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Medication-Related Osteonecrosis of the Jaw at the Site of a Presumed Pre-Existing Mandibular Dense Bone Island: A Longitudinal Cone-Beam Computed Tomography Case Report

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1 **Vasileios Venianakis** 
BD 2 **Georgios Ntagiantis** 
ABCDEFG 1 **Emmanouil Chatzipetros** 

1 Department of Oral Diagnosis and Radiology, Faculty of Dentistry
National and Kapodistrian University of Athens, Athens, Greece
2 Department of Oral and Maxillofacial Surgery, Faculty of Dentistry,
National and Kapodistrian University of Athens, Athens, Greece

Corresponding Author: Vasileios Venianakis, 2 Thivon Str, 11527, Goudi, Athens, Greece
Phone: +306944501891, e-mail: vasilis.venianakis@gmail.com
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Patient: Female, 70-year-old
Final Diagnosis: Medication-related osteonecrosis of the jaw
Symptoms: Pain
Clinical Procedure: —
Specialty: Dentistry • Radiology • Surgery

Objective: Rare disease

Background: Dense bone island (DBI), also known as idiopathic osteosclerosis, is a localized intraosseous radiopacity of unknown etiology that is typically asymptomatic and incidentally detected. It most commonly occurs in the posterior mandible as a well-defined, homogeneous radiopaque lesion without cortical disruption or effects on adjacent structures. Its behavior in patients receiving antiresorptive therapy remains largely unexplored. Medication-related osteonecrosis of the jaw (MRONJ) is a recognized complication associated with antiresorptive agents, including denosumab and bisphosphonates. This case report describes a 70-year-old woman receiving long-term denosumab therapy for osteoporosis who developed MRONJ at the site of a pre-existing mandibular lesion provisionally diagnosed as a DBI and was evaluated using cone-beam computed tomography (CBCT).

Case Report: A 70-year-old woman receiving long-term denosumab therapy for osteoporosis developed Stage 2 MRONJ at the site of a presumed pre-existing mandibular DBI. CBCT initially demonstrated a hyperdense lesion in the left posterior mandible. Four years later (at age 74), the patient presented with an intraoral fistula. Follow-up CBCT revealed a mixed osteolytic-osteosclerotic process at the same site, with mandibular canal involvement, and sequestrum formation. Surgical excision and histopathologic examination confirmed MRONJ.

Conclusions: This case highlights the value of longitudinal CBCT in documenting the radiographic evolution of MRONJ at the site of a previously identified lesion provisionally diagnosed as a DBI. However, the observed temporal and spatial association does not establish a causal relationship between the baseline lesion and subsequent development of MRONJ.

Keywords: Cone-Beam Computed Tomography • Denosumab • Osteonecrosis • Osteoporosis • Osteosclerosis

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Introduction

A dense bone island (DBI) is defined as a localized intraosseous radiopacity of unknown etiology that is not attributable to any other identifiable pathological condition [1]. It is most commonly detected incidentally during routine radiographic examinations, given that it is typically asymptomatic [1]. DBIs exhibit considerable size variability, generally ranging from around 2 mm to around 2 cm in diameter; in rare cases, they may reach large dimensions, extending to involve nearly the entire vertical height of the mandibular body [1,2]. Morphologically, DBIs can vary in shape, border definition, and radiographic density. They may be located in close proximity to adjacent tooth roots or be completely separated from such roots by intervening normal trabecular bone [1,2]. When identified in tooth-bearing regions of the jaws, these lesions have been described using various terms, including idiopathic osteosclerosis and focal sclerotic bone [1]. The differential diagnosis of DBI includes diffuse sclerosing osteomyelitis, particularly when secondary infection is suspected [1,2]. In such cases, careful correlation of inflammation-indicating clinical findings with radiographic features is essential [1,2]. A well-defined, homogeneous, structureless radiopacity favors a diagnosis of DBI, whereas ill-defined sclerotic areas containing residual marrow spaces are more suggestive of reactive osteosclerosis [1,2]. Histologically, DBI closely resembles compact osteoma and normal cortical bone—all are composed of dense lamellar bone with minimal or absent marrow spaces. However, unlike true neoplastic lesions, DBI does not typically cause displacement of adjacent teeth or anatomical structures, nor does it exhibit expansile growth. These distinguishing features are critical for differentiating developmental or non-neoplastic osseous variations from benign bone tumors [1,2].

