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內文：

#### 1. Introduction

- First reported case of osteonecrosis of the jaw (ONJ) : Marx 2003
  - Occurring in patients with multiple myeloma treated with intravenously administered bisphosphonate
- Bisphosphonate : treat bone resorbing diseases
  - multiple myeloma and bone metastasis
  - whose typical origins are breast cancer and prostate cancer
  - Specific target cell of BP : osteoclast
- Nitrogen-containing BP (nBP) has more potent ability to inhibit mineral dissolution and higher potency to induce BRONJ than early BP without nitrogen-containing side-chain

#### 2. risk factors for BRONJ

- glucocorticoids (GCs), anti-cancer drugs, alcohol, smoking, and malnutrition, tooth extraction and other surgical procedures
- Tooth extraction raised the incidence of BRONJ about 8-fold

#### 3. Diagnostic criteria and stage classification of BRONJ

- 2007 American Association of Oral and Maxillofacial Surgeons
  - (1) current or previous treatment with a BP
  - (2) exposed bone in the maxillofacial region that has persisted for more than 8 weeks → DD : chronic suppurative osteomyelitis
  - (3) no history of radiation therapy to the jaws → DD : ORN
- Staging classification of BRONJ (2007)
  - Stage 1 : only an exposure of the bone without infectious signs.
  - Stage 2 : not only a bone exposure, but also inflammatory symptoms by bacterial infection such as pain and swelling.
  - Stage 3 : when the lesion extends to the jaw itself beyond the alveolar level , where the bone necrosis or osteolysis may extend to the inferior border of mandible with or without extraoral fistula and pathological fracture
- Stage 0 (2009)
  - no clinical evidence of necrotic bone, but nonspecific clinical findings and symptoms
  - diffuse alveolar swelling, gingival redness, or internal dental fistula

#### 4. Relationship between stage 0 and suppurative osteomyelitis of the jaw

- Actinomyces

#### 5. Mechanism of nitrogen-containing BP actions

- Small GTPases → cytoskeletal arrangement, vesicular trafficking, and membrane ruffling which are involved in the processes of bone resorption by osteoclasts, including their migration to bones, adhesion on bone surface and transportation of bone-resorbing enzymes to the ruffled border
- Therefore, the inhibition of FPP synthase with nBP can prevent osteoclasts

from destructing the bones

- These data suggest that nBP brings about the functional disorder, rather than the depletion, of osteoclasts

Other target cells of BP

- Osteoblasts
- Osteocytes
- Vascular endothelial cells
- Macrophages/monocytes

7. Why does BRONJ occur in the jaws?

- (1) the turnover rate of jaws, especially alveolar bones, is so rapid
- (2) jaws have teeth and gum that may become an easy entrance for bacterial infection

10. Treatment of BRONJ

- stage 3 : surgical removal of the jaw which contains the necrotic bones
- stage 1 or stage 2 : conservative therapy
  - local irrigation with saline or the use of oral antimicrobial rinse
- Drug holiday : Discontinuation of BP therapy
  - more than 3 months before tooth extraction if the patients have received oral BP therapy for more than 3 years
- Hyperbaric oxygen
- it is expected to improve the hypoxia condition in the jaw and generate reactive oxygen species (ROS) to stimulate the differentiation and activity of osteoclasts
- Teriparatide (recombinant human parathyroid hormone 1–34)
- treatment of BRONJ, teriparatide may cause activation of osteoblasts

| 題號    | 題目                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
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| 1     | Treatment of BRONJ stage 3<br>(A) Local irrigation<br>(B) surgical removal of the jaw which contains the necrotic bones<br>(C) oral antimicrobial rinse<br>(D) All above                                                                                                                                                                                                                                                                                                                       |
| 答案(D) | 出處： Tetsuro Ikebe; 2012 Japanese Stomatological Society.                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 題號    | 題目                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| 2     | 以下有關 BRONJ 的分類何者為正確?<br>(A) Stage 0: no clinical evidence of necrotic bone, but nonspecific clinical findings and symptoms<br>(B) Stage 1: not only a bone exposure, but also inflammatory symptoms by bacterial infection such as pain and swelling.<br>(C) Stage 2 : where the bone necrosis or osteolysis may extend to the inferior border of mandible with or without extraoral fistula and pathological fracture<br>(D) Stage 3 : only an exposure of the bone without infectious signs. |
| 答案(A) | 出處： Tetsuro Ikebe; 2012 Japanese Stomatological Society.                                                                                                                                                                                                                                                                                                                                                                                                                                       |