TREATMENT FAILURE IN OSTEORADIONECROSIS INVOLVING THE MANDIBLE FOLLOWING ENBLOCK RESECTION OF THE AFFECTED BONE: A CASE REPORT

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Abstract

Osteoradionecrosis (ORN) of the jaws is a relatively common side effect of radiotherapy of head and neck tumours. It is a chronic condition that progresses slowly and does not tend to heal spontaneously. Irradiation brings about histological changes in hard and soft tissues, such as loss of ostoecytes, absence of osteogenic precussor cells, replacement of bone marrow by loose connective tissues and reduced expression of collagens and bone morphogenic protein by fibroblasts. Secondary lesions of these hypoxic tissues may then lead to an infection of the previously weakened bone and soft tissue and to development of a chronic, non-healing wound. Resection of bone without viable cells that remain around the area of resection will not facilitate revitalization. A case is presented of 35-year-old female with ORN of the mandible who presented with failure of wound healing following enblock resection of the affected part of bone. The possible causes of treatment failure and their management are discussed.

Key Words: Osteroradionecrosis, Treatment Failure, Mandible

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Introduction

Osteoradionecrosis (ORN) of the jaws is a relatively common side effect of radiotherapy of head and neck in patients suffering from malignant tumours. It is a chronic side effect of radiotherapy which progresses slowly and does not tend to heal spontaneously. It occurs more commonly in the mandible than the maxilla, most likely due to the relatively poor vascularisation of the lower jaw.[1] Many risk factors have been associated with ORN by different authors.[2,3] These include poor health status, tooth extractions due to poor dental status, radiotherapy after surgery and treatment using combined radio-/or chemotherapy before surgery. Abuse of alcohol and tobacco has also been identified by some studies as a risk factor in development of ORN.[4]

The development of ORN results from reduced vascularity and cellularity of oral hard and soft tissues as a result of radiation induced endarteritis. Irradiation brings about histological changes in hard and soft tissues, such as loss of osteocytes, absence of osteogenic precursor cells,

replacement of bone marrow by loose connective tissues, reduced expression of collagens and bone morphogenic protein by fibroblasts. Secondary lesions of these hypoxic tissues may then lead to an infection of the previously weakened bone and soft tissue and to the development of a chronic, non-healing wound.[5] ORN can lead to intolerable pain, fracture, sequestration of devitalized bone and fistulas which make oral feeding difficult or impossible.

The acute effects of radiotherapy in irradiated patients such as radiation mucositis occur during therapy and heal completely within several weeks. The cause of early stage ORN in less than 2 years after radiotherapy is high radiation and/or radiation trauma. Late stage ORN is observed for several years after radiotherapy and is related to trauma within the hypovascular – hypocellular hypoxic tissue[6]. This article reports treatment failure in a case of ORN and discuss the possible causes and management.

Case report

In May 1999, a 35 year-old female presented at the ENT-clinic with a 10 year- history of progressive swelling on the left submandibular region. The swelling extended to the submental region, left angle of the mandible and left sternocleidomastoid muscle. It was firm with some cystic areas. It was non-tender on palpation and the overlying skin was intact. The patient had undergone an operation in 1997 for a lesion on the same site but there was no histological result to show what kind of lesion it was. The Social history showed that she was married, a mother of six children of all of whom were alive. She is a house wife and does not drink or use tobacco. Clinical diagnosis of a submandibular neoplasm was made and patient was subjected to investigations. X-ray (orthopantomography-OPG), fine needle aspiration, full haemogram, urea and electrolytes were requested.

Full haemogram, orthopantomography, urea and electrolytes were normal. Fine needle aspiration (FNA) showed a highly cellular smear of multilayered sheets of benign epithelial cells in a solid and ductal arrangement. These features were suggestive of pleomorphic adenoma of the submandibular gland. In June 1999, she was operated under hypotensive General Anaesthesia. An elliptical incision over the skin overlying the mass was made and the whole mass was exposed and excised. Healing was uneventful and on 26th July 1999 she was also subjected to postoperative radiotherapy treatment.

In December 2002, (three years later) she reported to the same clinic (ENT), and this time presented with a wound on the left side of the mandible. Clinical examination revealed a large wound discharging pus and exposed body and angle of the mandible. Intra orally, there was poor oral hygiene and decay of teeth numbers 36, 37, 34 and 35 with roots only remaining. She was referred to the dental clinic for further evaluation. An OPG was ordered to evaluate the mandible. There was a gross destruction of the left body of the mandible from the angle to the region of the lower left lateral incisor with apparent dead bone (sequestra) within this area (Figure1).

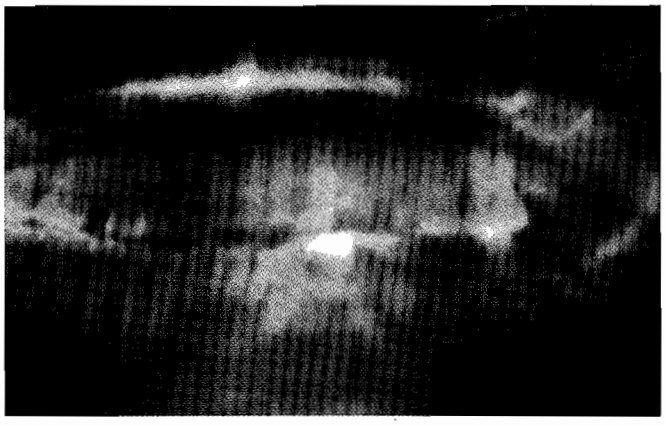

Figure1. Destruction of left body of the mandible due to osteoradionecrosis.

