

Osteoradionecrosis

Pathophysiology and Hyperbaric Effects

The recent introduction of radiation therapy for the treatment of solid tumors allows previously untreatable cancers to be cured. Now physicians face the challenge of aiding survivors. Unfortunately, the radiation beam used to fight cancer damages more than the tumor. Normal tissue in the path of the beam often sustains damage. Destruction of tissue also occurs. Even today, many physicians consider chronic radiation effects as irreversible, but hyperbaric oxygen therapy (HBOT) offers opportunities to repair damage.

Both bone and soft tissue suffer damage from therapeutic radiation (see Soft Tissue Radionecrosis Protocol for a detailed discussion of the radiopathologic change that tissue undergoes.) Bone is 1.8 times as dense as soft tissue and thereby absorbs a proportionately larger dose of incident radiation than does soft tissue. The effects of radiation on adult bone are a consequence of injury to its cellular and vascular components.

High doses of radiation cause a proliferative endarteritis causing ischemia, and eventually death of bone in the distribution of the involved blood supply. Additionally, radiation upsets the normal balance of osteoclastic destruction and osteoblastic reconstruction occurring in bone. Cell death of these osteocytes and osteoblasts leads to osteoporosis and eventually to osteonecrosis.

Clinically significant osteonecrosis (ORN) usually develops over a period ranging from four months to several years. There is no satisfactory treatment for radiation necrosis using available conventional means. One barrier to healing involves nutrients: providing adequate nutrition and oxygen to radiation devascularized tissue presented a previously insurmountable challenge. Radiation ulcers are painful, and the prolonged use of narcotic analgesics can lead to addiction. High failure rates confront reconstructive surgeons working in irradiated areas, due to problems with healing.

Osteoradionecrosis becomes clinically significant when it develops at four anatomic sites: chest wall, mandible, pelvis, vertebral column, and skull. Damage to the ribs and sternum can result following radiation therapy for tumors of the breast, chest wall, or lung. Pathologic fractures in irradiated ribs can result from coughing, or from merely deep breathing.

Irradiation damage to the skull from treatment of orbital or brain tumors is rare, primarily because of the use of highly fractionated doses of radiation, but does occur. The radiotherapy treatment of pelvic neoplasms can lead to radionecrosis of the lumbar vertebrae, femur, or pelvis; pathologic stress fractures can result from injury to these weight-bearing structures. Doses of radiation necessary to produce adequate tumor kill in head and neck cancers are accompanied by an unfortunately high incidence of osteoradionecrosis. The mandible is often involved following radiotherapy of these tumors, and is over represented in osteoradionecrosis. Hyperbaricists offer much experience in treating ORN in the mandible.

Mandibular Osteoradionecrosis

Because of the mandible's low vascularity and great density, the incidence of osteoradionecrosis is highest at this site. The mandible is often involved because head and neck cancers are common, and radiation therapy in these cancers is very effective.

The presence of teeth in the jaws, as well as the functional and cosmetic importance of the mandible, means that osteoradionecrosis of the mandible most dramatically impacts on the patient's quality of life.

Radiographically, osteoradionecrosis demonstrates a wide spectrum of presentations. These include normal morphology and trabeculation all the way to local osteolysis. Other morphologies include pathologic fractures. Still others include simple, dramatic, and massive osteolysis. The radiographic image does not necessarily correlate with the severity of the disease, and often does not detect its presence. Radiographically normal bone may be associated with large areas of exposed non-viable bone; conversely, if a small area is exposed the disease may spread into normal bone.

Because the clinical and the radiographic pictures fail to match and no laboratory tests or reliable irradiation tissue tolerance curves exist, physicians rely on a simple working definition of osteoradio-necrosis. Any exposed bone in a field of irradiation failing to heal after a trial of conservative treatment earns the ORN label. So does the presence of radiographically demonstrated osteoradionecrosis.

Beginning in 1979, Marx and others demonstrated that osteoradionecrosis is a wound healing defect related to a chronic hypoxic state. In 1984, Marx published a study of 150 cases of osteoradionecrosis in the mandible. In his examination, Marx divided the disease into three stages of advancing clinical activity. This staging and the HBOT treatment of osteoradionecrosis he described became the standard for planning the treatment of mandibular and soft tissue ORN. The strategy has implications for the treatment of ORN in other tissues as well.

