Introduction

Bisphosphonates, which are inhibitors of osteoclastic bone resorption,1 are useful for the treatment of osteoporosis and bone metastases.2-6 However, they are also implicated in the onset of medication-related osteonecrosis of the jaw (MRONJ).1,7,8 Patients with MRONJ are often referred to a larger hospital for the evaluation of bisphosphonate-induced changes in the jaws, along with the differential diagnosis of other diseases of the jaws, such as osteoradionecrosis (ORN) or osteomyelitis.9

ORN is a pernicious complication of radiotherapy for head and neck carcinomas.10 The most common cause of ORN is radiation arteritis,11-13 which leads to the onset of a hypocellular, hypovascular, and hypoxic environment. Jaws with MRONJ or ORN must be evaluated before any medical procedure is performed.9

Tc-99m hydroxymethylene diphosphonate (HMDP) scintigraphy is capable of demonstrating physiologic changes in bone, and it has been shown that scintigraphy is effective for detecting MRONJ.14 Furthermore, multiple imaging modalities, such as Tc-99m HMDP scintigraphy, computed tomography (CT), and magnetic resonance (MR) imaging, are useful for detecting MRONJ.8 However, to the best of our knowledge, the imaging features of MRONJ and ORN on scintigraphy, CT, and MR imaging have not been pre-
sented in the literature. The aim of this study was to evaluate the Tc-99m HMDP scintigraphy, CT, and MR imaging findings of osteonecrosis in the mandible, especially ORN and MRONJ.

**Materials and Methods**

Thirteen patients with MRONJ and 7 patients with ORN in the mandible underwent Tc-99m HMDP scintigraphy, CT, and MR imaging at Radiology, The Nippon Dental University Niigata Hospital from July 2013 to December 2017. Table 1 characteristics of the patients with ORN and MRONJ.

The images were acquired using a 16-MDCT apparatus (Aquilion TSX-101A; Canon Medical Systems, Otawara, Japan), a 1.5-T MR imaging system (EXCELART Vantage MRT-2003; Canon Medical Systems, Otawara, Japan), and a SNC-5100R scintigraphy apparatus (Shimadzu, Kyoto, Japan) with Tc-99m HMDP (Clear Bone Injection; Nihon Medi-Physics, Tokyo, Japan), following our institutional

| Table 1. Characteristics of the patients with osteoradionecrosis (ORN) and medication-related osteonecrosis of the jaw (MRONJ) |
| --- |
| **Number of patients** | **ORN (n = 7)** | **MRONJ (n = 13)** | **Total (n = 20)** |
| **Age (years)** |  |  |  |
| Mean ± standard deviation | 67.6 ± 9.6 | 75.6 ± 10.0 | 72.8 ± 10.4 |
| Range | 52-84 | 56-89 | 52-89 |
| **Sex** |  |  |  |
| Male | 6 | 0 | 6 |
| Female | 1 | 13 | 14 |
| **Primary disease** |  |  |  |
| Tongue cancer | 3 | 3 | 6 |
| Oropharyngeal cancer | 3 | 3 | 6 |
| Floor of the mouth cancer | 1 | 1 | 2 |
| Osteoporosis | 9 | 9 | 18 |
| Osseous metastases of breast cancer | 4 | 4 | 8 |
| **Medication** |  |  |  |
| Alendronate | 6 | 6 | 12 |
| Risedronate | 1 | 1 | 2 |
| Minodronate | 1 | 1 | 2 |
| Zoledronate | 1 | 1 | 2 |
| Bevacizumab | 2 | 2 | 4 |
| Denosumab | 1 | 1 | 2 |
| Ibandronate | 1 | 1 | 2 |

| Table 2. Comparison between osteoradionecrosis (ORN) and medication-related osteonecrosis of the jaw (MRONJ) with computed tomography (CT), magnetic resonance image (MRI) and bone scintigraphy |
| --- |
| **Imaging features** | **ORN (n = 7)** | **MRONJ (n = 13)** | **P-value** |
| **Bone scintigraphy** |  |  |  |
| Increased uptake | 7 (100%) | 13 (100%) | – |
| **CT images** |  |  |  |
| Osteolytic changes of the jaws | 6 (85.7%) | 12 (92.3%) | 0.639 |
| Sequestrum separation | 6 (85.7%) | 10 (76.9%) | 0.639 |
| Periosteal bone proliferation | 1 (14.3%) | 9 (69.2%) | 0.019 |
| **MR images** |  |  |  |
| Low-signal intensity on T1WI | 7 (100%) | 13 (100%) | – |
| High-signal intensity on T2WI | 4 (57.1%) | 10 (76.9%) | 0.357 |
| High-signal intensity on STIR | 7 (100%) | 13 (100%) | – |
| High-signal intensity on DWI | 5/5 (100%) | 8/8 (100%) | – |
| Low-signal intensity on ADC map | 5/5 (100%) | 8/8 (100%) | – |

