

CASE REPORT

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Anti-resorptive related osteonecrosis of the jaw in a patient with hemodialysis: Rapid progression and pathologic fracture in a short phase

Chihiro Kanno, Takehiro Kitabatake, Momoyo Kojima, Morio Yamazaki, Tetsuharu Kaneko

ABSTRACT

Introduction: Anti-resorptive agent-related osteonecrosis of the jaw (ARONJ) is a slowly progressive disease occurring due to the chronic use of anti-resorptive agents (e.g., bisphosphonates) and rarely presents with pathologic fractures. The frequency of pathologic fractures is rare, especially in patients with osteoporosis who are prescribed, low-dose bone-modifying agents. Herein, we report a case of rapidly progressive ARONJ with a pathologic fracture in a patient with hemodialysis.

Case Report: A 64-year-old woman with hemodialysis due to the microscopic polyangiitis who was treated with corticosteroids, immunosuppressants, and ibandronate presented with tooth pain of left mandibular second premolar and second molar, necessitating extraction. After extraction, ARONJ developed in the left mandibular. Anti-resorptive agent-related osteonecrosis of the jaw progressed rapidly during the follow-up at the 12th and 15th months, furthermore,

ARONJ also developed in the right mandibular second premolar and second molar lesion, requiring extensive surgery. We performed curative segmental and marginal mandibulectomy in the left and right hemimandible, respectively. The postoperative course was uneventful.

Conclusion: We report a rare case of rapidly progressive ARONJ with pathologic fracture in a patient with hemodialysis. This report suggests a potential role of hemodialysis as a risk factor for disease progression and pathologic fracture development. Further studies regarding factors that inhibit the healing of ARONJ are still needed.

Keywords: ARONJ, Hemodialysis, Low dose BMA, Pathologic fracture, Rapid progression

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INTRODUCTION

Eighteen years since its discovery, anti-resorptive related osteonecrosis of the jaw (ARONJ), an adverse effect of anti-resorptive drugs with unclear pathophysiology and treatment, is still impairing the quality of life in many patients [1]. The incidence of ARONJ is lower in osteoporotic patients receiving low-dose bone modifying

agents (BMA) than in those receiving high-dose BMA [2, 3]. Most ARONJ cases are chronic and progress slowly. To date, rapidly progressive ARONJ has been rarely reported. Herein, we report a case of rapidly progressive ARONJ with a pathologic fracture induced by low-dose BMA in a patient with hemodialysis.

CASE REPORT

A 64-year-old postmenopausal woman was admitted for tooth pain. She underwent left mandibular second premolar and second molar extraction due to periodontitis. Four months after extraction, she was diagnosed with ARONJ stage 1 [4] at the extraction site (Figure 1A). At this point, she desired conservative therapy (i.e., oral hygiene and antibiotic therapy for acute inflammation), not curative surgical therapy. The course silently elapsed since diagnosis, however, during the period of 12- and 15-month follow-up, jaw pain and inflammation surrounding the left mandibular body worsened rapidly and panoramic radiography revealed a rapid spread of bone destruction, resulting in pathologic fracture of the left mandibular body (Figure 1B and C), which prompted a referral to our clinic.

Four years before the consultation, she was diagnosed with microscopic polyangiitis (MPA), which required hemodialysis, and had been treated with corticosteroids, immunosuppressants, and ibandronate. Physical examination revealed malocclusion, left inferior mandibular nerve paresthesia, and an extraoral fistula on submandibular skin. In the right mandibular second premolar and second molar region, exposed bone was detected in the periodontal pocket of these teeth. Radiologic examination revealed stage 3 and stage 1 ARONJ in the left and right hemimandible, respectively (Figure 2A–E). The causes of ARONJ were considered as tooth extraction in the left lesion and periodontitis in the right lesion. Approximately 17 months after first diagnosis, segmental and marginal mandibulectomy was performed in the left and right hemimandible, respectively. Mandibular reconstruction was not performed because of her poor health condition and difficulty in rigid fixation. Mandibular reconstruction was not performed because of her poor health condition and difficulty in rigid fixation. The oral mucosa was sutured tightly for wound closure. Histopathologic examination of the resected bone showed bone necrosis with infiltration of inflammatory cells and *Actinomyces* granules (Figure 3A) in the absence of MPA. Twelve months after surgery, panoramic radiographs revealed that there was no recurrence of inflammation or bone destruction (Figure 3B). The postoperative course was uneventful. After 15 months of surgery, there were no findings of recurrence of inflammation.

