Chapter 2.2.8

RADIO-INDUCED LESION IN NORMAL TISSUES

David Pasquier¹, Jörg Schmutz² and Eric Lartigau¹

¹ Department of Radiation Oncology, Centre O. Lambret, University of Lille, France
² Hyperbaric Center, Basel, Switzerland

Abstract: Late complications are one of the major factors limiting radiotherapy treatment, and their treatment is not codified. Hyperbaric oxygen (HBO) has been used for over half a century in an attempt to treat late complications. This prompted European Society for Therapeutic Radiotherapy and Oncology and European Committee for Hyperbaric Medicine to organise a consensus conference in October 2001, dealing with the HBO indications on radiotherapy for the treatment and prevention of late complications. This updated literature review is part of the documents the jury based its opinion on. Despite the small number of controlled trials, HBO may be indicated for the treatment of mandibular osteoradionecrosis in combination with surgery, haemorrhagic cystitis resistant to conventional treatments and the prevention of osteoradionecrosis after dental extraction, whose level of evidence seems to be the most significant though randomised trials are still necessary.

Keywords: radiotherapy, late complications, osteoradionecrosis, soft tissue radionecrosis, post radiation proctitis, post radiation cystitis, post radiation laryngeal necrosis

1. OSTEORADIONECROSIS

Osteoradionecrosis is one of the most serious complications arising from head and neck radiation therapy, and so one of the most studied. Mandibular bone is by far the first site concerned, with a few cases reported involving maxilla or temporal bone¹,². Since its description in the 1920s, its incidence, causality, contributing factors and management have been a topic of debate.

Most authors define the entity in terms of clinical parameters in their studies. Incidence reporting for osteoradionecrosis may not be as accurate as for other diseases due to the lack of standard definition. Certain authors define osteoradionecrosis as an bone exposure longer than 3 months\textsuperscript{3-6}. Marx and Johnson\textsuperscript{7} define it as an area of exposed bone that has failed to show any evidence of healing for at least 6 months. Radiographically, periosteal thickening and lytic destruction are common\textsuperscript{8}. A tumor recurrence must be excluded. Necrosis or irritation of adjacent tissues are common. As necrosis persists, secondary infection, fistula formation or fracture may ensue.

1.1 Incidence and pathophysiology

The reported incidence is variable. Comparison is difficult because of differences between studied population (radiotherapy alone, technique of radiation, brachytherapy, surgery more radiotherapy, policy of dental management…). Overall the incidence has considerably decreased for the last twenty years and in recent series the incidence is inferior to 5 \textsuperscript{%}\textsuperscript{5,9-12}.

Early the role of vascular damage in the pathophysiology of osteoradionecrosis has been advocated\textsuperscript{13,14}. Its pathogenesis has been studied in a animal model in which high dose, fractionated megavoltage (equivalent to 70 Gy in 35 fractions of Cobalt 60) was administered to the mandible of rhesus monkeys\textsuperscript{15}. Blood vessels in the periodontum, periosteum, haversian bone and marrow were reduced in number and calibre (by obliterative endarteritis, fibrosis, periarteritis).

Similar histologic changes have been observed in human specimens, with fibrosis of the marrow spaces\textsuperscript{7,16,17}. The vascularisation of the mandible is precarious. All areas of the craniofacial skeleton other than the mandibular body are supplied by periosteal and muscular perforators that are very redundant. The entire posterior segment of the mandible receives most of its blood supply from the surrounding musculature\textsuperscript{18}. In contrast, the inferior alveolar artery has been shown to be primary nutrient source of the mandibular body\textsuperscript{18,19}. Additionally, the atherosclerotic changes in the inferior alveolar artery precede those in the others vessels of the head and neck\textsuperscript{20}.

Initially sepsis was considered as an very important factor of the pathogenesis of osteoradionecrosis. Meyer\textsuperscript{21} defined the classic triad as radiation, trauma and infection. Osteoradionecrosis and osteomyelitis were synonym. Introduction of sepsis by a trauma in avascular bone produced osteomyelitis. Irradiated bone was thought to be susceptible to infection because of its inability to defend against bacteria due to decreased vascularity\textsuperscript{13-15,22-26}. The presence of bone sepsis hasn’t been clearly demonstrated in early studies. Epstein\textsuperscript{5} cultured the necrotic sites of 26 cases of osteoradionecrosis with aerobic techniques, however no pathogens has