ORN Staging System

Stage I

All patients who meet the definition of osteoradionecrosis except those with cutaneous fistulae, pathologic fracture, or radiographic evidence of bone resorption. (These three subsets of patients are classified as Stage III.) Stage I patients receive 30 HBOT treatments. Wounds are maintained with irrigation only or with saline rinses. No bone is surgically removed. If, after 30 treatments, the wound shows improvement, as evidenced by decrease in amount of exposed bone; less resorption or spontaneous sequestration of exposed bone; or decreased softening of exposed bone; the patient completes another 10 treatments. The total 40 HBOT treatments are meant to achieve full mucosal cover. If there is no clinical improvement after 30 HBOT treatments or complete resolution, such as extended or continued exposure of bone, absence of mucosal proliferation, or presence of inflammation, the patient is advanced further to Stage II. (See Technical Treatment Protocol for suggestions on pressure levels and duration of individual treatments.)

Stage II

Surgeons attempt a local surgical debridement to identify those patients with only superficial or cortical bone involvement, and who can be resolved without jaw resection. A transoral alveolar sequestrectomy is performed with fine saline-cooled, air-driven saws. Minimal periosteal manipulation is done for labial access to the mandible. The lingual periosteum is allowed to remain completely attached until the specimen is delivered, and then only that which is attached to the specimen is reflected from bone. The resultant mucoperiosteal flaps are closed in three layers over a base of bleeding bone. If healing progresses without complication, HBOT is continued with 10 additional sessions. If the wound dehisces, leaving exposed non-healing bone, the patient is

advanced to Stage III. In those patients who initially present with orocutaneous fistulae, with pathologic fracture, or with radiographic osteolysis to the inferior border, the initial 30 HBOT treatments are given, and the patient enters Stage III directly.

Stage III

After 30 HBOT treatments, the patient undergoes a transoral partial jaw resection, the margins of which are determined at the time of surgery by the presence of bleeding bone. The segments of the mandible are stabilized either with extraskelatal pin fixation or with maxillo mandibular fixation. If there was an orocutaneous fistula, or large soft tissue loss, primary closure or soft-tissue reconstruction is accomplished during this surgery. HBOT is continued for another 10 treatments, and the patient is advanced to Stage III-R.

Stage III-R

These patients present the most difficult cases. Early reconstruction and rehabilitation produces the best results. Ten weeks after resection, the soft tissues are healing, and the potential graft bed is free from contamination and infection. Bony reconstruction is undertaken from a strictly transutaneous approach without oral flora contamination. Ten post-reconstructive HBOT treatments are given, and the jaw fixation is maintained for eight weeks. If no further surgery is required, the patient begins appointments with a maxillofacial prosthodontist for full prosthetic rehabilitation one month after release of his fixation. If additional surgery is required, such as a tongue release, vestibuloplasty, or excision of redundant tissue, surgeons schedule procedures one month after fixation is released. After surgery, the patient is referred to a maxillofacial prosthodontist.

Results

In Marx's reported study, 14 percent of patients with mandibular ORN resolved in Stage I, 18 percent in Stage II, and 68 percent in Stage III. Most of the patients (70 percent) were refractory cases treated elsewhere for months to years.

This staging and protocol is the most widely accepted regimen in treating ORN today, though some patients with particularly recalcitrant disease may require additional therapy and some surgeons enjoy alternative management techniques for particular patients. It is a logical, progressive sequence. Applied to all ORN and soft tissue radionecrosis patients, the regimen produces consistent disease resolution without recurrences. The protocol resolves most cases with one treatment sequence, retaining or reconstructing the jaw to an acceptable integrity. Patients are less disfigured, no longer require supplemental feedings (through feeding tubes or oral supplements), and are less depressed.

Consensus

The 1990 Consensus Paper of the National Cancer Institute on the Oral Complications of Cancer therapies states: "The treatment of ORN with antibiotics and surgical debridement frequently fails, with progressive involvement of the remaining mandible. The keystone of the treatment of ORN is the provision of adequate tissue oxygenation in the damaged bone. This is best done by using hyperbaric oxygen therapy (HBOT). In the event that dental extractions are required following radiation, meticulous surgical technique and antibiotic prophylaxis are necessary."

ORN of Other Areas

Osteoradionecrosis of the chest wall can be life threatening, and difficult to manage surgically. Hart and Strauss (1986) reported 20 cases of osteoradionecrosis of the chest wall following radiation therapy. All patients recovered with complete healing, after

HBOT. The researchers also reported cases of osteoradionecrosis of the vertebrae that also fully resolved.

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