

Conservative Approach of a Severe Case of Osteoradionecrosis of the Mandible- Case Report

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Case Report

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Crossref doi: <https://doi.org/10.36437/ijdrd.2020.2.3.G>

ABSTRACT

Osteoradionecrosis (ORN) of the jaw is a severe, complex, and multifactorial complication of radiotherapy (RT) for head and neck cancers. Most cases of ORN develop during the first 3 years with a peak between 6 months and 2 years after completion of RT however the patient is considered at risk of developing this condition many years later. The management of ORN is usually based on conventional medical care by focusing on comorbidity factors. However, in some refractory ORN cases, the condition requires extensive surgical resection. Based on the "the radiation-induced fibro-atrophic theory" introduced by Delanian, a new conservative approach of ORN seems to be promising by combining antioxidant agents: pentoxifylline and Tocopherol (PtxE) in the treatment of severe cases of ORN.

The aim of this paper was to report the case of a severe case of ORN of the mandible stabilized by a conservative approach combining antibiotics, antiseptic agent as well as antioxidant therapy (PtxE), and to discuss the efficacy of this approach.

Keywords: Osteoradionecrosis (ORN), fibro-atrophic theory, Mandible, Conservative Approach.

Introduction

Osteoradionecrosis (ORN) of the jaw is a severe, complex, and multifactorial complication of radiotherapy (RT) for head and neck cancers. According to the most recent literature, ORN of the jaws was defined as "an exposed irradiated bone that fails to heal over a period of 3 months without any evidence of persisting or recurrent tumor".¹

Ewing² was the first to use the term 'radiation osteitis' to describe changes that occur in the bone after the radiotherapy. Later, several terms were used to name these changes in the irradiated bone, such as radiation osteitis, ORN, and avascular bone necrosis.³



In 1983, Marx defined ORN as 'an area larger than 1 cm of exposed bone in a field of irradiation that failed to show any evidence of healing for at least 6 months'.⁴

In 1987, Marx and Johnson suggested the definition of ORN as: 'The exposure of non-viable bone which fails to heal without intervention'.⁵

Most cases of ORN develop during the first 3 years (70%–94%), with a peak between 6 months and 2 years after completion of RT, however, the patient is considered at risk of developing this condition many years later.⁶

The most important inducing factor is a surgical trauma, commonly a dental extraction. However, Other trauma causing mechanical injuries as well as poor dental status can induce the necrosis as well (1). In less than 10% of the cases, ORN occurs spontaneously.⁷

The pathophysiology of ORN has evolved through the time. First, microorganisms were considered to play an important role in the occurrence of ORN in irradiated bone. Meyer concluded to his theory of a classic triad of radiation, trauma, and infection.⁸ Later, Marx proposed the 3 H theory of hypoxia, hypocellularity, and hypovascularity.³

Recently, a new theory was proposed by Delanian⁹: "the radiation-induced fibroatrophic theory". This theory proposed that the progression of ORN is due to the activation and the deregulation of fibroelastic activity that leads to atrophic tissue in the irradiated area.

The management of ORN is usually based on conventional medical care focusing on comorbidity factors. Basically, by the optimization of oral hygiene, infection control with antibiotics and antiseptic agents, and the removal of the devitalized bone when possible. However, the Refractory ORN requires extensive surgical resection.¹⁰

Based on the recent theory of the radiation-induced fibroatrophy, a combination of an antioxidant treatment combining pentoxifylline and tocopherol (PtxE) with or without the adjunction of Clodronate (PENTOCLO) was suggested and tested on phase II clinical trial.¹¹

However, the reported results remained controversial. In some cases, there were good results with a healing rate that reached 100%¹² but in other reports, there was only little improvement with higher toxicity.¹³

The aim of this paper was to report the case of a severe ORN of the mandible stabilized by a conservative approach combining antibiotic, antiseptic as well as antioxidant (PtxE) therapy, and to discuss the efficiency of this approach compared to a more radical one.

