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Maxillofacial Osteoradionecrosis: Review

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Abstract

Osteoradionecrosis is a severe, late-onset radiation-induced injury characterized by necrosis of bone tissue and failure to heal. Cases of osteoradionecrosis present to the clinician with features such as mucosal or skin pain, drainage, and fistula formation associated with exposed bone in previously irradiated areas. Predisposing factors are tumor size and location, radiation dose, occurrence of local trauma, tooth extraction, infection, immunodeficiency, and malnutrition. A better understanding of the risk factors that lead to the development of osteoradionecrosis and its underlying pathophysiology could improve the ability of clinicians to prevent the development of osteoradionecrosis and improve the prognosis of this complication. It might help. Although the frequency of osteoradionecrosis has decreased since newer methods of radiotherapy were introduced, this review focuses on etiology, pathophysiology, clinical features, radiological features, diagnosis, and treatment modalities.

Keywords: Jaws, management, osteoradionecrosis, physiopathology, risk factors

Introduction

Osteoradionecrosis (ORN) of the maxilla is the most serious and important complication of radiotherapy (RT) used in patients with head and neck cancer. RT is usually prescribed as adjuvant therapy after tumor surgery. However, it can be given alongside chemotherapy or as palliative treatment (1). Osteoradionecrosis is defined as an area of exposed necrotic bone at one or more sites of the alveolar process of the maxilla or mandible that does not heal for at least 3 months. ORN can occur spontaneously in one-third of all cases, but it usually manifests after tooth extraction, after oral surgery, or due to inflammation from ill-fitting dentures. In most cases, the disease is chronic, progressive, more widespread and painful (2,3). Marx (3) defined ORN as a result of RT effects i.e. hypovascularization, hypoxia, and hypocellularity – these conditions adversely affect tissue repair capacity. A pro-trophic mechanism characterized by changes in bone metabolism and formation of free radicals is now proposed causing inflammation and microvascular thrombosis leading to necrosis of the affected tissue (4). Clinically, ORN is a latent, asymptomatic disease until lesions are visually recognized or patients present with bone loss, pain, swelling, suppuration, and formation of cutaneous fistulas or pathologic fractures. remains (5). Treatment should aim to relieve pain, control infection, and prevent or reduce the spread of ORN. Conservative management is recommended in the early stages and classically includes antibiotics, antiseptics, and hyperbaric oxygen therapy (HBO), although the latter is currently the subject of much controversy (6). Surgery has been used in more advanced stages of ORN characterized by extensive osteolytic areas, sequestrations, cutaneous fistulas, or pathologic fractures. First, lesion ablation surgery is performed, followed by reconstructive surgery (7,8). At the most advanced stages, lesion progression has proven more difficult to treat and contain.

Definition:

Given by Wong, Wood, and McLean (1997) "A slow-healing radiation-induced ischemic necrosis of bone with associated soft tissue necrosis of variable extent occurring in the absence of local primary tumour necrosis, recurrence, or metastatic disease that may or may not:

- Be superinfected (and accompanied by fistulation or cellulitis)
- End in pathologic fracture
- Resolve without surgery, hyperbaric oxygen therapy or both."

Pathogenesis

The pathogenesis of osteoradionecrosis is not absolutely understood. The most distinguished etiological issue is the impact of radiation at the endothelial linings of the vessels ensuing in hypocellularity, vasculitis followed via obliterate endarteritis, ischemia, fistula and pathological fracture of the bone(9). Osteoradionecrosis is the result of hypoxic, hypovascular and hypocellular tissue, accompanied through tissue breakdown main to a nonhealing wound(3). Mandibular ORN develops maximum generally after neighborhood trauma, consisting of dental extractions, biopsies, related most cancers surgical operation and periodontal tactics, however it could also occur spontaneously. Shop et al (10) the usage of DNA hybridization demonstrated that micro organism might also play a essential position inside the pathogenesis of ORN; teeth present inside the discipline of irradiation might constitute the port of access for microorganisms. He demonstrated the life of a numerous microbiota of the medullar elements of the mandible, visualized with the aid of scanning and transmission electron microscopy and via DNA-DNA hybridization in a checkerboard assay. based totally on evaluation of irradiated bone biopsies from a high number of patients with postoperative complications, Hansen et al also verified an affiliation among actinomyces and infected osteoradionecrosis (ORN)(11). A brand new hypothesis proposes that ORN takes place by a radiation-prompted fibro-atrophic mechanism, inclusive of loose radical formation, endothelial disorder, infection, microvascular thrombosis, fibrosis and remodeling and ultimately bone and tissue necrosis(12). The important thing occasion inside the development of ORN is consequently the activation and dysregulation of fibroblastic interest that results in atrophic tissue in the formerly irradiated region(4).