Diagnosis of osteoradionecrosis (ORN) was reached. Treatment plan was to resect the mandible from the angle to a region between 31 and 32 and to reconstruct the area later using a stainless steel plate when the infection had resolved.

In September 2005, she was taken to the theatre where resection of the mandible on the left side was done from angle to area between 31 and 32. The wound was cleaned with antiseptic solution (3% hydrogen peroxide) and closed primarily. She was put on antibiotics (cefuroximine and metronidazole intravenously) for five days. Three days postoperatively, the wound showed signs of infection and there was a massive pus discharge. On the 4th day postoperatively, the wound opened and there was complete communication with the oral cavity. Pus for culture and sensitivity was taken and at the same time a nasogastric tube was inserted for feeding (figure 2).

The results of culture and sensitivity showed heavy growth of citrobacter species which was sensitive to Augumentin, Cefuroximine, Gentamycin, Piperacillin and Ceftazidine. Ceftazidine was chosen. Despite using the antibiotic according to C/S results and daily dressing with antiseptic (rifocin), no improvement was observed and the condition got worse. She later developed tracheo-oesophageal fistula and neck contracture. The patient was referred to the ENT-department for management of the fistula. She improved and is currently being followed up on a half yearly basis.

Figure 2. Wound necrosis with communication with oral cavity on day four following resection of necrotic bone.

Discussion

Osteoradionecrosis has been associated with risk factors such as poor oral health status, tooth extractions due to poor dental status, radiotherapy after surgery, treatment using combined radio-/chemotherapy before surgery and abuse of alcohol and tobacco.[2] As radiotherapy reduces the proliferation of bone marrow, periostal, endothelial cells and the production of extracellular matrix especially collagen, irradiated areas have reduced vascularity and cellularity of both hard and soft tissues. Therefore, secondary affliction of these hypoxic tissues may then lead to an infection of previously weakened bone and soft tissue and to the development of a chronic, non-healing wound. Even when apparently complete recovery from acute effects of radiotherapy has taken place, the stem cell pool of rapidly dividing tissue is often depleted. For example, taking biopsy of soft tissue in a previously irradiated area can lead to an area of localized necrosis which may not heal. Care must be taken in maintaining good oral hygiene before radiotherapy treatment or extractions of teeth, performing major surgical procedures in a previously irradiated area and the use of combined radio/chemotherapy before surgery. Furthermore chemotherapy is likely to weaken the local immune response by damaging the cellular immune system. Chemotherapy has an anti-angiogenic potential which is important for anti-tumoural effects. It also reduces the level of vascular endothelial growth factor (VEGF).

The present case reported back 3-years later after radiotherapy treatment with large wound on the irradiated area and which was massively discharging pus. She was also having poor oral hygiene with teeth 36, 35, 34 and 25 gross caries with only roots remaining. This was certainly a late stage of ORN which is usually related to trauma or infection within the hypovascular-hypocellular hypoxic tissues. Poor dental status implies a high risk for osteoradionecrosis. Radiotherapy with a total reference dose of 50 Gy is considered to produce compromised soft and hard tissues. Radiation level needed to kill malignant cells ranges from 40-70Gy[7]. Therefore, apart from ORN other side effects of radiotherapy treatment include xerostomia, stomatopyrosis, high caries activity, epithelial atrophy, mucosal ulcer, candida infection and alopecia[8].

Osteoradionecrosis can be confused with chronic osteomyelitis as clinically and radio graphically they resemble each other. However, they can be differentiated histologically because ORN demonstrates bone with irregular trabeculae without osteoblastic activity. The marrow is usually replaced by acellular fibrous tissue with bone debris and usually lack inflammatory cells. On the other hand, chronic osteomyelitis demonstrate bone with irregular trabeculae due to osteoclastic and osteoblastic activity and bone marrow replaced by fibrous tissue. Inflammatory cells are present. Therefore all tissues removed from areas suspected of an ORN should be submitted for histological evaluation to rule out other conditions such as osteomyelitis and metastatic lesions.
Literature review showed that several methods have been tried to treat ORN. These methods include:

- Application of vascularised bone graft following resection of affected bone part.
- Application of cytokines (cytokines amplifies the sleeping residual population of cells in the host bone).
- The use of hyperbaric oxygen (HBO) which induce the neovascularisation of irradiated bone.
- Block resection of the affected area (i.e. resection with preservation of the lower border of mandible)

Some of these methods are still debatable. However, Merx and Johnson 1985, [6]reported about the efficacy of HBO treatment for prophylaxis in tooth removal after radiotherapy. Hyperbaric oxygen treatment has been used to promote revascularisation of the irradiated tissues. In the present case, resection of the mandible was carried out, followed by primary closure and antibiotic cover of the patient. This was followed by wound dehiscence 3-days postoperatively and profuse pus discharge. The reason for this is that the bone and soft tissue of the previously irradiated area were already weak. They had reduced vascularity and cellularity and hence regeneration and vascularisation were poor. Resection of bone without viable cells that remained around would not be able to revitalize dead bone. Radiation apparently has deleterious effects on osteocytes, osteoblasts and endothelial cells, causing reduced capacity of bone to recover from injury. Therefore, conservative surgical removal of necrotic bone would have assisted the patient in the healing process. This has been demonstrated by Ruggiero[9]; that the proper protocol in management of ORN should include antibiotic therapy, irrigation with hydrogen peroxide associated with 2% potassium iodide, sequestrectomy and surgical debridation. If resection of the affected bone is contemplated then application of vascularised bone graft should be mandatory. The use of HBO chamber would add an advantage since HBO induces neovascularisation of irradiated bone. The proper management of this case would have been the use of the above protocol in combination with HBO which unfortunately is not available in our setting.

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