# Bisphosphonate induced osteonecrosis on the peri-implantation area : A case report

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## Ⅰ. Introduction

Every year, an estimated 30 million bisphos-phonate prescriptions are written in the U.S. alone. It is estimated that pamidronate and zoledronate have been used in over 2.5million patients worldwide[1]. Some patients who have Paget's disease and osteolysis with metastatic bone disease may not be able to survive without bisphosphonate therapy. Others suffered from a osteoporosis may develop further spontaneous fractures if bisphosphonates are discontinuated.

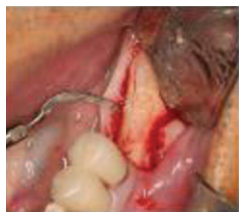
But, there is a serious oral complication of bisphosphonate therapy involving the exposure of necrotic maxillary or mandibular bone[2]. That is a bisphosphonate induced osteonecrosis and it is recently recognized clinical entity. The first report of this painful avascular necrosis of the bone in the mandible and maxilla in patients receiving the bisphosphonates was published by Marx et al. and new cases are being reported daily.[3]

Clearly, patients receiving bisphosphonates intravenously are more susceptible to bisphosphonate induced osteonecrosis of the jaw than are those receiving oral forms. Thus, it is not common to see bisphosphonate induced. However, beginning in 2006, cases began to apprear in the literaure.[4-7]

In this report, we present a case of a 84-year-old patient who received for 2 years oral forms of bisphosphonate induced osteonecrosis of the mandible.

## Ⅱ. Case

A 84-year-old man came for seeking to have his missing teeth - the mandibular left first molar and second molar - restored. After thorough clinical and radiographic examination. A treatment plan was proposed that included initial periodontal therapy and implant placement. After periodontal treatment, 2 tapered scew vent implnats (Zimmer, USA) were placed in the area of the missing teeth (fig. 1).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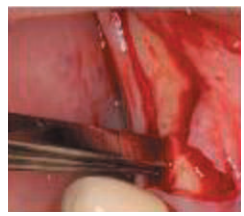
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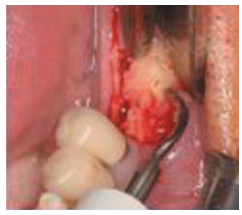
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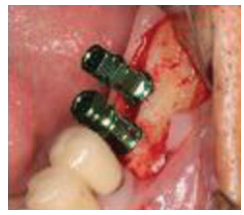
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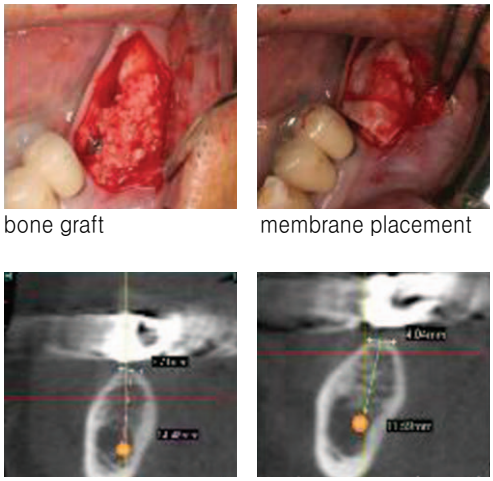


Fig. 1. Operation procedure for implantion.

Post-operative wound healing was uneventful. During the 5 months follw up period, no discomfort reported by patient. Solid abutments were conneted to the implants, and crowns were fabricated without any problems(fig.2).

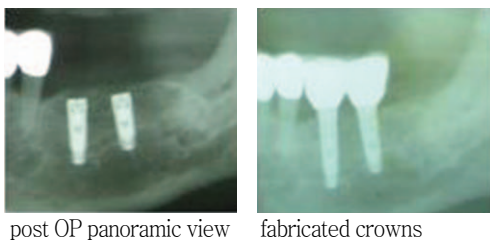


Fig. 2. post operative wound healing was uneventful.

However, some inflammatory signs and symptoms were observed on the second molar area 1month later and the peripheral bone of the implant was exposed. First, the crowns were disconnected and the inflammatiory area was disinfected by Erbium YAG laser periodically and local rinses with chlorhexidine. Additionally, long-term antibiotics therapy were performed. As a result, inflamatory signs and symptoms were thought to be improved(fig.3).