DISCUSSION

In the present case, ARONJ progressed rapidly during the follow-up at the 12th and 15th months,

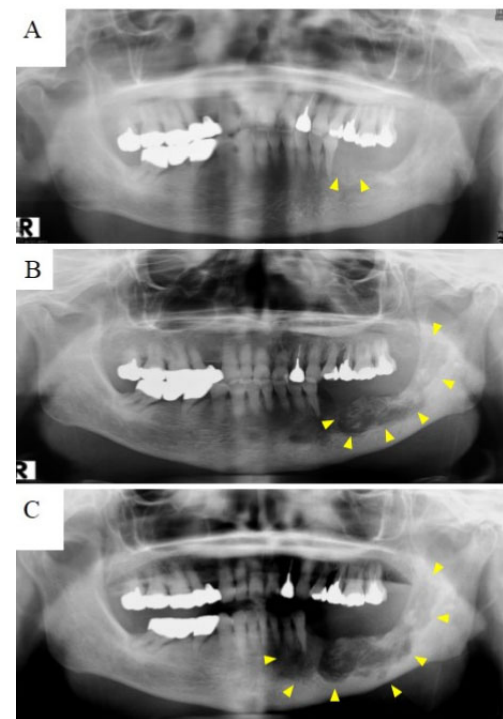


Figure 1: Radiologic progression of anti-resorptive related osteonecrosis of the jaw (A) at the time of diagnosis; (B) 12 months after diagnosis; and (C) 15 months after diagnosis. The arrowhead indicates the lesion with bone destruction. ARONJ: Antiresorptive related osteonecrosis of the jaw.

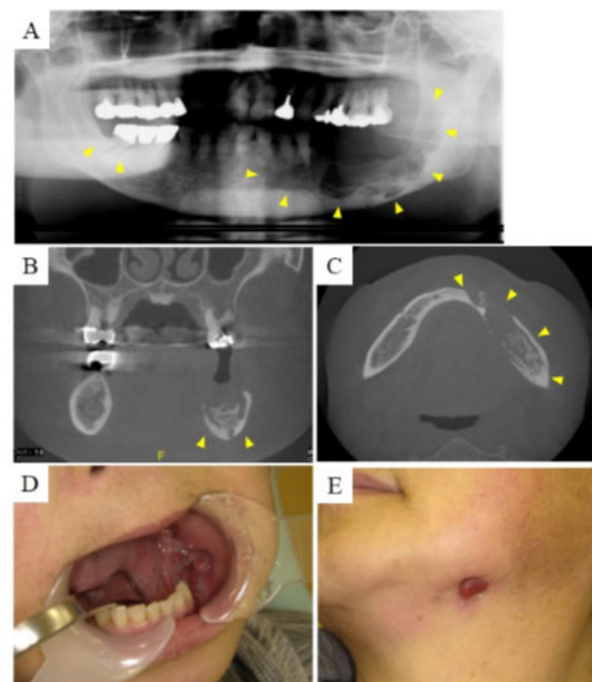
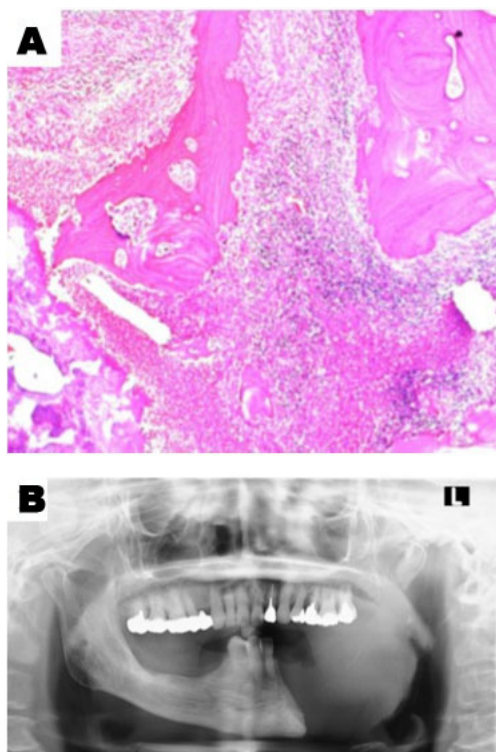