Radiographically, DBI appears as a well-defined, intensely radiopaque lesion with a homogeneous internal structure, typically lacking medullary spaces and a surrounding radiolucent or cortical halo [3]. The lesion may vary in size and occur as a solitary or, less commonly, multiple foci [1]. DBIs are most commonly located adjacent to tooth roots; however, they can also occur in edentulous regions [1,2]. They generally do not cause cortical expansion, although mild expansion may occasionally occur, and they typically exhibit long-term radiographic stability [2]. Epidemiologically, DBIs are more frequently observed in the mandible (particularly in premolar and molar regions) and are more prevalent in women, most commonly during the second to fourth decades of life [3]. Although initially considered developmental anomalies, DBIs are now more widely regarded as reactive osseous formations, potentially arising in response to chronic low-grade inflammatory stimuli or persistent occlusal trauma [1-3]. The diagnosis of DBI is primarily established through radiographic assessment in conjunction with clinical evaluation. Diagnostic criteria include the presence

of a well-defined, dense radiopaque lesion within the maxilla or mandible, absence of a surrounding radiolucent border and associated clinical symptoms, and exclusion of alternative pathological conditions based on comprehensive clinical examination [1,3]. The widespread use of cone-beam computed tomography (CBCT) has substantially improved the detection and characterization of DBIs in the jaws. Compared with conventional 2-dimensional imaging modalities, CBCT provides superior 3-dimensional visualization, allowing more precise assessment of lesion morphology, dimensions, anatomical location, and relationship to adjacent structures. Despite these advantages, awareness of the radiographic variations and clinical implications of DBIs remains limited among clinicians, particularly in the context of preoperative evaluation for dental implant placement [3].

Medication-related osteonecrosis of the jaw (MRONJ) is a well-recognized complication associated with antiresorptive agents, including denosumab and bisphosphonates [4-6]. These agents suppress osteoclast-mediated bone resorption through distinct mechanisms. Denosumab is a monoclonal antibody that binds receptor activator of nuclear factor- κ B ligand (RANKL), thereby inhibiting osteoclast formation, function, and survival. In contrast, nitrogen-containing bisphosphonates inhibit farnesyl pyrophosphate synthase within the mevalonate pathway, disrupting osteoclast function and survival [4,5,7]. The incidence of MRONJ varies according to the underlying condition, type and duration of antiresorptive therapy, and other risk factors. Diagnosis is primarily based on clinical assessment, including the presence of exposed bone or bone that can be probed through an intraoral or extraoral fistula in the appropriate clinical setting. Management depends on disease severity and can range from conservative measures and infection control to surgical treatment when indicated [8]. Osteoporosis is the most common indication for antiresorptive therapy, although these agents are also used to manage malignant bone disease and other metabolic skeletal disorders [4,5]. CBCT is widely used to evaluate maxillofacial pathologies, providing high-resolution imaging of osseous structures with substantially lower radiation exposure relative to conventional computed tomography. Characteristic CBCT findings in MRONJ include osteolytic defects, sclerosis, lamina dura thickening, periosteal reaction, cortical disruption, and sequestrum formation [6]. To our knowledge, no published reports have described longitudinal CBCT documentation of MRONJ developing at the site of a radiopaque lesion provisionally diagnosed as a DBI.

This case report describes the clinical and radiographic evolution of a pre-existing radiopaque lesion provisionally diagnosed as a DBI (idiopathic osteosclerosis) in a 70-year-old woman receiving long-term denosumab therapy for osteoporosis; it also documents subsequent development of MRONJ at the same site. Furthermore, the report illustrates the value