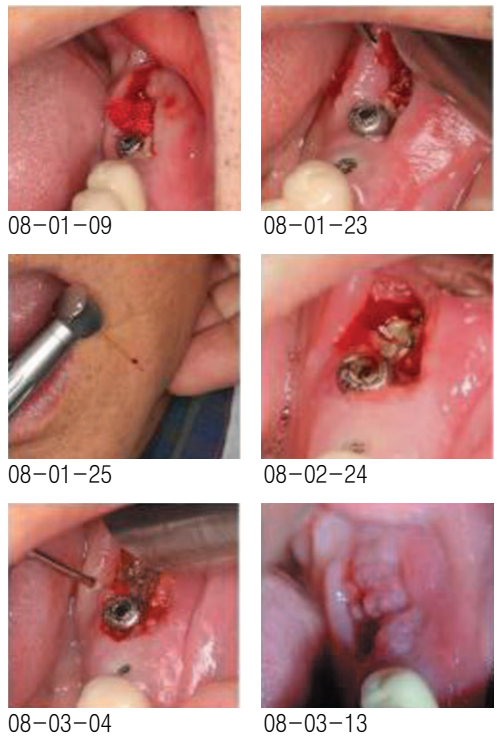


Fig. 3.Inflammatiory signs and symptoms were observed. After 3months later, it is thought to be improved.

but, the exposed bone became mobile and panoramic radiograph revealed that sequestrum was formed on the second molar area. The sequestrum was removed with the implant(fig. 4).

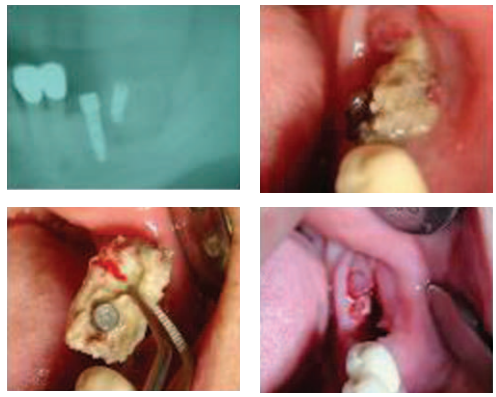

Fig. 4. The exposed bone was formed sequestrum and it was removed with the implant

Frequent follow up check and oral hygiene maintenance was done and the large osseous defect was healed. 2 months later, the first molar implant was restored with crown and has remained symptom free(fig. 5).

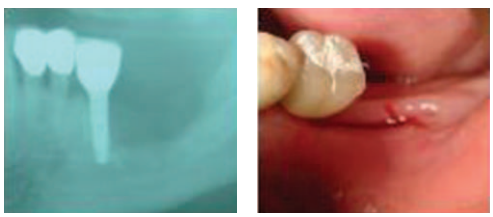

Fig. 5. The large osseous defect was healed and the first molar implant was restored with crown.
The patient is called regularly for evaluation and maintenance care.

## Ⅲ. Discussion

Bisphosphonate induced osteonecrosis can be defined as " The unexpected development of necrosis in the oral cavity of a patient who has received bisphosphonates but not radiotherapy to the head and neck"[8].

The exact mechanism of bisphophonate induced osteonecrosis of the jaws is unclear. Bisphosphonates bind to bone and incorporate in the osseous matrix. During bone remodeling, the drug is taken up by osteoclasts and internalized in the cell cytoplasm, where it inhibits osteoclastic function and induces apoptotic cell death. Bisphosphonates also inhibit vascularity which could potentiate the ischemic effects. As a results, bone turnover becomes suppressed[2,9,10].

The presence of teeth may lead to exposure of the environmental bone which requires an increase in bone turnover because of repeated inflammation, abscess formation, and tooth extraction. Edentulous patients often have poor fitting dentures which may lead to chronic irritation and inflammation to the gingiva and underlying alveolar bone. It may induce osteonecrosis of the jaw.[2,11]

The most common clinical presentation associated with bisphosphonate induced osteonecrosis of the jaw is an ulcer with exposed bone in a patient who has had a dental extraction. An ulcer from a ill fitting prosthetic device has also been implicated in the initiation of this pathologic process. Similar to osteo- radionecrosis, in the early stages of bisphosphonate induced osteonecrosis of the jaw, radiographic manifestations can not be seen. Patients may be asymptomatic but may have severe pain because of the necrotic bone becoming infected secondarily after it is exposed to the oral environment. The osteonecr-osis often is progressive and may lead to extensive areas of bony exposure[8,12].