Figure 2: (A–C) Panoramic radiograph and computed tomography taken 17 months after diagnosis show the wide lesion of bone destruction extending from the midline of the left side of the mandible to the mandibular notch and bone destruction in the area surrounding right mandibular second molar; (D) intraoral view shows left gingiva replaced with granulation tissue and presence of necrotic bone; and (E) extraoral fistula is visible. The arrowhead indicates the lesion with bone destruction.



Figures 3: (A) Histopathologic examination of the resected bone revealing bone necrosis with infiltration of inflammatory cells and *Actinomyces* granules and (B) panoramic radiograph taken 10 months after surgery showing no recurrence of inflammation and bone destruction.

requiring extensive surgery. During the general course of ARONJ, patients receiving low-dose BMA have a slower progression of the disease than those receiving high-dose BMA. Furthermore, pathologic fractures develop only after a few years in patients receiving high-dose BMA, with an incidence rate of 2.9–4.3% [5–7]. However, to the best of our knowledge, in the English literature, only a few cases of pathologic fractures have been reported in patients treated with low-dose BMA [5–8]. This study presented a case of ARONJ with pathologic fracture that worsened rapidly in the period of 12 to 15 months from diagnosis, nevertheless, the silent course was seen until then. This is considered extremely rare in a patient being treated with low-dose BMA.

In the present case, we hypothesized about the cause of rapid exacerbation, first, the role of hemodialysis is considered as a potential factor. During wound healing, hemodialysis is strongly related to poor healing. Patients with hemodialysis have a higher tendency of wound infection and wound dehiscence [9, 10]. The factors related to inhibition of wound healing in patients with hemodialysis are arteriosclerosis, impaired peripheral blood flow, and reduced immunity. Additionally, use of corticosteroid and the impairment of calcium metabolism due to renal dysfunction might concerned. Impaired calcium concentration results in low bone density and fragility of bone. In contrast, in the development of

ARONJ, hemodialysis is defined as a risk factor in many guidelines of ARONJ; however, it is not stated as a healing inhibitor. Moreover, resolution of bacterial infection, necrotic bone separation, and epithelization are the crucial factors in ARONJ healing; thus, correlation with hemodialysis may be hypothesized.

Next, the role of MPA is considered. MPA is a systemic disease that causes necrotizing vasculitis of the small and medium blood vessels [11], and occurs multi-organ dysfunction in whole body especially in the kidneys, lungs, skin, and ears. Nevertheless, long-term treatment with glucocorticoids and immunosuppressants is crucial for its management [12–14], little progress has been made with multiple comorbidities. The histopathological feature of necrotic vasculitis is distinctive in MPA. According to the pathophysiology of MPA, the course of this atypical case could be explained. However, in the present case, it was difficult to evaluate MPA histopathologically, because in the resected sample was just necrotic bone, not the healthy bone. Although the distinctive histopathological feature is not often observed in the target organs [11], whether MPA exacerbates ARONJ is unclear.