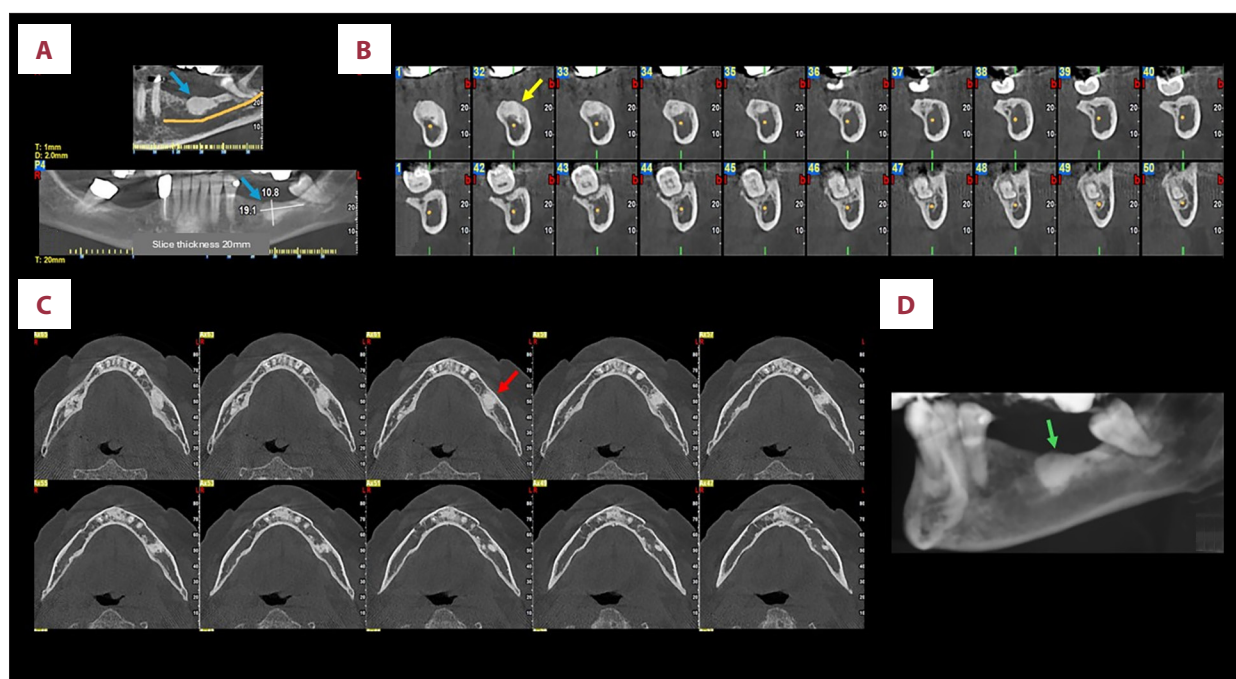


Figure 1. Baseline cone-beam computed tomography (CBCT) scan performed in 2021 in a 70-year-old Greek woman, demonstrating a hyperdense lesion in the left posterior mandible, provisionally diagnosed as a dense bone island (DBI). **(A)** Panoramic CBCT reconstruction showing the presumed DBI (blue arrow). **(B)** Cross-sectional CBCT images showing the presumed DBI (yellow arrow). **(C)** Axial CBCT images showing the presumed DBI (red arrow). **(D)** Three-dimensional CBCT reconstruction showing the presumed DBI (green arrow).

of CBCT for longitudinal assessment of lesion transformation over time. Because this observation is based on a single case, any potential relationship between DBI and susceptibility to MRONJ should be regarded as hypothesis-generating and requires confirmation in additional studies.

Case Report

A 70-year-old non-smoking Greek woman was referred to our private practice in 2021. The patient reported mild discomfort in the left posterior mandible; however, no clinical or radiographic findings at baseline suggested that the discomfort was attributable to the radiopaque lesion. The patient sought implant-supported rehabilitation as part of a comprehensive dental treatment plan. Her medical history was notable for long-standing osteoporosis, for which she had received teriparatide therapy from 2009 to 2012, followed by subcutaneous denosumab (60 mg every 6 months) from 2012 to 2021. Denosumab therapy was initially discontinued in 2021 based on the recommendations of her treating physician. However, the patient subsequently received 2 additional doses, administered approximately in August 2024 and February 2025; the latter was the most recent dose. Apart from her osteoporosis treatment, the patient's medical history was otherwise non-contributory. Her dental history revealed that teeth in the

affected mandibular region had been extracted before 2009. No history of inflammatory disease or other local pathological conditions in the affected area was reported before the initial CBCT examination.

Clinical examination revealed no serious intraoral abnormalities. CBCT was performed using a NewTom VGi unit (Cefla, Imola, Italy). The system was operated with variable acquisition parameters (110 kV, 2.5–4.1 mA, exposure time: 3.6 s) and a field of view of 12 × 8 cm. Image reconstruction was performed using a fixed isotropic voxel size of 0.30 mm. All scans were analyzed using NNT software. Baseline CBCT demonstrated a well-defined, homogeneous, hyperdense radiopaque lesion measuring approximately 1.9 × 1.1 cm within the left posterior mandible. The lesion exhibited well-circumscribed borders and was associated with mild expansion of the alveolar ridge. Based on its radiographic characteristics, a provisional diagnosis of DBI was established (**Figure 1**).

Concurrently, the referring dentist fabricated a removable partial denture with a metal framework. The patient wore the prosthesis daily for approximately 1.5 years until she developed discomfort associated with its use, after which she discontinued wearing it. Due to personal circumstances, she did not attend follow-up appointments. Four years later, in 2025 (at age 74), she returned with an intraoral fistula in the same region.

