concept¹⁸ this disease should be considered a nonhealing wound resulting from metabolic and tissue homeostatic disturbances. ORN is the result of hypoxic, hypovascular, and hypocellular tissue, followed by tissue breakdown leading to a nonhealing wound¹⁸. Healing may exist in such

compromised tissue but takes place very slowly, requiring months or even years; however, it may still lead to repair in the end²⁵.

There is no universally accepted treatment for ORN of the jaws. The management of ORN remains controversial, both radical and conservative treatment have been reported^{3,5,6,10,14,16,22,23,25}. Conservative treatments, which consist of systemic antibiotics, rinsing with topical antiseptics and also removal of small sequestrums, seem ineffective in controlling acute and progressive ORN and are only indicated when small necrotic bone areas are involved^{5,22,25}. Radical surgery is indicated in cases where conservative approaches are not successful and in symptomatic and rapidly progressive lesions. In recent years, treatment of ORN has focused on revascularization of irradiated tissues^{3,6,10,13,14,16,17,23}. Hyperbaric oxygen therapy (HBO) has

the capacity to increase the tissue oxygen tension levels and, thus, enhances wound healing in heavily irradiated tissues. Surgery in combination with HBO is denoted as being impractical by some authors because of costs and the time factor^{4,25}. An important consideration in the treatment of ORN is the role of microorganisms that are not the causative factor, but they complicate the process and the extent of treatment⁹. The general condition of the host, severity and location of the disease and availability of certain techniques such as HBO and microvascular free flaps are all factors that play an important role in the proper management of ORN.

In this study, we report on the treatment of ORN of the jaws using surgery and adjunctive HBO in 18 patients who failed to respond to conservative treatment, including antimicrobial therapy, rinsing with antiseptics and selective removal of small sequestrums.

Material and methods

The medical records of 18 patients with ORN of the jaws who received HBO in combination with surgery at the Stomatology Department, Hospital do Câncer – A. C. Camargo, São Paulo, Brazil, were reviewed. Only patients with a history of ORN with a duration of at least 3 months and a follow-up of at least 1 year were included in this study. The diagnosis of ORN was based on clinical and radiographic findings and the patient's history.

The primary tumor site, tumor stage and treatment given to the patients are shown in Tables 1 and 2. The time from radiotherapy until the onset of ORN varied from 3 months to 14.5 years with a mean of 27.9 months (Table 3). The factors believed to have caused ORN are shown in Table 4.

Radiotherapy consisted of external beam radiation and megavoltage delivery (linear accelerator 4 MeV) in all cases. Seven patients received preoperative radiotherapy and 11 patients received postoperative radiation. The total radiation dose ranged from 5.0 Gy to 7.2 Gy with a mean dose of 6.2 Gy. The dose rate/day varied from 0.12 Gy to 0.2 Gy with a mean of 0.18 Gy.

All patients had been previously treated with conservative measures for a mean period of 15.4 months and had failed to respond to this therapy. This conservative treatment consisted of systemic antimicrobial therapy (clindamycin 300 mg orally four times a day) in acute infectious episodes, local debridement of the wound and rinsing with antiseptic solutions (digluconate chlorhexidine 0.12%) and selective removal of small sequestrums when present. All sequestrectomies were carried out on an outpatient basis. The necrotic bone was removed by curetting and/or burring it out until normal bleeding bone appeared. If the patient did not respond and the ORN persisted, then radical surgery was carried out. This procedure aimed to eradicate the full extent of the disease by resecting all necrotic tissue, which

Table 1. Tumor clinical stage* and site in 18 patients

Variable	n
Location	
Lip	1
Tongue	5
Gingiva	2
Floor of the mouth	3
Soft palate	1
Retromolar area	1
Oropharynx	2
Tonsillar area	3
Clinical stage	
I	6
II	2
III	7
IV	3

* Tumor clinical stage – According to UICC, 1997.

Table 2. Oncologic treatment in 18 patients with osteoradionecrosis

Treatment	Cases
Radiotherapy only	4
Radiotherapy+chemotherapy	1
Radiotherapy+salvage surgery	5
Postoperative radiotherapy	7
Pre- and postoperative radiotherapy	1

usually resulted in a bone defect. Resection was carried out under general anesthesia through an extraoral or intraoral approach. All affected bone was removed by a Stryker drill under cooling with 0.9% NaCl solution.