Because there is no effective treatment ,the management of bisphosphonate induced of the jaws presents a challenge to dentists. The goal is to get the patient comfortable.

If the exposed bone is asymptomatic, maintenance with 0.12% chlorhexidine is all that is initially required. If the evidence of infection is present, antibiotics should be provided in addition to the chlorhexidine rinse. Penicillin is the drug of choice and if the patient is allergic to penicillin, doxycyclin is the second line drug. The antibiotics should provided for 14 days or until the pain is controlled and only restarted if pain returns. In patients refractory to these antibiotics the addition of metronidazole has proven effective. Clindamycin is not recommened due to its absent or low activity against the microorganisms seen in bisphosphonate

induced osteonecrosis cases[2,13].

A local debridement can be accomplished, if the exposed bone shows clinical or radiographic evidence of a sequestrum with the anticipation of uncomplicated healing[14]. In extensive cases where purulent exudates or sinus tracts are visualized, culture and microbial sensitivity testing may be warranted and may require more extensive surgical procedures[15].

Marx has suggested a management protocol for patients who receiving bisphosphonate therapy, bisphosphonate discontinuation and CTx monitoring may be needed before surgery[17]. CTx is the marker of the bone remodeling[16]. CTx level should be greater than 150 pg/mL before surgery.

The bisphosphonate would be discontinued for 3 months before the procedure if approved by the patient's physician. The patient would not take bisphosphonate for a further 3 months following surgery[17]. The patients who are about to start taken bisphosphonates, most reports of bisphosphonate induced osteonecrosis of the jaw occur after the patient has been taking bisphosphonates for 6 months or more, for 2 years in this case, so it may be possible to provide dental care early in the treatment for without development of osteonecrosis from dental treatment[13]. If possible institution of bisphosphonate therapy should be delayed for approximately 4 to 6 weeks after invasive procedures such as dental extractions to give the bone a chance to recover[2,14,18].

## Ⅳ. Conclusion

The treatment of patients receiving oral or intravenous bisphosphonate therapy is principally preventive. All potential sites of infection must be eliminited and frequent periodic follow up visits should be scheduled to reinforce the importance of oral hygiene maintenance.

If the patients are suffered from bisphosphonate induced osteonecrosis of the jaw, all dental treatments involving scailing and prophylaxis should be done atraumatically and gentlely. One should try to avoid dental extractions if possible and if necessary, should perform them as atraumatically as possible. Any existing prosthetic appliances should be re-evaluated to minimize soft tissue trauma.

Also, significant to dentists, It should be performed and given information about bisphosphonate induced osteonecrosis of the jaw to all patiens receiving bisphosphonate therapy and be made aware of the early signs of development of this condition.

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Abstract

# 경구 투여한 bisphosphonate 와 연관된 골괴사에 관한 증례보고

손효정, 장호열, 이장열, 안현정, 김현철, 박일해, 이상철

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Bisphosphonate는 paget병과 같은 대사성 골질환 및 전이성 암종과 연관된 골격성 질환과 골다공증의 예방 및 치료에 널리 사용되고 있는 약물이다. 정확한 약물의 작용기전은 알려져 있지 않으나 주요 약리학적인 작용은 파골세포를 억제시켜 정상적인 골치환 주기의 불균형을 가져와 골질에 문제를 일으키는 것으로 생각되고 있다.

본 보고는 경구로 2년간 bisphosphonate를 복용한 84세 남자 환자에서 하악 좌측 제1, 2 대구치부에 2개의 임프란트를 식립한 후 제 2대구치부 임프란트 주변 골에 괴사가 일어나 부골이 형성되어 임프란트를 포함한 부골을 제거한 경우이다. 주기적인 follow up을 통해 oral hygine 유지를 해주어 큰 골의 결손부는 회복되었고 제1대구치부 임프란트는 기능을 할 수 있게 되었다.

흔히 경구용 bisphosphonate를 복용했을 경우, 그리고 복용기간이 3년이 넘지 않았을 경우에는 심각한 부작용이 있을 수 있음을 간과하기 쉬우나 이같이 나타날 가능성이 있으므로 임프란트 식립 및 기타 치과 치료 시 이에 대한 고려가 충분히 필요하다고 생각되어 이를 보고하는 바이다.