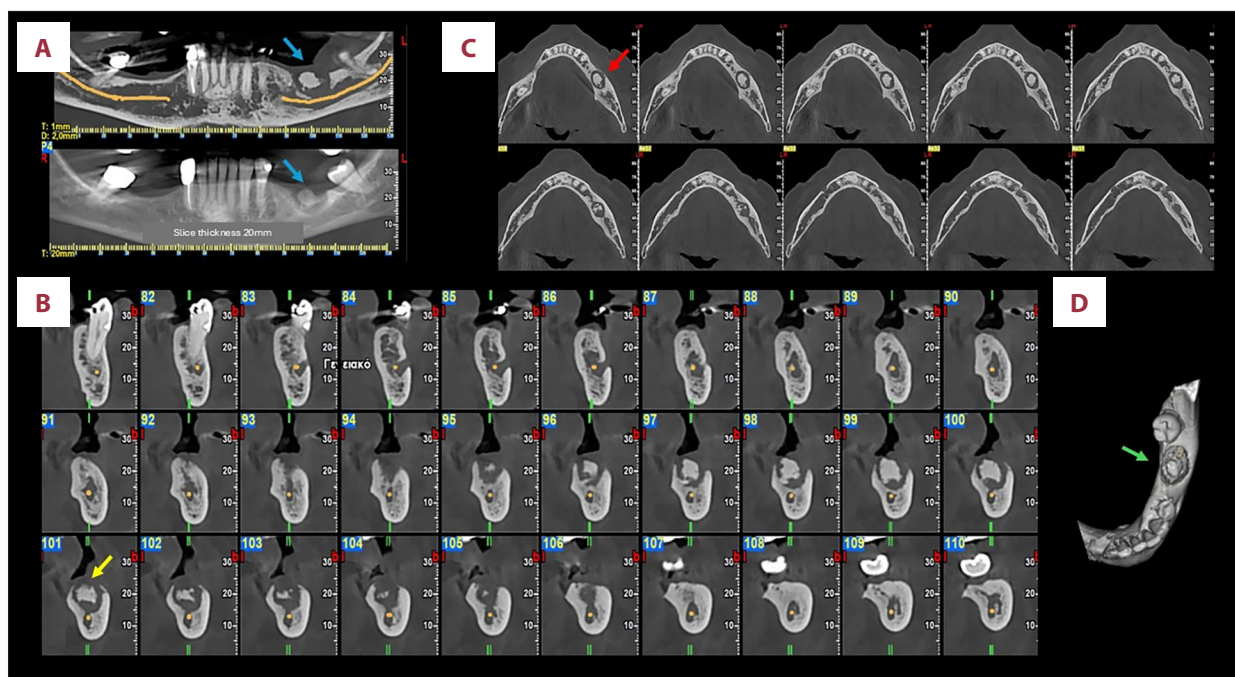


Figure 2. Repeat cone-beam computed tomography (CBCT) of the patient shown in Figure 1, obtained in 2025, revealing a mixed hyperdense and hypodense lesion at the site of the previously documented lesion provisionally diagnosed as a dense bone island (DBI), suggestive of bony sequestration associated with medication-related osteonecrosis of the jaw (MRONJ). (A) Panoramic CBCT reconstruction showing a mixed hyperdense and hypodense lesion due to MRONJ at the site of the previously documented lesion provisionally diagnosed as a DBI. (B) Cross-sectional CBCT images showing the mixed osteolytic-osteosclerotic lesion (yellow arrow). (C) Axial CBCT images showing the mixed osteolytic-osteosclerotic lesion (red arrow). (D) Three-dimensional CBCT reconstruction showing the mixed osteolytic-osteosclerotic lesion (green arrow).

A repeat CBCT scan revealed a mixed osteolytic-osteosclerotic lesion with ill-defined, moth-eaten borders at the site of the previously documented radiopaque lesion. The lesion measured approximately 1.4 cm in its greatest overall dimension; associated resorption of the alveolar crest extended to a depth of approximately 1.0 cm, and mandibular canal involvement was evident. Within the osteolytic area, a prominent hyperdense focus suggestive of sequestrum formation was observed. Additionally, generalized peripheral osteosclerosis was noted adjacent to the lesion margins (Figure 2).

Upon presentation in 2025, the patient reported mild pain in the affected region and an intraoral fistula that had been present for approximately 2 weeks. The fistula probed directly to bone. No purulent discharge, swelling, or erythema was observed. In accordance with the 2022 American Association of Oral and Maxillofacial Surgeons Position Paper, the lesion was classified as Stage 2 MRONJ based on the presence of an intraoral fistula probing to bone, associated infection/inflammation and mild pain, as well as radiographic evidence of sequestrum formation, and without evidence of pathologic fracture, extraoral fistula, or osteolysis extending to the inferior border of the mandible [5].

