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內文：

Background

1. Multiple myeloma is characterized by neoplastic **proliferation** of plasma cells clones.
2. The most frequent complications are anemia, renal failure, recurrent bacterial infections, pathological fractures, and hypercalcemia.
3. Bisphosphonates are used in the treatment of multiple myeloma because of their inhibitory effect on osteoclastic activity.
4. Bisphosphonates are grouped into nitrogen-containing and non-nitrogen-containing bisphosphonates; both result in cytotoxic effects to the osteoclast.
5. Adverse effects can be separated into four groups: acute-phase-reactions, upper aerodigestive tract issues, and effects concerning renal function. The fourth adverse effect, bisphosphonate associated osteonecrosis of the jaw (BP-ONJ), was described and has been subsequently diagnosed with increasing frequency.
6. According to the American Association of Oral- and Maxillofacial Surgeons (AAOMS), BP-ONJ is defined as the presence of exposed, necrotic bone in the maxillofacial region that has persisted for more than **eight weeks** in a patient with current or previous **bisphosphonate therapy** and no history of radiation to the jaws.
7. The aim was to evaluate the prevalence of BP-ONJ in multiple myeloma patients using two different study designs and to compare this with existing published data. Further aims were to detect additional factors that may be related to the development of BP-ONJ.

Methods

1. Two studies with two different populations were conducted: one retrospective study and one cross sectional study.
2. The retrospective study:
In the study time span from January 2000 to February 2006, 161 patients with multiple myeloma and bisphosphonate treatment were registered. All patients were contacted by letter and/or phone. In the end, we obtained data for 81 patients (50.3%).
3. The cross sectional study:
All 78 patients with multiple myeloma treated from October 2006 to March 2008, regardless of the date of diagnosis, were comprised. The same data elements were collected as in the retrospective study, but patients in the cross sectional study also underwent an additional examination.

Results

Retrospective study

1. 161 patients with multiple myeloma and bisphosphonate treatment were identified. Data for 81 patients (50%) could be obtained, 69 had passed away, and 11 either refused participation or we failed to locate them.
2. The 81 recruited patients (36 women and 45 men) had an average age of 69.8 years; the average age at the time of multiple myeloma diagnosis was 63.7 years. All administered bisphosphonates were nitrogen-containing bisphosphonates.
3. Four patients (5%), three men and one women aged 53, 71, 74 and 65 respectively, suffered from bisphosphonate associated osteonecrosis of the jaw. Two of these patients had only received zoledronate; the other two patients had been treated with pamidronate followed by zoledronate for an average duration of 64 months.

Cross sectional study

1. 78 patients (47 men and 31 women) with multiple myeloma and current bisphosphonate therapy with an average age of 63.5 years at oral examination had been treated in the specified time span of 10/2006 to 03/2008. The average age at the time of multiple myeloma diagnosis was 59.8 years.
2. 16 patients (21%) developed BP-ONJ. These patients had received an average of 48.4 bisphosphonate infusions compared to 23.3 infusions in patients without BP-ONJ.
3. Four of these patients had had only zoledronate. Nine patients had received pamidronate and zoledronate sequentially. One patient had first received ibandronate followed by zoledronate. Two patients had pamidronate, zoledronate and ibandronate sequentially.

Table 2: Data of the cross sectional study.

	All patients	Patients with BP-ONJ	Patients without BP-ONJ	Difference
Number (percentage)	78 (100%)	16 (21%)	62 (80%)	
Age at examination (SD)	63.5 (10.1)	61.9 (21.0)	64.1 (10.5)	p = 0.18
Age at MM diagnosis	59.8 (11.1)	54.1 (8.8)	61.3 (11.2)	p = 0.02
Men	47	9	38	p = 0.78
Women	31	7	24	
MM stage I	17 (22%)	3 (4%)	14 (18%)	
MM stage II	13 (17%)	2 (3%)	11 (14%)	p = 0.79
MM stage III	48 (62%)	11 (14%)	37 (47%)	
Bisphosphonate infusions	28.1	48.4 (range 9 - 111)	23.3 (range 1 - 104)	p < 0.001

Corticosteroids	59 (76%)	13 (17%)	46 (61%)	p = 0.75
Chemotherapy	64 (82%)	13 (17%)	51 (67%)	p = 1.0
Diabetes mellitus	6 (8%)	2 (3%)	4 (5%)	p = 0.6
Further malignant diseases	3 (4%)	0	3 (4%)	p = 1.0
Smoker	8 (10%)	1 (1%)	7 (9%)	p = 1.0

Discussion

1. In the retrospective study, the average age of the patients at the time of multiple myeloma diagnosis was 63.7 years. In the cross-sectional study the age was 59.8 years.
2. In both study populations, zoledronate was the bisphosphonate most often used.
3. The association between zoledronate and BP-ONJ is explained by the higher potency of zoledronate as compared to the other bisphosphonates.
4. Chemotherapy did not show an influence on BP-ONJ prevalence in this study.
5. Non-restorable teeth could be extracted and restorations could be done. After commencement of bisphosphonates therapy, improved oral hygiene could prevent further dental surgical procedures such as tooth extractions.
6. Across both studies, the most affected site was the mandible. This might be explained by the reduced blood supply in the mandible as compared to the maxilla.
7. In studies with such small numbers of patients, the detection or non-detection of a BP-ONJ has a huge influence on the resulting prevalence or incidence.

題號	題目
1	Which is not the clinical feature of multiple myeloma? (A) Hypocalcemia (B) Bone pain (C) Renal failure (D) Myelophthisic anemia
答案 (A)	出處：Oral & Maxillofacial Pathology, Brad W. Neville, DDS, 2002
題號	題目
2	Which is not the histopathologic feature of multiple myeloma? (A) Deposition of amyloid (B) Stained by Congo red, demonstrating apple-red with polarized light (C) Monoclonal gammopathy (D) Presence of myeloma protein
答案 (B)	出處：Oral & Maxillofacial Pathology, Brad W. Neville, DDS, 2002