Case report: A 59-year-old female patient was referred by her dentist for "severe pain due to a purulent lesion on the right side of the sub-mandibular area.

The medical history of the patient revealed that she was diagnosed with a T2B N1M0 undifferentiated carcinoma of nasopharyngeal type (UCNT) in 2012 and treated with combined Chemotherapy and conventional curative radiotherapy. The Total dose of the delivered radiotherapy was 74Gy with a fractioning of 2Gy per day, 5 days per week.

No systemic disease or chronic conditions were present.

The extra-oral examination of the patient revealed a painful, purulent, and indured lesion of her right sub-mandibular area. (figure1 and 2). No recent teeth pain or extraction was reported.



Figure1 and 2: Extra Oral Examination: Painful Purelent Lesion of the Sub- Mandibular area.

The patient had a severe limitation of her mouth opening as well as severe xerostomia that were both attributed to the side effects of the radiotherapy. (figure4)

The intra-oral examination, which was difficult to perform given the severe trismus, showed: very poor oral hygiene. All the remaining teeth were severely decayed. (figure 2 and 3).





Figure 3 and 4: Intra Oral Examination: Decayed Teeth and Severe Xerostomia

The purulent exudate was evident in the socket of 47. A small area of exposed bone was also noticed in the lower vestibule.

The panoramic radiograph showed that the roots of 47.46.45 and 44 were present and presented radiolucent images in their apical region combined with confluent radio opacities (figure5).



Figure5: Severe Limitation of the Mouth Opening

CT scan showed osseous abnormalities of the entire mandible, with focal lytic areas as well as cortical interruptions and loss of the spongiosa trabeculation on the symptomatic side. (figure6) The diagnosis of stage III of Epstein ORN of the mandible with submandibular fistulae was made. Our therapeutic approach consisted in the prescription of Amoxicillin-Clavulanic Acid (Augmentin) 3g/day in association with metronidazol (Flagyl) 1.5g/day for 2 weeks.

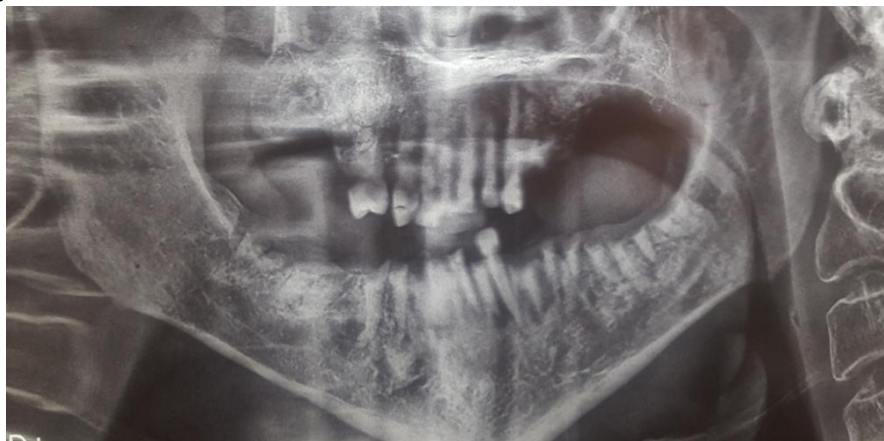


Figure 6: Panoramic Radiograph Showing Increased Radiodensity and Mixed Radioopaque/Radiolucent Lesion

We also prescribed Pentoxifylline (Torental) 800mg/day, Tocopherol 1000UI/day for 2 weeks Paracetamol 3g /day and Chlorhexidine mouthwashes 4 times/day. Pilocarpine 4mg 5 times daily The extraction of 47 was postponed.

Ten days later, we noticed an improvement in the fistulae which showed signs of resolution of the infection (figure 7 and 8). The patient also reported a decrease in her pain and an improvement of her mouth opening (figure 9).