After diagnosis, the patient underwent complete surgical excision of the affected area by the oral and maxillofacial surgery team. Intraoperatively, the lesion demonstrated sequestration and was surrounded by inflamed soft tissue. Local anesthesia was achieved using articaine hydrochloride with epinephrine (1: 100,000). An L-shaped mucoperiosteal flap with periosteal releasing incisions was elevated to allow tension-free primary closure, and the associated fistulous tract was de-epithelialized (Figure 3A, 3B). Wound closure was performed using absorbable 4-0 polyglycolic acid sutures (PGA Rapid, Belgium). The patient received oral antibiotic therapy comprising amoxicillin (500 mg) combined with clavulanic acid (125 mg), which was initiated 2 days before surgery and continued for 7 days postoperatively.

Histopathological examination of the excised osseous specimen (Figure 3C) revealed mature lamellar bone characterized by multiple empty osteocytic lacunae, irregular bone margins, and absence of osteoblastic and osteoclastic rimming; these findings were consistent with bone necrosis. Focal basophilic colonies of *Actinomyces* species surrounded by aggregates of neutrophils were identified within the marrow spaces, along with prominent reversal lines. The associated soft tissue specimen consisted of oral mucosa exhibiting pronounced acanthosis,

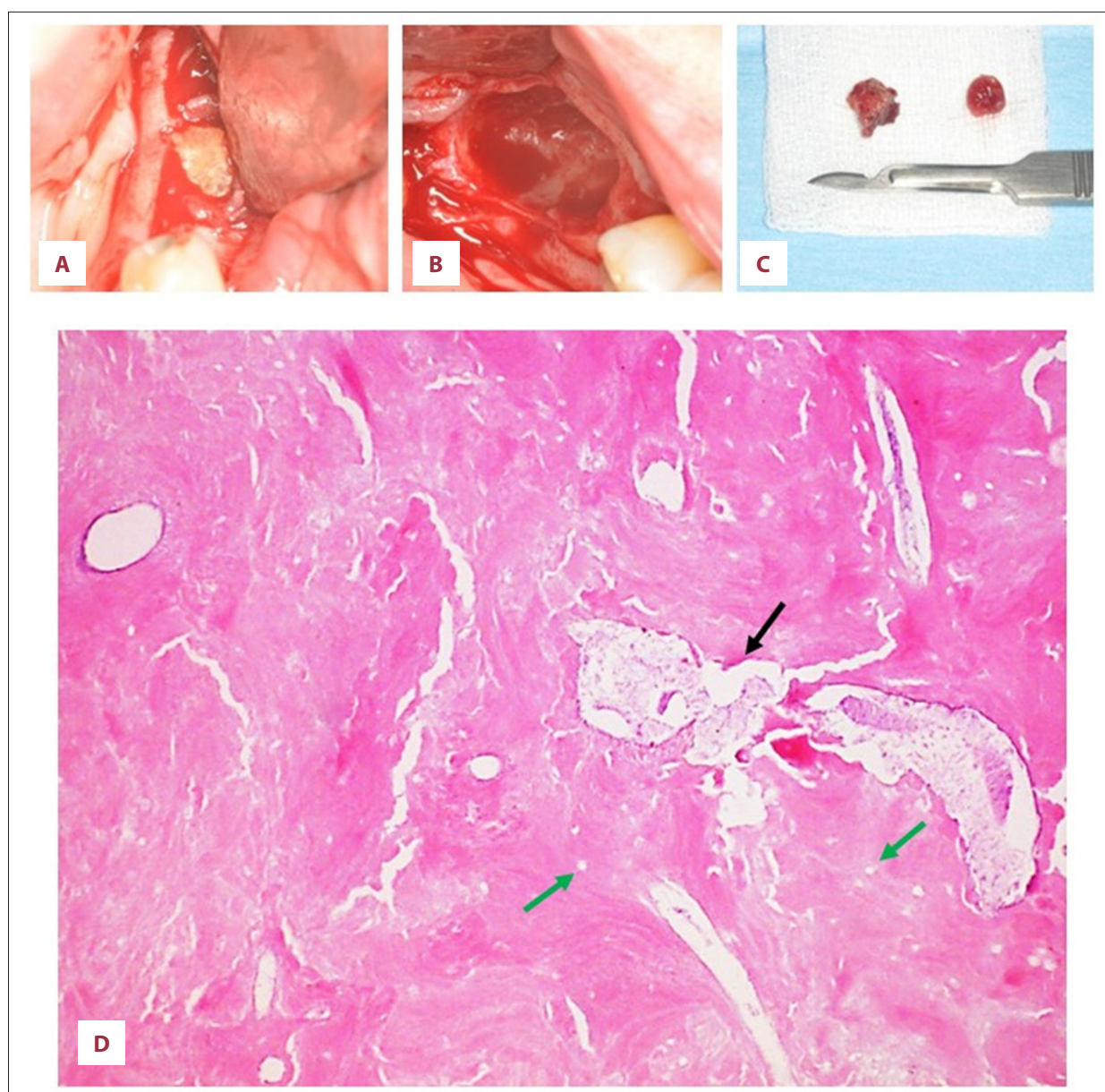


Figure 3. Intraoperative and histopathological views of the lesion in the patient shown in Figures 1 and 2. **(A)** Intraoperative view of medication-related osteonecrosis of the jaw (MRONJ) at the site of the previously documented lesion provisionally diagnosed as a dense bone island (DBI), after elevation of a full-thickness mucoperiosteal flap, revealing exposed necrotic bone