Predisposing factors

1. Radiation

Total dose of radiation and time factors(13): Doses of < 67.5 Gy delivered in < 6.5 weeks resulted in no case of ORN as compared to a 50% incidence with higher doses delivered in < 6.5 weeks

Energy source(14): Brachytherapy sources deposit a higher dose within a short period of time resulting in a higher risk of ORN. Higher energy photons have a higher exit beam dose, and are more likely to increase the risk of ORN.

Tissue density in radiated volume: Bone has density 1.6 to 1.8 times greater than soft tissue, absorbing more photons with higher energy deposition. The mandible has a higher density compared to maxilla, which may explain the higher incidence of mandibular involvement.

- **Trauma and Surgery**
  Trauma according to Marx(15) Trauma may or may not be an initiating factor. When trauma is associated, it is usually caused by tooth removal (88%). Role of trauma is part of comprehensive pathologic process, involving cellular death and collagen lysis, which places a greater energy, oxygen and other metabolic demands on tissues unable to meet them. Furthermore, a study by Bagan et al reported about 50% of spontaneous ORN appearing without history of previous tooth removal.16
  Surgical procedure to jaws after irradiation increases the risk for developing ORN, since vascularization of tissues is impaired(17). In addition, factors linked to preirradiation surgery are loss of periosteal blood supply due to a marginal mandibular resection, unstable fixation of the mandibular split osteotomy leading to malunion or nonunion and inadequate tissue coverage of the bone after resection of a tumor(18)

- **Habits and Drugs**

One of the most prevalent negative factors associated with the ORN patients is the continued heavy use of alcohol and tobacco by 86% of them(19). These strong tissue irritants significantly contributes to the breakdown of mucosa and exposure of bone.
Steroid use before or after radiation therapy reduced the risk of ORN by 96%, by preventing progression to thrombosis, atrophy and necrosis, credited to the protective effect related to inhibition to the initial inflammatory phase of ORN(20) On same lines, anticoagulant therapy use also significantly reduced the ORN risk.

Clinical Features

Symptoms of ORN may appear months or years after a patient has been irradiated. In some cases, lesions are discovered during a visual inspection of the oral cavity or due to discomfort in certain areas of the mouth. The most commonly affected location is the mandible (80%), in the premolar and molar regions. This is likely due to the higher bone density in these zones and less collateral circulation compared to the maxilla (21). Lesions present as ulcers with exposed, rough, necrotic bone. Although the lesions appear clinically small, imaging techniques such as computed tomography (CT) show larger lesion sizes (2). Overinfection, in turn, causes pain, and patients may experience paresthesia in certain areas and difficulty chewing and swallowing (21). Exposure to food in the affected area can cause bad breath. The disease tends to be chronic and progressive, alternating between asymptomatic and painful phases. This is especially noticeable in cases of hyperinfection of lesions. Symptoms depend on the location and extent of bone damage (22). In more advanced stages of ORN, bone sequestration, trismus, severe pain, swelling, cutaneous fistulas, and pathologic mandibular fractures may be observed.Diagnosis is usually based on clinical presentation and medical history and confirmed by radiographic and biopsy findings. Imaging techniques used to assess the extent of osteolysis include panoramic radiographs and CT (23). ORN and bisphosphonate-induced osteonecrosis of the maxilla may be clinically indistinguishable if the patient's medical history is unknown. Nevertheless, Bagan et al. (24) reported a number of important differences in his study of 20 cases of ORN and 53 cases of osteonecrosis of the maxilla. First, compared with bisphosphonate-induced osteonecrosis of the maxilla,

men were affected more frequently in the setting of ORN than women (80% vs. 37.7%), and addiction habits such as alcohol abuse and smoking had a significant impact on ORN (60% smoking, 40% alcohol). %). Spontaneous onset was also more frequent in ORN (50%), and the incidence of mandibular fractures (20%) and cutaneous fistulas (35%) was also higher in ORN.