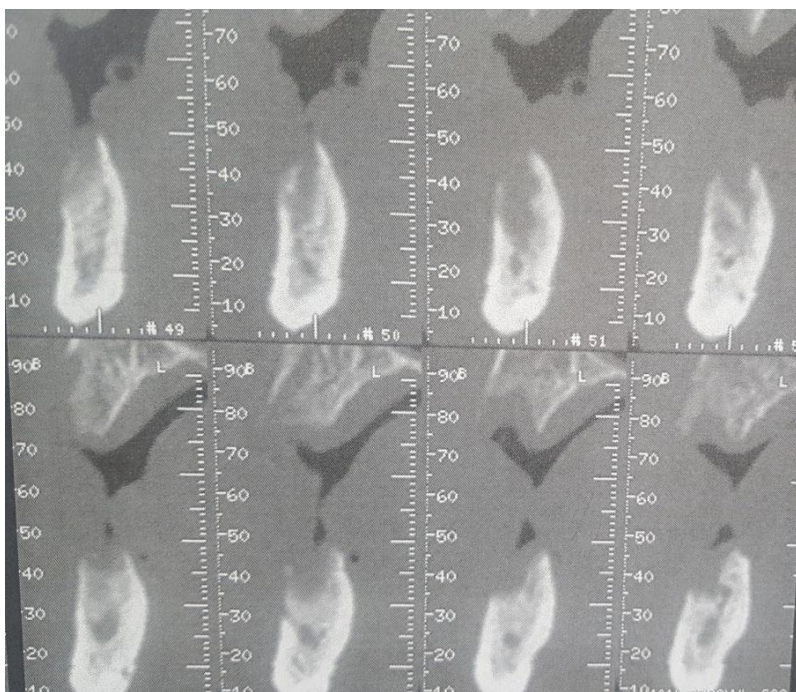


Figure7: CT Scan Cortical Bone Destruction





Figure 8 and 9: Control Images Showing Improvement of the Condition with Regression of the Infection and the Inflammation.

However, on the intraoral examination, we noticed that the socket of the tooth 47 was still infected. So we decided to perform the extraction of 47 under local anesthesia followed by a meticulous curettage of the socket using an antiseptic solution. No modification of medical therapy was made.

The patient was received 3 weeks later. She reported a significant improvement in her pain and her fistulae. The socket of 47 showed signs of good cicatrisation. However, the patient reported a severe intolerance to Pentoxifylline in the form of severe nausea which led her to stop taking it.

The patient was asked to continue her antibiotherapy, Vit E, and the pilocarpine as well as the use of the mouth wash. However, the use of Ptx was interrupted. Follow-ups were programmed monthly.

Discussion: ORN of the jaws remains among the most commonly encountered and severe complications of radiotherapy for head and neck cancers.³

This condition occurs more frequently in the mandible because of its relatively poor blood supply, which is exclusively provided by the inferior alveolar artery.¹⁵ Moreover, ORN is generally caused by local trauma such as a dental extraction however some other incriminated patient dependent risk factors are reported such as age, diabetes, collagen vascular disease but also poor oral hygiene and alcohol and tobacco consumption.¹⁵ In our case, no dental extraction was reported and the complication was attributed to bad oral hygiene.

Different staging and scoring systems of ORN have been proposed.

These systems are based either on the response to hyperbaric oxygen (HBO) therapy; Marx staging system (5) or on the degree of bone damage, clinical- radiological findings, duration of bone exposure and treatment required.^{16,17,18}

In our case, the patient was considered as a stage III of Epstein (table I), since her condition was progressive with purulent exudates in both the fistulae and the socket of 47 as well as the severe pain and trismus.