and surrounding inflammatory tissue. **(B)** Surgical site after complete excision and thorough debridement of necrotic bone, showing removal of non-viable tissue and healthy bleeding bone margins. **(C)** Excised tissue specimens submitted for histopathological examination, showing resected necrotic bone and associated soft tissue that measured approximately 1 × 1 × 0.6 cm and 0.6 × 1 × 0.6 cm, respectively. **(D)** Whole-slide histologic section at × 10 magnification after hematoxylin and eosin staining, demonstrating empty osteocytic lacunae (green arrows) and marrow spaces containing necrotic debris (black arrow).

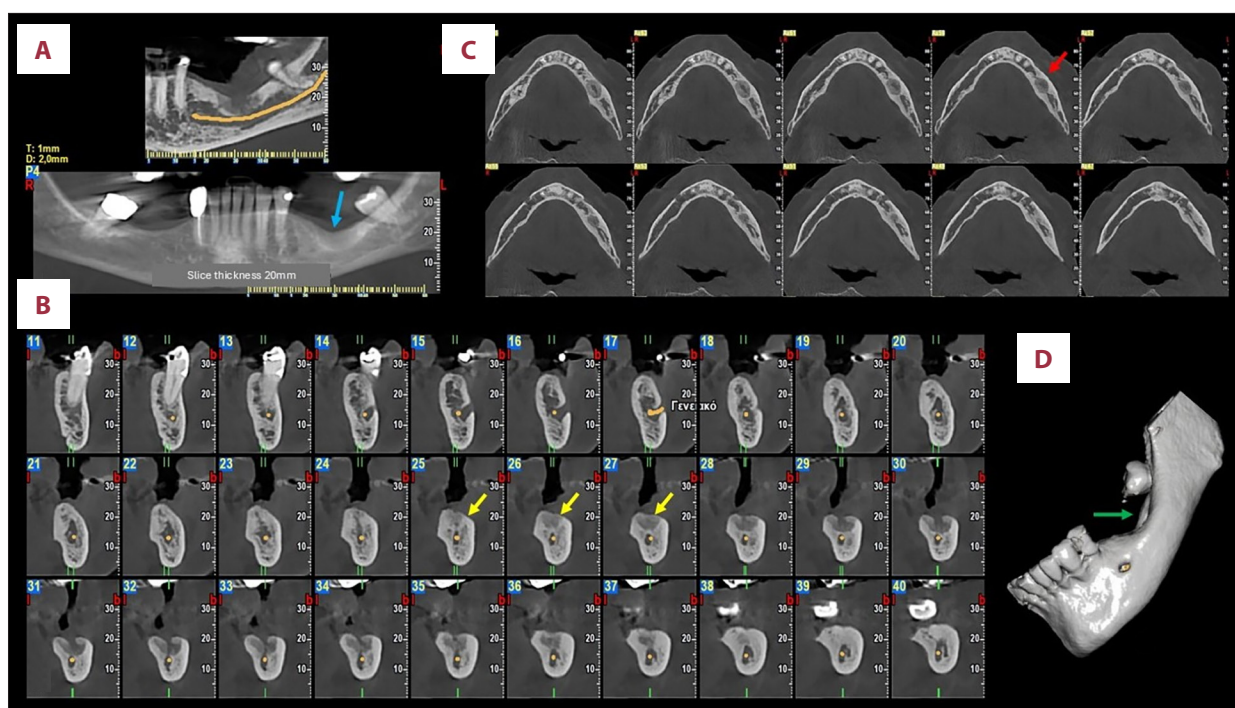


Figure 4. Follow-up cone-beam computed tomography (CBCT) obtained in 2026 regarding the patient shown in Figures 1-3. Six-month follow-up CBCT images demonstrate healing of the previously identified mixed osteolytic-osteosclerotic lesion, with a residual postoperative defect at the margin of the edentulous alveolar ridge. (A) Panoramic CBCT reconstruction demonstrating healing of the previously identified lesion (blue arrow). (B) Cross-sectional CBCT images demonstrating healing of the previously identified lesion, with a residual postoperative defect at the margin of the edentulous alveolar ridge (yellow arrows). (C) Axial CBCT images demonstrating healing of the previously identified lesion (red arrow). (D) Three-dimensional CBCT reconstruction demonstrating healing of the previously identified lesion (green arrow).

spongiosis, inflammatory exocytosis, and elongated rete ridges. The underlying connective tissue demonstrated edema, a moderate chronic inflammatory infiltrate, and focal interstitial hemorrhage. Collectively, these histopathological features confirmed the diagnosis of MRONJ (Figure 3D).

