Letter to the Editor

Medication-related osteonecrosis of the jaw; what should we do as prosthodontists?

Keywords:
- Bisphosphonate
- Denosumab
- Medication-related osteonecrosis of the jaw
- Prosthodontic treatment
- TRAP-positive mononuclear cells

Dear Editor,

Medication-related osteonecrosis of the jaw (MRONJ), which is a rare but severe impairment of oral wound healing in patients taking antiresorptive drugs, including bisphosphonates (BPs) and denosumab, mainly occurs after tooth extraction [1]. Due to their pharmacological action, oral and intravenous BPs have been widely used to treat osteoporosis, bone metastases of solid tumors, multiple myeloma and Paget’s disease in Japan and other countries [2]. Denosumab, which is a human monoclonal antibody against the receptor activator of nuclear factor-κB ligand (RANKL), has recently been approved for osteoporosis and malignant therapies in Japan. Denosumab is also antiresorptive, but has a different pharmacological action than BPs in that it binds to RANK, and targets both bone resorbing osteoclasts and pre-osteoclasts [3].

1. Common findings in BP- and anti-RANKL antibody-induced impeded wound healing

Estimates for developing ONJ after tooth extraction in malignant patients exposed to intravenous BPs are 1.6–14.8% [1,4]. Malignant diseases themselves are not associated with ONJ if BPs are not used [5]. Although it has been reported that BP-related ONJ is resolved by subcutaneous daily injection of parathyroid hormone (PTH) [6], the application of PTH is not suitable for patients with malignancies, thus PTH therapy does not resolve all ONJ cases. Furthermore, ONJ risks in cancer patients taking denosumab are comparable to those in cancer patients taking intravenous BPs [1]. Denosumab-related ONJ is thought to be spontaneously resolved if denosumab administration is stopped, but there is no evidence that the discontinuation of denosumab is able to resolve denosumab-related ONJ.

It is noteworthy that two drugs with different mechanisms of pharmacological action induce ONJ. This suggests that common pathological findings may be correlated with the etiology of ONJ. Recently, Kuroshima et al. demonstrated that BP and anti-RANKL antibody administration increased tartrate-resistant acid phosphatase (TRAP)-positive mononuclear cells (MNCs) in bone marrow and oral wounds in mice (“denosumab” is the generic name for humans, not mice) [7,8]. Therefore, osteoclast suppression and increased TRAP-positive MNCs may be associated with the onset of ONJ. Further studies are necessary to understand the monocyte-macrophage lineage influenced by both drugs.

2. MRONJ occurs after prosthodontic treatment

Although the causes of MRONJ are unknown, many significant risk factors including prosthodontic treatments such as ill-fitting denture fabrication, are associated with its development [1]. Denture use in malignant patients with intravenous BP has been correlated with high risk for ONJ occurrence (odds ratio; 4.9, 95% confidence interval; 1.2–20.1) [9]. Another study has indicated that denture wear in cancer patients with intravenous BP showed a 2-fold increased risk for ONJ [5]. Therefore, prosthodontists should assess mucosal trauma along with lingual flange and thin mucosa in bisphosphonate-taking edentulous patients wearing dentures in order to prevent ONJ. In addition, prosthodontists should carefully fabricate well-fitting dentures by taking accurate impressions and occlusal records, and performing try fitting and denture adjustment.

3. Prosthodontic considerations for ONJ in regenerative dentistry

As prosthodontists, our goal is not only to prevent or restore ONJ, but also to reconstruct missing dental tissue and ensure good oral health-related quality of life (OHRQoL). One of the distinct features of dental tissue is its non-regenerative nature; therefore, “classic” prosthodontics attempt to restore missing tissue using artificial materials, such as metals, polymers and ceramics. However, recent advances in regenerative dentistry
have enabled the reconstruction of missing dental tissue through the use of various biomaterials, including autologous tissue/cells, by complimenting the patients’ own regenerative capacity [10]. On the other hand, as compared with classic approaches, tissue regenerative approaches require surgical intervention; therefore, patients who suffer from serious systemic diseases or take medication with side effects gain little benefit from regenerative dentistry. As a result, we must carefully select the most appropriate prosthetic options for each patient, depending on their systemic condition. In patients taking either BPs or anti-RANKL antibody, classic, non-invasive prosthetic approaches might therefore remain the first choice for restoration. As disturbance of prosthodontic treatment by MRONJ affects OHRQoL, prosthodontists must clarify the etiology of MRONJ and develop therapeutic strategies in order to provide patients with better treatment outcomes.

Conflicts of interest statement

All authors have no conflicts of interest.

REFERENCES


Shinichiro Kuroshima DDS, PhD
Department of Applied Prosthodontics, Graduate School of Biomedical Sciences, Nagasaki University, 1-7-1 Sakamoto, Nagasaki-city, Nagasaki 852-8588, Japan

Masaru Kaku DDS, PhD
Division of Bioprosthodontics, Niigata University Graduate School of Medical and Dental Sciences, 2-5274 Gakkocho-dori, Chuo-ku, Niigata 951-8514, Japan

Takashi Matsuura DDS, PhD
Section of Fixed Partial Prosthodontics, Department of Oral Rehabilitation, Fukuoka Dental College, 15-1 Tamura 2-Chome, Sawara-ku, Fukuoka 814-0193, Japan

Ikiru Atsuta DDS, PhD
Section of Implant and Rehabilitative Dentistry, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

Yasunori Ayukawa DDS, PhD
Section of Implant and Rehabilitative Dentistry, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

Takashi Sawase
Department of Applied Prosthodontics, Graduate School of Biomedical Sciences, Nagasaki University, 1-7-1 Sakamoto, Nagasaki-city, Nagasaki 852-8588, Japan

*Corresponding author. Tel.: +81 95 819 7688; fax: +81 95 819 7689
E-mail address: kuroshima@nagasaki-u.ac.jp (S. Kuroshima)

28 October 2015
Available online 10 February 2016

http://dx.doi.org/10.1016/j.jpor.2016.01.004
1883-1958/(c) 2016 Japan Prosthodontic Society. Published by Elsevier Ltd. All rights reserved.