In fact, the clinical symptoms of ORN vary but generally include ulceration of the mucosa with exposure of necrotic bone that fails to heal for more than 3 months as well as pain, trismus and suppuration which were the main symptoms of our patient.¹⁸

Stage	Description	Symptoms
I	Resolved healed	None
Ia	No pathologic fracture	None or Controlled
Ib	Pathologic fracture	
II	Chronic persistent non progressive	
IIa	No pathologic fracture	
IIb	pathologic fracture	Jaw Dysfunction
III	Active progressive	Progressive
IIIa	No pathologic fracture	
IIIb	Pathologic fracture	Jaw Dysfunction

Table I ORN staging according to Epstein¹⁷

The progression of ORN may lead to pathological fractures and local or systemic infection. Difficulties in mouth opening, mastication and speech frequently arise and affect severely the patient's quality of life.¹⁸

The diagnosis of septic ORN appears to be easier. Marked by pain as a primary symptom¹⁷ However, in some cases, this complication is only revealed by radiographic images that show localized osteolytic areas, extensive osteolytic areas, sequestra and fracture.¹⁸

In our case, the radiographic alterations were in the form of increased radiodensity, as well as a mixed radioopaque/radiolucent lesion in which radiolucent areas represented bone destruction. (Figure 8)

The management of ORN is usually based on conventional medical care focusing on comorbidity factors. Basically by infection control with antibiotics and antiseptic agents as well as by the removal of the devitalized bone when possible.¹⁹

In our case, the infection was controlled with association of Amoxicillin - Clavulanic acid and Metronidazol as well as Antiseptic agent; Chlorohexidine mouth wash.

We also prescribed Pentoxifylline and Tocopherol (Vit E) following the protocol proposed by Delanian.¹¹

Pentoxifylline (PTX), is an antioxidant agent generally used to treat vascular diseases such as intermittent claudication. In vivo, it has been reported to have an anti-TNF α effect, increase erythrocyte flexibility, vasodilate, and inhibit inflammatory reactions.¹¹

The recommended dose used by the authors are: Pentoxifylline: 800mg /day, Tocopherol; 1000UI/day with a treatment duration that varies from 3 to 24 months.^{11,12}

McLeod et al. reported in their study of 12 patients who had received this protocol for an average of 14.8 months that 5 of these patients improved, 5 remained stable, and 2 deteriorated, requiring microvascular reconstructive surgery.²⁰

A modified protocol proposed by D'souza involved administering 800 mg/day of pentoxifylline, 1000 IU/day of tocopherol, and 100 mg/day of doxycycline. With the use of this protocol, the cure rate reached 70% among patients with stage I and stage II disease, whereas the disease remained stable in 40% of patients in stage III.²¹

In another retrospective analysis of 62 patients with established ORN, led by Patel et al, the success rate reached 56% in patients how received Ptx and Vit E association.²²

Even if this protocol seemed to be safe with minimum side effects,²³ our patients had developed a severe intolerance to pentoxifylline which justified the interruption of the treatment a few weeks later. Some other side effects of Ptx were reported in the literature such as vertigo, nausea and headache.²⁴

In some cases of ORN, surgical approaches such as small sequesters removal and debridement of superficial bone until bleeding were also reported in many studies as conservative management. In advanced or refractory cases of ORN, surgical treatment, including microvascular reconstructive techniques for bone and soft tissue, remains the only option available.²⁵

In our case, the extraction of the residual roots of 47 was indicated since they were infected with signs of alveolar abscess which also was incriminated in the onset of the ORN. however, no other surgical treatment was proposed due to the good results obtained with this conservative approach.

Conclusion

This case report showed that conservative treatment of ORN should be indicated and implemented whenever it is possible based on the infection control with antibiotic and antiseptics agent with minimal surgical debridement. This approach can improve the overall situation of the patient especially when the surgical treatment may cause severe morbidity and does not always guaranty the healing or the improvement of the condition.

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How to cite this Article: Touil Dorsaf¹, Hassouna Mariam El Ons², Abdel Mouleh Yosri³, Oualha Lamia⁴: *Conservative Approach of a Severe Case of Osteoradionecrosis of the Mandible- Case Report*

Int. J. Drug Res. Dental Sci., 2020; 2(3): 45-54.

Crossref doi: <https://doi.org/10.36437/ijdrd.2020.2.3.G>

Source of Support: Nil, **Conflict of Interest:** Nil.

Received: 16-7-2020 **Revised:** 19-8-2020 **Accepted:** 20-8-2020