Non-exposed bisphosphonate-related osteonecrosis of the jaw: a critical assessment of current definition, staging, and treatment guidelines.

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Authors: S Patel, S Choyee, J Uyanne, A L Nguyen, P Lee, P P Sedghizadeh, S K S Kumar, J Lytle, S Shi, A D Le

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Public Summary:
Bisphosphonates are used across a wide range of disciplines, including endocrinology, oncology, orthopedics, and dentistry. These antiresorptive drugs have been indicated for various diseases, including osteoporosis Paget's disease of bone, hypercalcemia of malignancies, bone metastases, and osteolytic lesions of multiple myeloma. Osteonecrosis of the jaw (ONJ) is a serious side effect of these medications that presents with high morbidity and challenging clinical management. The estimated incidence of this side effect for patients taking intravenous (IV) bisphosphonates for malignancies ranges from 0.8% to 12%, whereas for oral bisphosphonates, it ranges from 0.009% to 0.034%. Osteonecrotic lesions may be asymptomatic for a period of time. Common symptoms reported by patients prior to a clinically evident lesion, such as exposed necrotic bone, include pain, tooth mobility, mucosal swelling, and erythema. A key point in the case definition of BRONJ by both task forces is the presence of necrotic bone exposed in the oral cavity. However, bone exposure is not always observed in a subset of cases that otherwise have characteristic hallmarks of BRONJ. Recently, a clinical variant of BRONJ with unclear development and pathophysiology has been reported. Clinical features include persistent jaw bone pain, bone enlargement, and gingival swelling in the absence of both significant dental disease and clinical evidence of necrotic bone exposure. We critically assess the current guidelines and treatment recommendations for BRONJ and propose a modified treatment protocol for these atypical BRONJ cases. We present non-bone exposure BRONJ cases and propose a modified staging system for including non-exposed BRONJ lesion.

Scientific Abstract:
Non-exposed bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a newly reported complication arising from bisphosphonate therapy that presents with atypical symptoms and no apparent mucosal fenestration or exposure of necrotic bone. The clinical observation of the presence of necrotic bone underneath normal epithelial coverage was not conclusive for the diagnosis of BRONJ based on current guidelines established by the American Association of Oral and Maxillofacial Surgeons (AAOMS) and the American Society for Bone and Mineral Research (ASBMR), which specify the presence of clinically exposed necrotic bone for more than 8 weeks. Hence, the purpose of this review is to critically assess the current guidelines for diagnosis and management of BRONJ and propose a modified staging system and treatment guidelines to properly address the non-exposed variant of BRONJ lesions.

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