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The high risk of the development of medication-related osteonecrosis of the jaw in prostate cancer patients with bone metastasis: A case report

KEYWORDS

Medication-related
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Bone metastasis;
Antiresorptive drugs;
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The medication-related osteonecrosis of the jaw (MRONJ) is a serious complication of treatment with antiresorptive drugs such as bisphosphonates and denosumab. The MRONJ is a relatively common condition among dental patients treated with antiresorptive drugs. Among them, the incidence of MRONJ is ranged from 0.1% to 1%, depending on the drug type, duration, and route of drug administration. In addition to osteoporosis patients, the cancer patients with bone metastasis are also often treated with anti-bone resorption drugs.^{1,2} Those cancer patients with bone metastasis treated with antiresorptive drugs for reducing bone destruction have become a high-risk group for the MRONJ. Although the incidence of MRONJ is not high, once it occurs, it often affects the patients' quality of life and their subsequent medications. To avoid the occurrence of MRONJ after dental treatments, the patients and the dentists play a very important role. In this study, we presented a MRONJ case caused by the periodontitis of tooth 35 and the subsequent extraction of tooth 35 in a prostate cancer patient with bone metastasis who received the antiresorptive treatment of injection of Xgeva (denosumab).

This male patient born in 1952 came to the local dental clinic for the first time for the toothache of tooth 45 at the

age of 60. The panoramic radiograph taken at the age of 60 demonstrated his original teeth and jawbone condition (Fig. 1A). Four years later, the patient's teeth 14 to 18 had been replaced by a new dental bridge and the teeth 36 and 37 had been replaced by the dental implants, while the condition of the right mandibular posterior teeth gradually deteriorated (Fig. 1B). At the age of 66 when the patient was suffering from the toothache and mobility of tooth 35, the panoramic radiography revealed the periodontal ligament widening of tooth 35 (Fig. 1C). According to the patient's statement, he was diagnosed as having the prostate cancer and was treated by injection of Xgeva (denosumab) once per month due to the prostate cancer bone metastasis. The local dentist recommended the extraction of affected tooth 35 six months after the last injection of denosumab. When the patient's tooth 35 was extracted (in the dental clinic) 6 months later, the socket of tooth 35 and the jawbone of the dental implants of teeth 36 and 37 area still did not heal, and the MRONJ was diagnosed (Fig. 1D). This finding suggests that the long-term inflammation of the alveolar bone and the infection of the extraction socket may further cause osteonecrosis of the jaw bone, especially when the patients had been treated with

