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Case Report

Bisphosphonate-related osteonecrosis of the jaw successfully treated with surgical resection and its histopathological features: A long-term follow-up report



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ABSTRACT

Bisphosphonates (BP) are potent inhibitors of the osteoclast activity used in the treatment of metastatic bone disease and osteoporosis. Bisphosphonate related osteonecrosis of the jaw (BRONJ) is a rare, but severe complication as a pathological fracture, pain and tumor-induced hypercalcemia. Patients taking BP may subsequently develop BRONJ after dentoalveolar surgery or trauma of the oral mucosa. However, appropriate approaches for the prevention and treatment of BRONJ have not been established. One of reasons is that the pathogenesis of BRONJ is poorly understood. We reported a case of BRONJ in a 77-year-old woman that was successfully treated by segmental resection of the extensive necrotic bone and a pathological fracture in the mandible. We describe the rare histopathological features of the resected specimen.

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1. Introduction

The presence of metastatic bone deposits in cancer patients often results in complications including hypercalcemia, pathologic fracture and pain [1]. The primary benefit of bisphosphonates is the prevention of skeletal bone pain and fractures [2]. The bisphosphonate related osteonecrosis of the jaw (BRONJ), diagnosed in patients receiving bisphosphonate (BP), was first described in 2003 [3] and over 400 reports have since been published concerning BRONJ. BRONJ is defined by the presence of a positive BP drug history, exposed bone for a period that exceeds 8 weeks and the absence of previous irradiation to the head and neck region. The

American Association of Oral and Maxillofacial Surgeons proposed the four staging categories of BRONJ. Stage 0 is represented by the non-exposed variant, where other symptoms and signs as pain or radiologic markers are present. Stage 1 includes asymptomatic bone exposure. Stage 2 is the exposed bone with pain and infection. Stage 3 is the exposed bone in patients with pain, infection, and one or more of the following: pathologic fracture, extra-oral fistula, or osteolysis extending to the inferior border [4]. The osteonecrosis can develop spontaneously, but it is reported that tooth extraction, dental implants, apical surgery, and periodontal surgery with invasion of the bone may be risk factors [5]. These surgical dental procedures increase the incidence of BRONJ by more than sevenfold [5].

However, clear information on the pathogenesis of BRONJ has not been reported. There are a few studies that described histopathological features or the prognosis of BRONJ [6]. We report a case of the successful outcome of a stage 3 BRONJ patient with a pathological fracture of 3 years' duration after the surgical treatment. We also describe histopathological features of BRONJ.

[☆] AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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2. Case report

A 77-year-old woman was referred to the Department of Oral and Maxillofacial Surgery, Hiroshima University Hospital in April 2007 with a 1-year history of a contact pain in the left sub-mandible region and a local swelling with fistulas in the submental region (Fig. 1A and B). The left lower first and second molars were extracted by a private dentist in September 2005. The patient then received anti-inflammatory agents, antibiotics and curettage in a hospital. Her medical history revealed breast cancer with a metastatic disease affecting the spinal column. The patient received an intravenous infusion of 180 mg of pamidronate followed by 36 mg of zoledronate from April 2005 to September 2006. At presentation, the patient had an exposed and necrotic bone, contact pain and gingival swelling of the left side of the mandible with trismus. The patient also had three orocutaneous fistulas with pus discharge in the submental region (Fig. 1A). Panoramic radiography

showed an extensive osteolysis in the mandibular body (Fig. 1C). A CT-scan revealed a cortical osteolysis of the mandible (Fig. 1D). Based on the criteria of the American Association of Oral and Maxillofacial Surgery, the diagnosis of BRONJ stage 3 was made.

The patient received various types of oral and intravenous antibiotics (penicillin, cepheids, macrolides and clindamycin), mouthwashes and cleaning fistulae for 16 months. The symptoms did not completely resolve after this treatment and gradually exacerbated, accompanied by the development of trismus. Radiographic presentation showed the progression of bone loss 9 months after the initial visit. A conservative treatment was continued for another 7 months. A radiograph revealed a pathological fracture in the left mandibular body and additional bone destruction (Fig. 1E and F). In September 2008, we decided to perform the segmental resection of the extensive necrotic bone and a pathological fracture in the mandible with 1-cm margins via an extraoral approach under general anesthesia (Fig. 2A–C). She underwent reposition and