In ARONJ treatment outcome, curative surgical therapy, such as necrotic bone removal, with surrounding healthy region is expected to have a better outcome compared to conservative therapy. As the first choice of ARONJ treatment, conservative therapy is recommended in some guidelines [4, 15, 16]. On the other hand, the efficacy of surgical therapy has been reported [17, 18]; however, it is still controversial. In the present case, the clinical course was rapidly exacerbated in a short term during the conservative therapy, consequently, extensive surgery was performed. Our patient exhibited two factors that were related to wound healing complications, both the factors had the possibility of causing inhibition of healing in ARONJ, though it is unclear. In light of this case, surgical therapy should be considered in the early clinical stage in ARONJ with several healing inhibiting factors, such as hemodialysis or MPA, to avoid rapid exacerbation and extensive surgery to provide a better quality of life to the patients.

CONCLUSION

We reported a case of rapidly progressive ARONJ with a pathologic fracture in a patient with hemodialysis. This study suggests a potential role of hemodialysis as a risk factor for disease progression and pathologic fracture development in ARONJ. Nevertheless, further research is still required to determine the exact role of hemodialysis in patients with ARONJ.

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Author Contributions

Chihiro Kanno – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Takehiro Kitabatake – Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Momoyo Kojima – Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Morio Yamazaki – Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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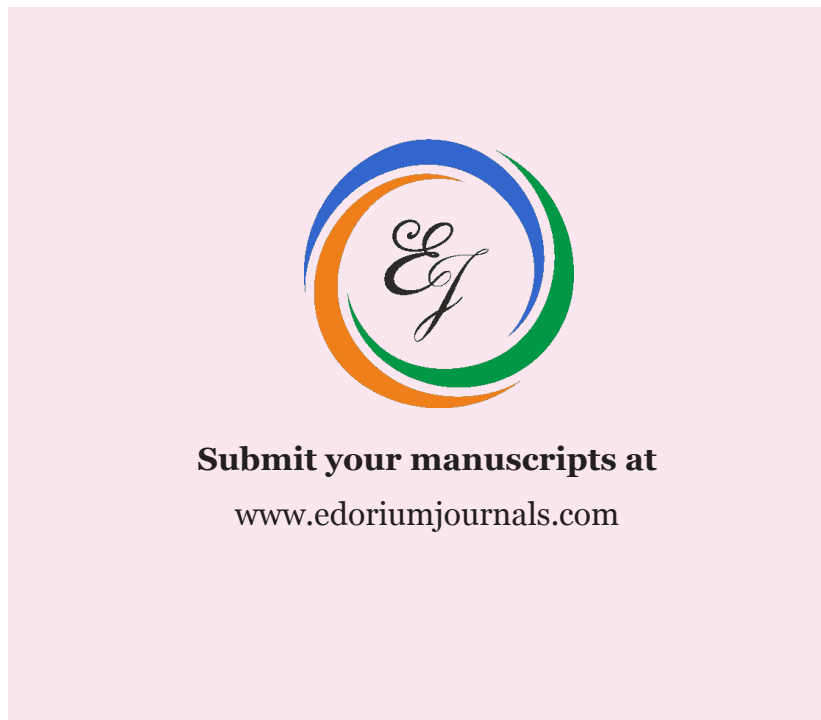
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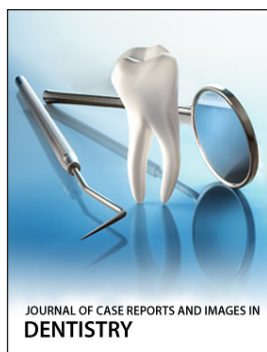
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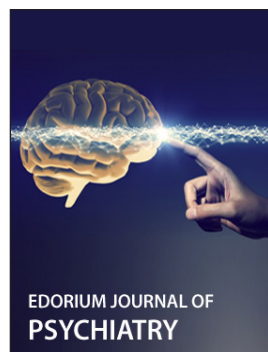
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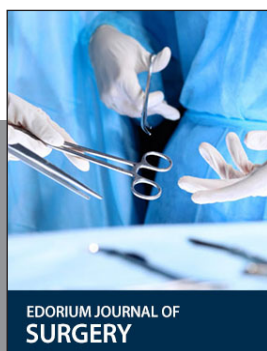
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