Radiological features

The presence of osteoradionecrosis cannot always be diagnosed radiographically and often clinically obvious signs of exposed necrotic may not be accompanied by significant radiologic changes. Plain radiography shows an ill-defined cortical destruction without sequestration. The periphery may be ill-defined as in osteomyelitis. Bone pattern can be granular. Scattered regions of radiolucency may be seen, with or without central sequestra. The most common effect on surrounding bone is stimulation of sclerosis. Computed tomography plays an important role in diagnosis of osteoradionecrosis since it is hard tissue lesion. Anterior-posterior and supero-inferior extent of the osteolytic lesion is best judged with CT scans comparatively. Hence, from diagnostic purpose to the surgical intervention, CT is recommended as far as osteoradionecrosis is concerned(26). MRI reveals development of new heterogeneous signal within the marrow of an irradiated area (intermediate or low T1 signal, intermediate or high T2 signal). Adjacent muscles may appear oedematous and show intense enhancement, which can be difficult to differentiate from recurrent tumour if bone changes are not visible on CT(25). PET scan is helpful to differentiate between osteoradionecrosis and recurrent tumour(25). Radionuclide bone scanning with technetium methylene diphosphonate (99mTc-MDP) can identify pathophysiologic changes in bone earlier than conventional radiography because scan changes reflect osteoblastic activity and good blood flow(25). Infrared spectroscopy is a noninvasive method. This shows a reduction of the amount of deoxygenated haemoglobin at sites of osteoradionecrosis, confirming that it is a hypovascular and hypoxic tissue with decreased metabolic rate(25).

Prevention

Preventive measures should be evaluated in terms of reducing the risk or severity of ORN. Poor dental hygiene and oral decay have been shown to increase the risk of osteoradionecrosis. Similarly, an edentulous patient has a three-fold lower incidence of ORN than dentulous patient. This is likely due to the trauma associated with the need for post-irradiation tooth extraction and the high number of bacteria present. Prior to treatment, a thorough dental examination is necessary when evaluating teeth with poor prognosis due to caries, periodontal Illness or potential infection. Restoration should be limited to truly restorable teeth and teeth with a reasonable chance of survival. In such cases, he should undergo extraction at least 2-3 weeks prior to treatment. For preserved teeth, this period should be even longer. Another after treatment to reduce risk of ORN(27)(28) Less optimally, the tooth can be extracted within 4 months after the end of treatment. All patients should be instructed in proper oral hygiene and fluoride should be applied daily to the dentition via a specially shaped splint. Patients should be monitored weekly during radiotherapy and then monthly for the first 6 months. After this initial follow-up phase, the patient should see her dentist every months. The rationale for this "close follow-up" plan is to monitor patient adherence to meticulous oral hygiene and daily use of topical fluoride. Cervical root caries, which is common in xerostomia patients, should be treated promptly to avoid involvement of the pulp chamber and damage to the structure of the clinical crown. If a tooth extraction is needed more than 4 months after radiotherapy, it should be treated with HBO. The Marx protocol has become the de-facto standard, where he does 20 dives at 2.4 atmospheres, 90 minutes per dive on the before extraction, and 10 dives after extraction.

Advances in the delivery of radiotherapy, such as intensity-modulated radiotherapy (IMRT), have increased compliance by prescribing higher doses to conserve more mandibular volume and improve uniformity, thereby improving bone health. It promises to reduce the incidence of radiation necrosis (ORN). dose The main treatment factors that influence the likelihood of developing ORN include the total radiation dose ([60 Gy]), the volume of the mandible that receives the dose, the portion of the mandible that is irradiated, and the dose fractionation (fraction size [2 Gy]). Spontaneous ORN are associated with doses of 60 Gy and may occur at a rate of 5-15% with older techniques, whereas recent techniques using three-dimensional (3D) conformal therapy and IMRT That percentage has decreased to 6% or 6%. Less than. In a study comparing 3D and IMRT approaches, mandibular volume irradiated above 50, 55, and 60 Gy can be reduced in oral cancer patients undergoing IMRT when appropriately restricted. has been shown to have potential. There were also fewer mandibular hot spots and a lower maximum dose. Multiple studies reported that he developed ORN after IMRT. The Radiation Therapy Oncology Group study (RTOG-0022) reported an ORN incidence of 6% in patients with oropharyngeal cancer treated with a fraction size of 2.2-66 Gy without chemotherapy. did.

The University of Michigan reported his 176 patients treated with IMRT. At a median follow-up of 34 months, there were no cases of ORN. This is thought to be due to careful dental hygiene and salivary gland sparing as well as adherence to IMRT, which may reduce risk of caries. Similarly, Studer reported ORN incidence of 1.3% after parotid-sparing IMRT. Therefore, to date, the best results of IMRT with ORN have been limited dose to at-risk organs (mandible, oral cavity, and parotid), use of conventional fractionation techniques, and careful dental care. (30)(29).