At the 6-month follow-up after surgical excision, clinical examination revealed no signs or symptoms. A follow-up CBCT scan performed at the same time demonstrated healing of the previously identified mixed osteolytic-osteosclerotic lesion, with a postoperative surgical defect at the margin of the edentulous alveolar ridge. No evidence of recurrence was observed (Figure 4).

Discussion

This case demonstrates the value of longitudinal CBCT assessment in documenting the development of MRONJ at the site of a lesion previously provisionally diagnosed as a DBI in a patient receiving long-term antiresorptive therapy. Serial CBCT examinations provided an opportunity to monitor the lesion longitudinally and identify radiographic changes that preceded

and accompanied the onset of osteonecrosis. To our knowledge, no published cases describing MRONJ arising at the site of a previously documented mandibular DBI were identified in available literature during the preparation of this report.

DBI, also termed idiopathic osteosclerosis, represents a localized increase in compact bone extending from the cortical plate into the cancellous compartment and radiographically manifests as a well-defined radiopaque lesion with variable size and morphology [1]. Its reported prevalence is approximately 5% in the general population; DBI is typically asymptomatic and detected incidentally, most commonly in the posterior mandible [2]. Although the precise etiology remains uncertain, some authors have suggested an association with occlusal trauma or low-grade local stimuli [2]. Longitudinal studies generally indicate these lesions are stable over time, despite occasional reports of dimensional variation [1,2]. Histologically, DBIs consist of dense, mature lamellar bone with minimal or absent marrow spaces [2]. The differential diagnosis includes diffuse sclerosing osteomyelitis and compound odontoma, among other radiopaque jaw lesions [1,2].

Epidemiologic data indicate that DBIs are most frequently identified in adolescents and young adults in their second and third decades of life, without a clear sex predilection [1]. Conversely, other studies have detected a higher prevalence between the second and fourth decades, with a female predominance [1,2]. Consistent with the literature [1], the radiopaque lesion in the present case was clinically asymptomatic; no clinical or radiographic findings were specifically attributable to the lesion. Although some studies have shown a higher prevalence in the premolar region, multiple authors have identified the mandibular first molar region as the most common site [1]. DBIs are typically located adjacent to tooth roots but can also occur in edentulous regions without causing cortical expansion. They demonstrate a clear predilection for the mandible, which has been involved in approximately 95% of reported cases [2]. The clinical and radiographic features of the present case largely align with these established patterns.

Radiographically, DBIs are described as well-circumscribed, homogeneous radiopaque lesions that may cause mild cortical expansion but do not exhibit bone destruction [1-3]. Although mild cortical or alveolar ridge expansion has been reported in association with some DBIs, this feature is non-specific and should not be considered diagnostic in isolation. In the present case, initial CBCT imaging revealed a well-circumscribed hyperdense intraosseous lesion measuring 1.9 × 1.1 cm, with alveolar ridge expansion in the absence of osteolysis. These findings are consistent with previously published radiographic descriptions [1-3]. CBCT enabled precise 3-dimensional localization and delineation of the lesion borders, supporting current recommendations that CBCT is the imaging modality of choice for assessing osseous lesions of the jaws [6]. Because histopathological confirmation was not available during the initial CBCT examination, the diagnosis of DBI was based on characteristic radiographic features and clinical correlation. However, given the patient's long-term receipt of denosumab therapy, an early osteosclerotic manifestation of MRONJ at the time of the initial CBCT examination cannot be definitively excluded. Therefore, although radiographic characteristics were considered compatible with a DBI, the absence of histopathological confirmation at baseline represents an important limitation of the present case. Alternative radiopaque lesions, including condensing osteitis, osteoma, focal cemento-osseous dysplasia, and diffuse sclerosing osteomyelitis, were considered [1,2]. Nevertheless, the lesion's well-defined borders, homogeneous internal structure, and absence of associated symptoms were considered most consistent with a provisional diagnosis of DBI [1-3].