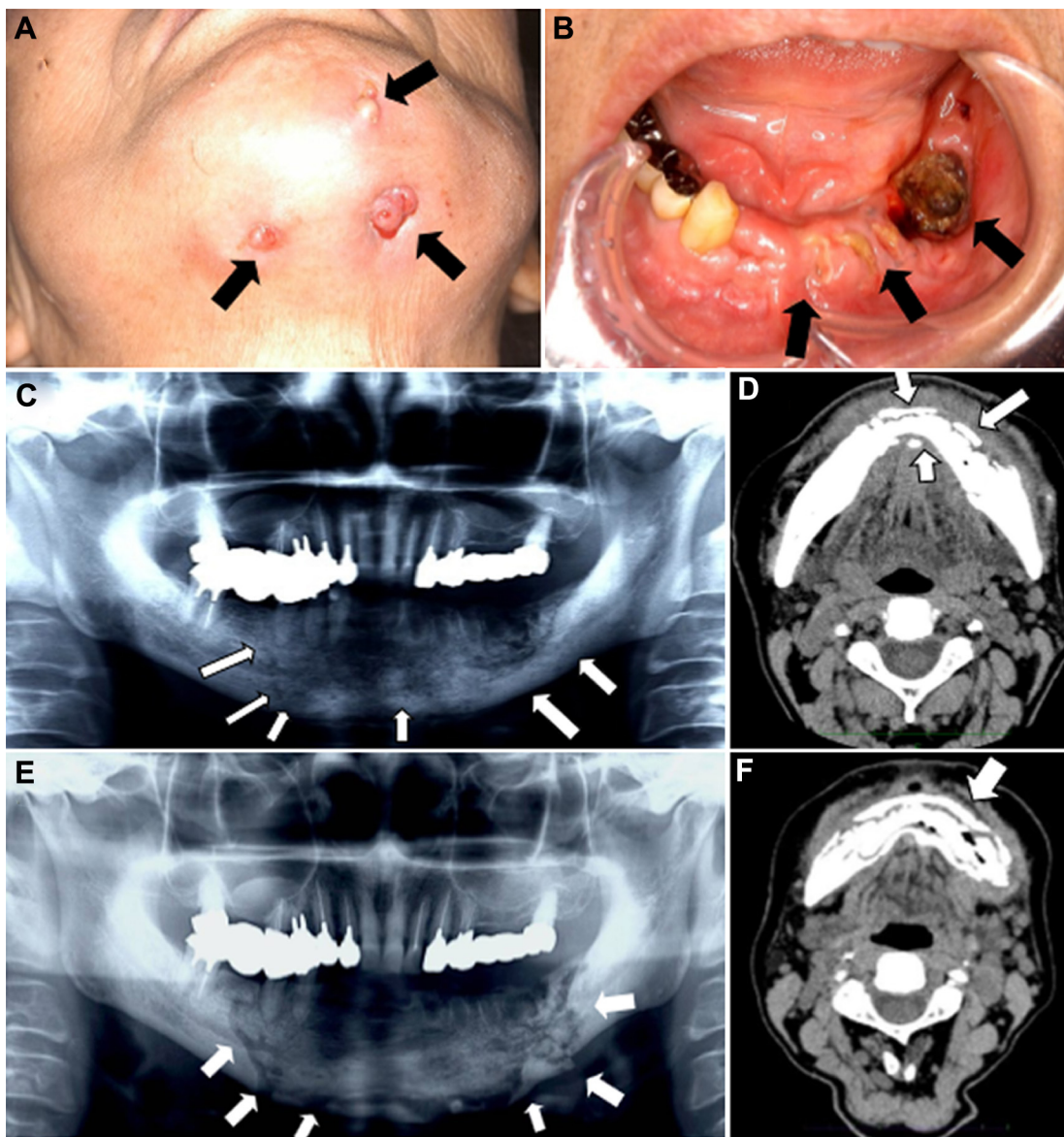


Fig. 1. Bisphosphonate-related osteonecrosis of the jaw (BRONJ) in a 77-year-old woman. (A) Extraoral view; (B) intraoral view; (C and D) radiographic and CT images at the initial visit; and (E and F) radiographic and CT images at 16 months after conservative treatments. The patient had fistulas in the mental region of the skin (A). In her left molar region of the mandible, the exposed necrotic bone is located (B). Panoramic radiograph reveals bone destruction over a wide region of the mandible (C). A CT-scan identified the appearance of the necrotic cortical bone in the left and anterior mandible (D). Panoramic radiograph reveals an advanced bone destruction and a pathological fracture in the left mandible (E). A CT-scan confirms the presence of an advanced disease (F).

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