T1WI: T1-weighted image, T2WI: T2-weighted image, STIR: short TI inversion recovery image, DWI: diffusion-weighted image, ADC: apparent diffusion coefficient
Fig. 1. Medication-related osteonecrosis of the right side of the mandible in an 86-year-old woman. A. Axial bone tissue algorithm computed tomography shows an osteolytic lesion with sequestrum separation and periosteal bone proliferation in the right mandible (arrow). B. On magnetic resonance imaging, an axial T1-weighted image shows heterogeneous, low-signal intensity (arrow). C. An axial T2-weighted image shows heterogeneous, low-signal intensity (arrow). D. An axial short TI inversion recovery image shows heterogeneous, high-signal intensity (arrow). E. An axial diffusion-weighted image shows heterogeneous, high-signal intensity (arrow). F. An axial apparent diffusion coefficient map shows heterogeneous, low-signal intensity (arrow). G. A maximum intensity projection (diffusion-weighted image) shows the lesion in an improved way (arrow). H-J. Bone scintigraphy shows increased uptake in the mandible (arrow).
Fig. 2. Radiation-related osteonecrosis of the left side of the mandible in an 84-year-old man. A. Axial bone tissue algorithm computed tomography shows an osteolytic lesion with sequestrum separation in the left mandible (arrow). B. On magnetic resonance imaging, an axial T1-weighted image reveals heterogeneous, low-signal intensity (arrow). C. An axial T2-weighted image shows heterogeneous, high-signal intensity (arrow). D. An axial short TI inversion recovery image reveals heterogeneous, high-signal intensity (arrow). E. An axial diffusion-weighted image shows heterogeneous, high-signal intensity (arrow). F. An axial apparent diffusion coefficient map shows heterogeneous, low-signal intensity (arrow). G. A maximum intensity projection (diffusion-weighted image) shows the lesion in an improved way (arrow). H-J. Bone scintigraphy shows increased uptake in the mandible (arrow).
protocol. The findings of Tc-99m HMDP scintigraphy, CT, and MR imaging of ORN and MRONJ were evaluated by 2 oral radiologists. Scintigraphy was used to analyze areas of increased uptake. CT was used to evaluate osteolytic changes of the jaws, sequestrum separation, and periosteal bone proliferation. In MR imaging, T1-weighted images (T1WI), T2-weighted images (T2WI), short inversion time inversion recovery images (STIR), diffusion-weighted images (DWI), and apparent diffusion coefficient (ADC) maps were obtained.

The associations of scintigraphy, CT, and MR imaging findings with MRONJ and ORN were analyzed using the chi-square test with the Pearson exact test. \( P < 0.05 \) were considered to indicate statistical significance.

**Results**

The bone scintigraphy, CT, and MR imaging findings are compared between MRONJ and ORN in Table 2. Thirteen patients with MRONJ and 7 patients with ORN in the mandible showed low signal intensity on T1WI and ADC mapping, high signal intensity on STIR and DWI, and increased uptake on scintigraphy. Periosteal bone proliferation on CT was observed in 69.2% of patients with MRONJ (9 of 13) versus 14.3% of patients with ORN (1 of 7) \( (P = 0.019) \). Figures 1 and 2 show images of MRONJ and ORN, respectively.

**Discussion**

Imaging findings are unclear both in the early stages of ORN and when the disease is advanced. Although the radiological findings are nonspecific, they do appear to play a role in the management of MRONJ. In this study, we have presented the characteristic imaging findings of MRONJ and ORN on bone scintigraphy, CT, and MR imaging.

Tc-99m HMDP scintigraphy is an effective diagnostic tool for detecting bone changes, and has a higher sensitivity than that of radiography. Many authors have reported that scintigraphy showed increased uptake at sites affected by MRONJ. In our study, all cases (ORN and MRONJ) showed low signal intensity on T1WI and high signal intensity on STIR and DWI, and increased uptake on scintigraphy. Periosteal bone proliferation on CT was observed in 69.2% of patients with MRONJ (9 of 13) versus 14.3% of patients with ORN (1 of 7) \( (P = 0.019) \). Figures 1 and 2 show images of MRONJ and ORN, respectively.

Regarding the reasons underlying the different imaging characteristics of MRONJ and ORN, we propose that periosteal bone proliferation on CT in association with ORN is rare because ORN is caused by radiation arteritis. All cases of MRONJ and ORN in our study showed low signal intensity on T1WI and ADC maps, high signal intensity on STIR and DWI, and increased uptake on bone scintigraphy. We suggest that the increased uptake on bone scintigraphy may be correlated with MR imaging findings, especially those on DWI and ADC maps, although the sample was relatively small in this study.

In conclusion, this study presented the characteristic imaging findings of MRONJ and ORN on bone scintigraphy, CT, and MR imaging. Our results suggest that CT can be effective for detecting MRONJ and ORN.

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