Antiresorptive agents, including bisphosphonates and denosumab, suppress bone resorption through distinct mechanisms involving inhibition of osteoclast formation, function, and/or survival. These agents are widely prescribed for the management of osteoporosis and other metabolic or malignant bone

diseases [4,5,7,9]. The resultant suppression of bone turnover, particularly within the highly remodeling alveolar bone, predisposes susceptible individuals to impaired healing and the development of MRONJ [5,9]. In the present case, the patient had received long-term denosumab therapy for osteoporosis, placing her within a well-recognized risk group [5]. The occurrence of MRONJ in an older female patient is thus consistent with established epidemiologic data [5,8]. However, MRONJ arising at the site of a pre-existing DBI appears to represent a highly unusual clinical occurrence for which there is limited evidence in published literature.

In the present case, 4 years after the initial diagnosis, the patient presented with an intraoral fistula. Repeat CBCT demonstrated a mixed osteolytic-osteosclerotic lesion characterized by moth-eaten borders, cortical destruction, mandibular canal involvement, and radiographic evidence of sequestrum formation. These findings closely correspond to the characteristic imaging features of MRONJ, including osteolysis, sclerosis, periosteal reaction, and sequestrum formation, as described in the contemporary literature [6]. Thus, the radiographic progression observed in the present case is consistent with current diagnostic criteria for MRONJ [5]. The diagnosis was supported by the patient's antiresorptive medication history, the presence of an intraoral fistula probing to bone, characteristic CBCT findings, and subsequent histopathological confirmation. Management consisted of surgical excision of the affected area, along with removal of sequestered bone and debridement of the involved tissues, followed by histopathological examination. This approach was selected based on the clinical and radiographic extent of the lesion; it is consistent with individualized treatment strategies recommended for MRONJ [5]. The subsequent clinical course was favorable, without signs or symptoms or evidence of recurrence at the 6-month follow-up. Follow-up CBCT demonstrated healing of the previously identified mixed osteolytic-osteosclerotic lesion, although a residual postoperative surgical defect remained.

Patients with a history of antiresorptive therapy who undergo prosthetic rehabilitation require meticulous and continuous follow-up, particularly when mucosa-supported removable prostheses are utilized [4]. Ill-fitting dentures and chronic mucosal trauma are recognized non-surgical triggering factors for MRONJ [4,10]. In the present case, the patient wore the removable partial denture daily for approximately 1.5 years until she developed discomfort associated with its use, after which she discontinued wearing it. Although a potential contribution of prosthesis-related mucosal trauma cannot be excluded, this possibility remains speculative, and its contribution to the development of MRONJ cannot be determined from the present case. The literature emphasizes the importance of optimal prosthetic design, periodic relining, and close follow-up, typically every 2 to 3 months, in high-risk individuals [4]. The present

findings reinforce these recommendations and highlight the need for vigilant prosthodontic management and close clinical monitoring in patients receiving antiresorptive therapy.

Several contextual factors should be considered when interpreting our observations. The patient was an older woman receiving long-term denosumab therapy, a recognized risk factor for MRONJ [5]. The clinical presentation, characterized by mild pain and an intraoral fistula probing to bone, was consistent with clinical features used to diagnose and stage MRONJ [5]. Additionally, a removable partial denture had been fabricated for the affected region, and the patient reported persistent discomfort associated with the prosthesis, raising the possibility of chronic local mucosal irritation. Because these factors were present concurrently, the relative contributions of the pre-existing DBI, antiresorptive therapy, and potential prosthesis-related trauma cannot be determined. Consequently, the findings should not be interpreted as evidence that DBI alone is associated with or predisposes to the development of MRONJ.

Overall, the patient's demographic profile, medication history, lesion location, and radiographic findings are consistent with current knowledge of MRONJ [5,6,9]. The notable aspect of this case is the temporal and spatial co-localization of MRONJ with a previously documented DBI. Although this observation raises the possibility that local osseous characteristics may be associated with site-specific patterns of occurrence, the present report cannot establish a causal relationship or determine whether DBI represents a site of increased susceptibility to MRONJ. Instead, the case should be viewed as a rare co-occurrence warranting further investigation in additional patients.

Conclusions

This report documents the development of MRONJ at the site of a previously identified presumed mandibular DBI in a patient receiving long-term denosumab therapy. The principal contribution of this case is the longitudinal CBCT documentation of

radiographic change at the site of a previously documented radiopaque lesion to MRONJ. Although the temporal and spatial association between the 2 findings is noteworthy, this observation does not establish a causal relationship between the baseline lesion and the subsequent development of MRONJ. Importantly, it generates a hypothesis that may be explored in future studies and additional case reports but does not imply causation or preferential susceptibility. CBCT proved valuable for the detection, characterization, and documentation of disease progression. Careful prosthodontic management and long-term follow-up remain important in patients receiving antiresorptive therapy.

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Institution Where Work Was Done

Clinical data collection and subsequent analysis for this case report were performed exclusively within a private Oral and Maxillofacial Surgery Practice (Athens, Greece).

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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