HBO was given in a Sechrist monoplace chamber at 2.4 ATA (atmosphere absolute), with the patient breathing 100% oxygen for 120 minutes per dive. During this period, the first 10 minutes were used for successive compression up to 2.4 ATA. The pressure was then

Table 3. Interval between radiotherapy and onset of osteoradionecrosis in 18 patients

Interval (months)	Cases
0–12	9
12–24	3
24–36	2
36–48	1
>48	3

Table 4. Contributing causative factors in 18 patients

Factors	Cases
Salvage surgery	10
Postradiation dental extractions	3
Periodontal disease	1
Denture pressure	2
No obvious factor	2

Table 5. Treatment of osteoradionecrosis in 18 patients

Treatment ORN	Cases
HBO+sequestrectomy	7
HBO+radical resection	11

kept constant for 90 minutes and decompression lasted 20 minutes. The chamber temperature was kept at +23°C by a water cooling system. The HBO treatment was performed once daily and a total of 30 consecutive dives were given in patients who were submitted to sequestrectomy (7 cases). A different protocol was used for patients submitted to radical resection (11 cases), that included HBO once daily, with a total of 20 dives preoperatively and 10 dives postoperatively.

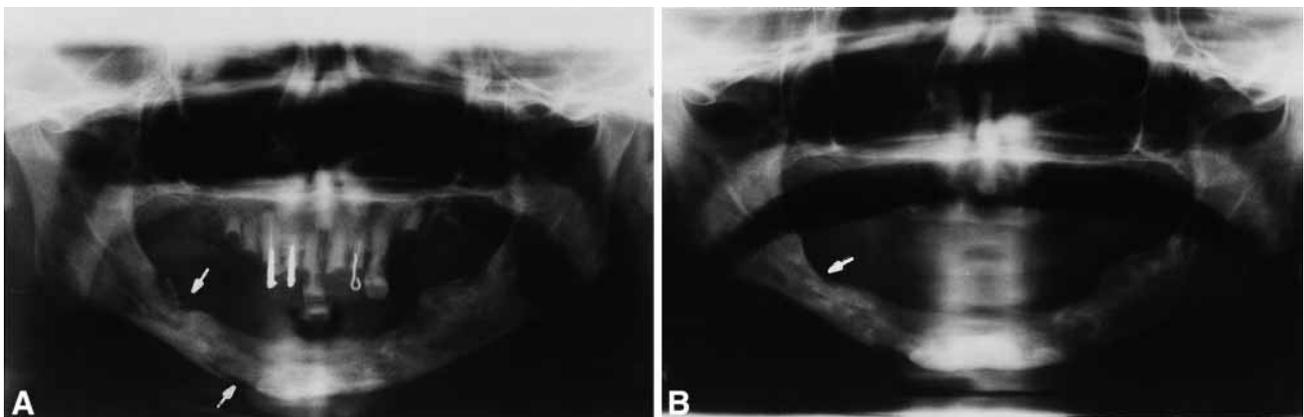


Fig. 1. A. Panoramic radiograph showing ORN involving the inferior border (white arrow) and the right body (lower white arrow) of the mandible, which developed after salvage surgery 4 months after radiation therapy. B. Panoramic radiograph of healing mandible following sequestrectomy and HBO. Note: white arrow points to healed bone with remucosalized defect over vital bone.

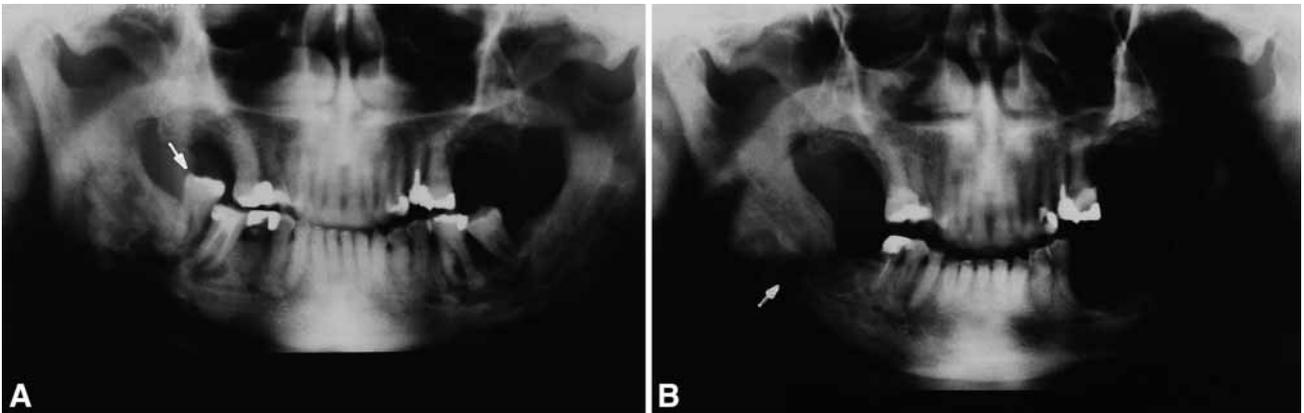


Fig. 2. *A.* Panoramic radiograph showing bilateral ORN of the body of the mandible, which developed from sites of periodontal disease activity. Note: white arrow points to upper level of right second molar tooth because of pathologic fracture of the mandible. *B.* Panoramic radiograph of healing mandible following surgery and HBO. Bony callous formation and healed fracture of the right body of the mandible (white arrow).