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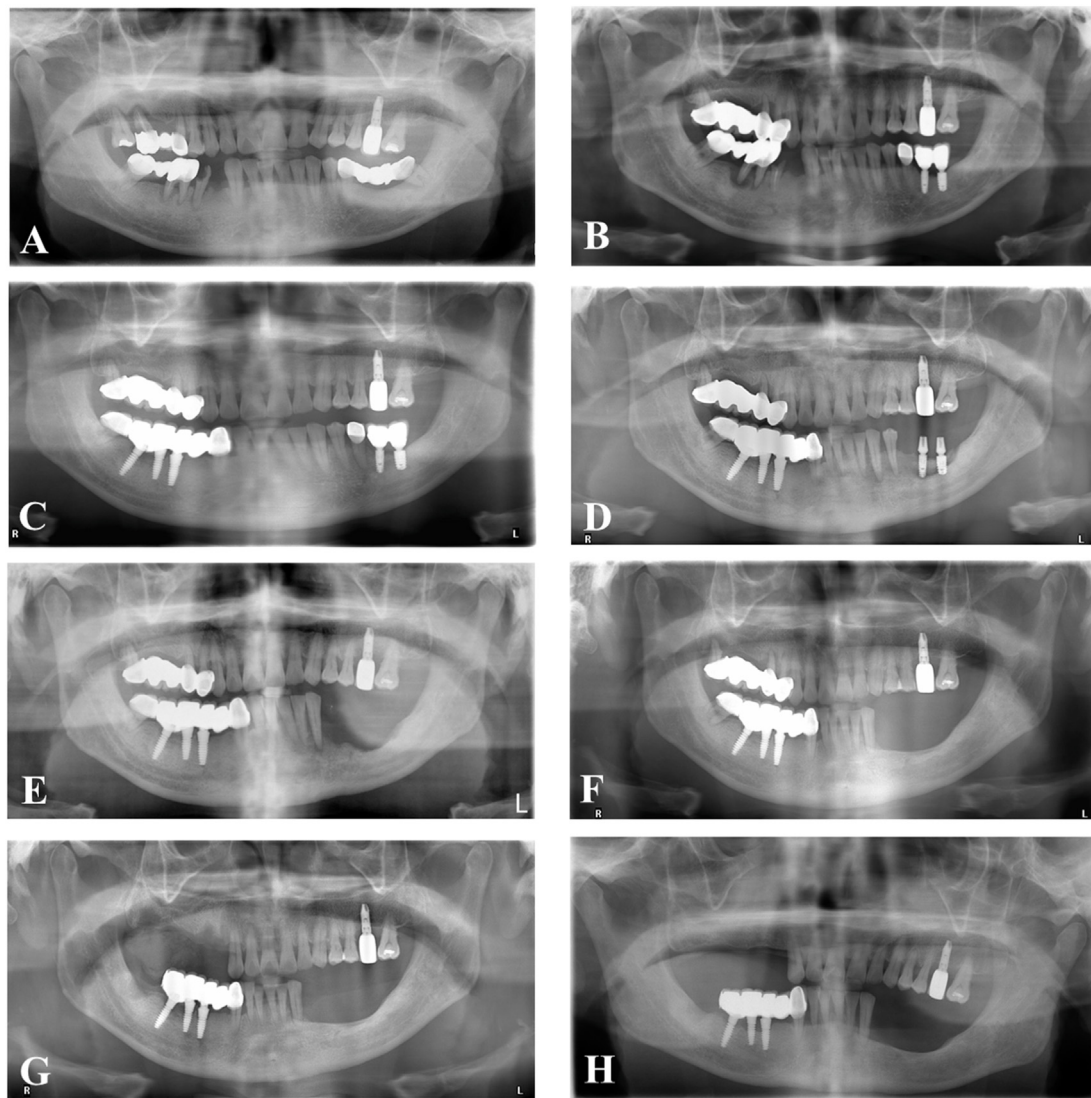


Figure 1 A series of panoramic radiographs of our patients with the medication-related osteonecrosis of the jaw (MRONJ). (A) The panoramic radiograph taken at the time when the patient visited the local dental clinic for the first time for the toothache of tooth 45 at the age of 60, demonstrating his original teeth and jawbone condition. (B) Panoramic radiograph taken at the time when the patient was 64 years old, showing the teeth 14 to 18 having been replaced by a new dental bridge and the teeth 36 and 37 having been replaced by the dental implants, while the condition of the right mandibular posterior teeth in a state of gradual deterioration. (C) Panoramic radiograph taken at the time when the patient was suffering from the toothache and mobility of tooth 35 at the age of 66, revealing the periodontal ligament widening of tooth 35 and the teeth 43 to 48 having been replaced by a new dental bridge combined with the dental implants. According to the patient's statement, he was diagnosed as having the prostate cancer and was treated by injection of Xgeva (denosumab) once per month due to the prostate cancer bone metastasis. The local dentist recommended the extraction of affected tooth 35 six months after the last injection of denosumab. (D) Panoramic radiograph taken at the time when the patient's tooth 35 was extracted (in the dental clinic) 6 months later, showing that the socket of tooth 35 and the jawbone of the dental implants of teeth 36 and 37 area still did not heal, and the MRONJ was diagnosed. (E) Panoramic radiograph taken at the time when the patient completed the treatment of sequestrectomy at the posterior area of the left mandible and the removal of the dental implants of teeth 36 and 37 (in the hospital), showing the well-healed operation site at the posterior edentulous area of the left mandible in the early postoperative period. (F) Panoramic radiograph taken at the time two years after the sequestrectomy was performed, indicating a good clinical outcome of the operation site at the posterior edentulous area of the left mandible, while the periodontal condition of the right maxillary posterior teeth in a state of gradual deterioration. (G) Panoramic radiograph taken at the time when the patient completed the treatments of extraction of teeth 14, 15 and 18 and alveolar bone debridement at the corresponding area, showing the well-healed operation site at the posterior edentulous area of the right maxilla in the early postoperative period. (H) Panoramic radiograph taken at the time 4.5 years after the sequestrectomy was performed and 2.5 years after the right maxillary posterior teeth were extracted, indicating a good clinical outcome of the operation sites at the posterior edentulous area of the left mandible and at the posterior edentulous area of the right maxilla.