Conservative Management

'Conservative management' includes topical rinsing (saline, NaHCO3 or 0.2% chlorhexidine), systemic antibiotics in acute episodes of infection, avoidance of irritants (tobacco, alcohol, dentures), and oral hygiene. consists of instructions. In addition to these conservative measures, 'simple management' refers to the gentle removal of isolated in case of isolated lesions (without local anesthesia). Resection, HBO therapy, or both were initiated in cases of refractory pain, unresponsiveness to conservative therapy, and progressive deterioration (including pathologic fractures). The treatment period ended on the day of resections or the first HBO dive (13).

Hyperbaric Oxygen Therapy

The rationale for using hyperbaric oxygen (HBO) for radiation-induced tissue injury is to revascularize the irradiated tissue and improve fibroblast density. This limits the amount of non-viable tissue that needs to be surgically removed, improving wound healing and reducing tissue damage. Preparing for reconstruction if needed Marx and Ames first outlined a standard approach for treating established osteonecrosis of the jaw with additional his HBOT. They proposed an approach known as the "Wilfred Hall Protocol" . This consists of his three stages of his described below.

Stage I. 30 consecutive treatments. If a wound does not show definitive clinical improvement, an additional 10 irradiations are performed up to 40 complete cycles of irradiation. If does not heal after 3 months, condition has progressed to Stage II.

Stage II. Exposed bone is removed by alveolar isolationectomy followed by 20 additional HBO treatments, up to for a total of 60 exposures. If wound dehiscence or failure to heal occurs, the patient progresses to stage III.

Stage III. Criteria for this category are her radiographic evidence of stage II failure, pathologic fracture, orocutaneous fistula, or resorption at the mandibular junction. Recommended treatment begins with a protocol of 30 exposures with surgical resection of the bleeding bone and/or bone reconstruction, followed by soft tissue dressing. 10 more treatments are recommended. If healing fails, additional surgery is performed , at which point 10 more HBOT exposures of him (31).

Surgical Management

The most important advances in the surgical treatment of ORN concern reconstructive surgery. The development of myocutaneous flaps and the use of microvascular free bone flaps have significantly altered the decision-making process regarding the extent of surgical ablation of extensive ORNs. Replacing dead bone with vascularized bone fragments not only restores the continuity of the mandible, but also results in non-irradiated soft tissue coverage with an intact blood supply. Flaps frequently used are the fibular flap, the iliac crest flap, and the scapular-parascapular flap (32).

Discussion

The incidence of ORN, a significant radiotherapy-related consequence, has not decreased in recent years. ORN responds to various types of treatment because it can be thought of as a non-healing wound brought on by metabolic and tissue homeostatic abnormalities. After radiation therapy for head and neck cancer, the incidence and prevalence of ORN of the jaws are unknown. Clayman discovered an overall incidence of 11.8% before 1968 and 5.4% after that, based on the literature. Osteoradionecrosis (ORN) is characterised by a delay in bone repair as a result of radiation damage. The average prevalence of the condition is 10%, and tooth extractions are a common trigger. It typically manifests between 6 months and 5 years after radiotherapy, with 90% of the lesions in the mandible.

Clinical management of ORN is challenging and typically entails receiving medical attention, abstaining from toxic behaviours, improving oral hygiene, controlling infections with antibiotics and antiseptics, and, once complications have manifested, removing necrotic tissue with more aggressive surgery (pathological fractures). Conservative treatment has been favoured by some writers to control minor necrotic regions, but refractory and acute ORN may make this therapy ineffective. Additionally, even though its usage is debatable, numerous clinical manuals note the potential use of hyperbaric oxygen therapy as a coadjuvant strategy. HBO therapy is successful in treating ORN, according to prospective random control trials undertaken by Annane et al., Marx et al., and a recent Cochrane review by Bennet et al. (6). In any case, there is currently no widely accepted clinicotherapeutic approach for treating this condition. Both a conservative strategy and surgery/HBO treatment have been successful in the past. Radical resection of the affected segment and adjuvant HBO is a suitable alternative in the management of ORN of the jaws in advanced cases where the results of conservative treatment alone are poor.

Conclusion

ORN can lead to intolerable pain, fracture, sequestration of devitalized bone and fistulas, which makes oral feeding impossible. ORN is an expensive disease to manage no matter what course of treatment is used. Effective management of any disease process initially requires diagnosis before treatment. Criteria used to identify ORN vary even among identical authors at different points in time. So, it is important to make a correct diagnosis before initiating a treatment.

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