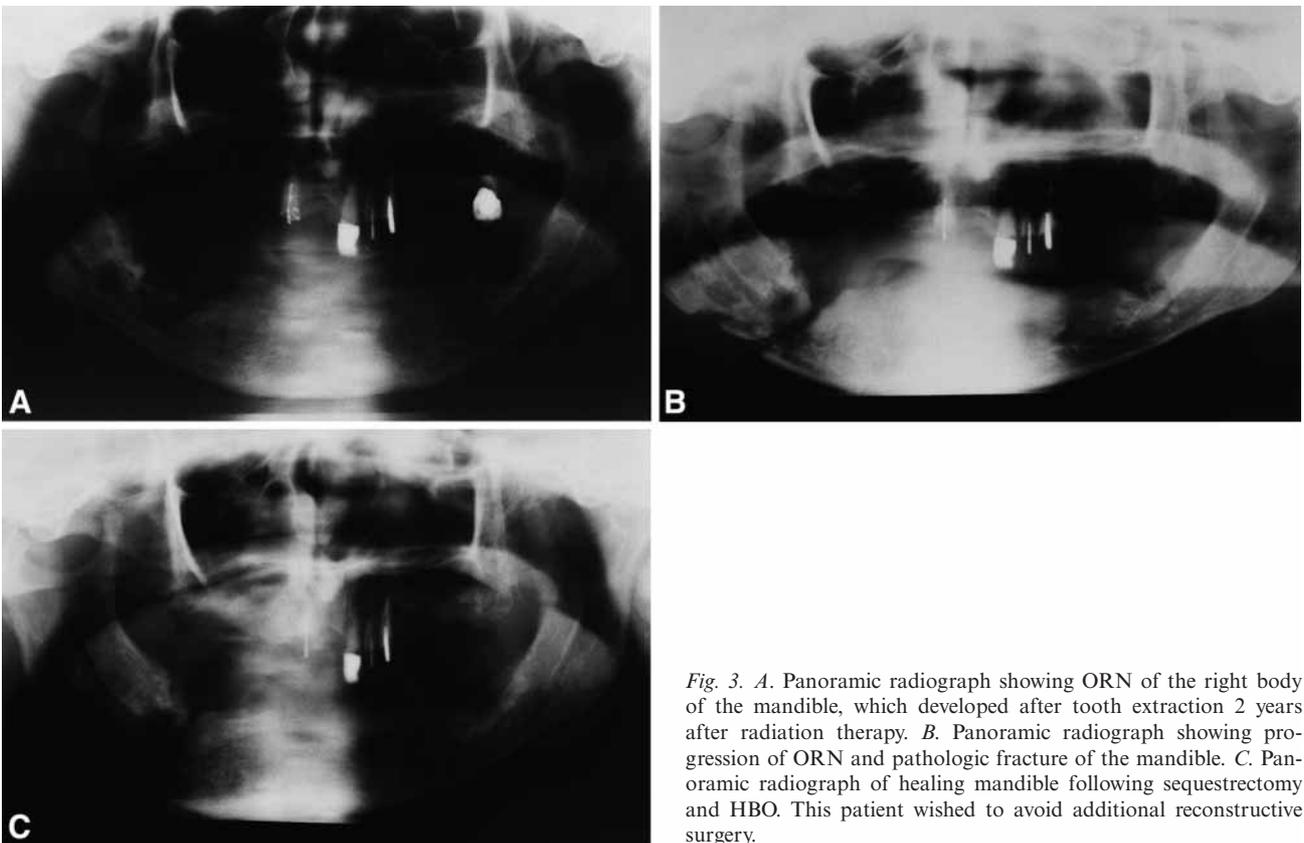


Fig. 3. *A.* Panoramic radiograph showing ORN of the right body of the mandible, which developed after tooth extraction 2 years after radiation therapy. *B.* Panoramic radiograph showing progression of ORN and pathologic fracture of the mandible. *C.* Panoramic radiograph of healing mandible following sequestrectomy and HBO. This patient wished to avoid additional reconstructive surgery.

Results

Between 1992 and 1997, 18 patients (14 men and 4 women) were submitted to surgery and adjunctive HBO therapy for treatment of ORN of the jaws (Table 5). The age of the patients varied from 40 to 77 years with a mean age of 55.6 years. Seventeen patients were

Caucasian and one was Japanese. ORN was located in the mandible in 16 cases and in the maxilla in 2 cases. Of the 18 patients, 2 cases had no obvious causative reason, whereas 16 cases were induced by trauma.