antiresorptive drugs. There were two clinical characteristics of this case. Although the osseointegration between the dental implants and the surrounding alveolar bone still existed, the whole block of the surrounding alveolar bone together with the dental implants finally became a block of sequestrum and separated from the adjacent healthy alveolar bone. Subsequently, after the patient received the treatment of sequestrectomy at the posterior area of the left mandible and the removal of the dental implants of teeth 36 and 37 (in the hospital), the operation site of the posterior edentulous area of the left mandible healed well in the early postoperative period (Fig. 1E). Two years after the sequestrectomy was performed, the panoramic radiography revealed a good clinical outcome of the operation site at the posterior edentulous area of the left mandible, while the periodontal condition of the right maxillary posterior teeth gradually deteriorated (Fig. 1F). Then, after the patient received the treatments of extraction of teeth 14, 15 and 18 and alveolar bone debridement at the corresponding area, the operation site at the posterior edentulous area of the right maxilla healed well in the early postoperative period (Fig. 1G). In addition, 4.5 years after the sequestrectomy was performed and 2.5 years after the right maxillary posterior teeth were extracted, there was still a good clinical outcome of the operation sites at the posterior edentulous area of the left mandible and at the posterior edentulous area of the right maxilla (Fig. 1H). Finally, the patient's two posterior edentulous areas were reconstructed with two removable partial dentures. Although it needed time to adapt to the use of the two removable partial dentures, the patient had no other complaints.

The occurrence of MRONJ is often related to the long-term tooth-related inflammation (such as periodontal disease or tooth pulp necrosis-caused periapical lesion), which may cause spontaneous MRONJ. In addition, antiresorptive drugs can lead to the osteosclerosis and thus result in the reduced bone blood circulation and metabolism. Therefore, if there is a bacterial infection after tooth extraction or dental implant surgery, the patients may suffer from the poor healing of the jawbone wound or the inability to regenerate new bone, finally resulting in the MRONJ. For our patient, the long-term periodontal disease of tooth 35, the bacterial infection of the extraction socket of tooth 35, and the long-term peri-implantitis of the dental implants of teeth 36 and 37 might be the major etiologies of MRONJ in our patient.

The dental professionals, especially the dentists, can and must play a key role in the prevention of MRONJ by identifying patients at a high risk for this disease through a thorough medical and dental history taking and careful treatment planning.^{3,4} Therefore, it is important that the dentists are fully aware of the complications of anti-resorptive therapy, the risk factors for MRONJ, and the latest treatment guidelines for the patients taking bisphosphonates and/or denosumab in the dental procedure.⁴ However, the majority of previous surveys showed inadequate awareness and unsatisfactory practices among the dentists regarding the MRONJ. These results are very

alarming. Thereby, an urgent action is required to help improve dentists' knowledge for preventing the MRONJ during the dental practice. The dentist continuing education courses, including workshops, seminars, and conferences, should address this gap.⁵ Knowing the optimal drug holidays of antiresorptive medications is very crucial to prevent the serious consequence of MRONJ. Hence, the dentists should be aware of the guidelines for the prevention of MRONJ.^{3,5}

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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