Current follow-up of the patients ranges from 12 to 68 months with a mean of 24.8 months. After surgery/

HBO therapy, 14 patients had complete healing, 3 patients had improved and one patient did not show any improvement (Figs 1, 2). Of the 14 patients who had complete recovery, only four still had a discontinuity defect of the mandible but they declined additional reconstructive surgery (Figs 3A–C).

Discussion

ORN is still a serious complication resulting from radiotherapy and its incidence has not decreased in the last years^{1,4,5,7,11,12,18,20,21,24}. Because ORN may be considered a nonhealing wound resulting from metabolic and tissue homeostatic disturbances, it responds to different forms of treatment. Some authors have preferred conservative treatment to control small necrotic areas, but this therapy may be insufficient in refractory and acute ORN^{5,25}. The rationale for the use of HBO in association with surgery in irradiated tissue is to increase the blood-to-tissue oxygen tension, which enhances the diffusion of oxygen into the tissues. This revascularizes the irradiated tissue and improves the fibroblastic cellular density, thus limiting the amount of nonviable tissue to be surgically removed^{16,17}. Treatment of ORN should aim at local debridement of the wound, removal of nonviable tissue, antimicrobial therapy and revascularization of the tissues^{3,6,10,13,14,16,17,23}.

In 1973, GREENWOOD & GILCHRIST⁸ reported for the first time the benefits of HBO on wound healing in postradiation patients. Since then, several authors have reported the beneficial effects of HBO in the management of ORN of the jaws. In 1975, MAINOUS & HART¹³ treated 14 cases of refractory osteoradionecrosis of the mandible with HBO and hemimandibulectomy, with complete resolution of all cases. In 1981, MANSFIELD et al.¹⁵ treated 12 patients with refractory ORN of the mandible with HBO therapy, resulting in complete healing in 11 cases.

The benefits of revascularization of irradiated tissues have been shown in many clinical and experimental studies^{3,6,10,13,14,16,17,23}. MARX¹⁸ treated successfully 58 cases of refractory ORN and developed a staging protocol for its treatment, considering the clinical aspects and the possibilities of hard/soft tissue reconstruction. MCKENZIE et al.²⁶ published treatment with HBO of postradiation ORN of the mandible in 26 patients and concluded that resolution occurred in 69% (18 of 26) patients, improvement occurred in 12% (3 of 26) but 19% (5 of 26) of the patients did not show any improvement. MERKSTEYN et al.¹⁹ reported a combination of surgical debridement, antimicrobial therapy and HBO in 27 patients and concluded that 20 (69%) had com-

pletely healed after this treatment. EPSTEIN et al.³ reported the results of a long-term follow-up study with the same group of patients previously published by MCKENZIE et al. Of the 20 patients followed, 12 had completely healed, improvement had occurred in two patients and five of the patients still had chronic persistent ORN. NEOVIUS et al.²³ reported results on treatment with HBO after surgery in the irradiated head and neck in 15 consecutive patients and compared them with a group of patients treated without HBO. The authors concluded that 12 out of 15 patients treated with HBO had healed completely and that only seven of 15 patients with similar signs of ORN had healed after therapy without HBO.

In this study, complete healing was achieved in 14 of the 18 patients. This result is in agreement with other studies which shows the benefits of surgical/HBO treatment in ORN of the jaws^{3,6,10,13,14,16,17,23}. Although the benefits of adjunctive HBO therapy in irradiated tissues have been demonstrated in a series of reports, some authors do not agree with the use of HBO for treatment of ORN^{5,25}. WONG et al.²⁵, in a retrospective study of 28 patients with mandibular ORN managed by conservative measures only, showed that 14 patients had complete healing. A previous study², in which 104 patients with ORN were treated with conservative approaches (local debridement/gentle sequestrum removal), supports this statement, because it resulted in healing of 42.3% of patients.

Serious complications resulting from HBO therapy are extremely rare, but toxic effects of oxygen may be observed in the central nervous system, eye, liver and tracheobronchial tree. Optic neuritis, active viral infection, malignant disease and forms of chronic pulmonary disease have been pointed as contraindications to HBO therapy⁶. In the current study, no signs of oxygen toxicity were observed in the patients under treatment.

Osteoradionecrosis of the jaws produces considerable morbidity and its management is still a matter of debate. The results of both a conservative approach and surgery/HBO treatment are well documented. Our results in 18 patients suggest that, in advanced conditions, the results of conservative treatment only are poor and under these cir-

cumstances, radical resection of the involved segment and adjuvant HBO is a satisfactory option in the management of ORN of the jaws.

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