Reports related to the drug/Report legati al farmaco

ONJ IN A YOUNG ADULT PATIENT AFTER SHORT TERM USE OF CORTISONE AND OMALIZUMAB

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Background. MRONJ is an adverse reaction induced by different categories of drugs. We describe a recent case of a young male adult who had osteonecrotic bone exposure following the use of a monoclonal antibody in association with cortisone therapy.

Case Presentation. A 30-year-old male patient has been experiencing pain, swelling, and gingival erosion with erythematous borders in the lingual gum area of tooth 3.7 for about a month. He suffers from asthma and is being treated with beclomethasone dipropionate and formoterol fumarate dihydrate spray, omalizumab i.m. 3 times every 15 days, and tiotropium spray. Recently, he took betamethasone tablets 1 mg 4 tablets/day, gradually reduced, and prednisone tablets 25 mg 1/2 tablets daily for 15 days for otitis.

During the first clinical examination, the patient expelled a small bone fragment, resulting in a 3mm bone exposure on the lingual side of the mandible, 2 mm under the gingival margin. The exposed bone had a probing depth of approximately 6 mm, with bleeding on probing and pain, and bony spicules appeared in the central location. The adjacent teeth (3.6-3.7) were vital and did not present mobility or gingival pockets. The patient reported the last omalizumab administration the week before the first clinical examination. The CBCT revealed an irregularity of the ridge profile, consistent with the presence of an osteonecrotic focus.

The patient was monitored every 2 weeks for two months, to decide if surgery was necessary. The prescribed therapy included hyaluronic acid gel, chlorhexidine gel 0.5%, antibiotic therapy (amoxicillin and clavulanic acid tablets 1g twice a day for 7 days and metronidazole tablets 250mg twice a day for 7 days), and anti-inflammatory therapy (ibuprofen tablets 600 mg). The patient skipped the omalizumab intake session with the agreement of the allergist specialist. There was a gradual improvement of the bone exposure. At the final follow-up, no signs of bone exposure or gingival inflammation were present.

Conclusions. Omalizumab is a type of medication used to treat persistent allergic asthma. It is a humanized monoclonal antibody that may cause drug-related pharyngeal irritation, abdominal pain, fever, headache, and other adverse events during treatment. However, no cases of oral bone exposure have been reported with this medication.

On the other hand, people with asthma who rely on oral corticosteroids are at risk of bone loss and an increased risk of fractures in the hip and spine. A recent study conducted on mice showed that taking prednisone orally for three weeks can inhibit endochondral ossification, delay the healing process, and reduce bone biomechanical properties. This can adversely affect the formation of hard callus (woven bone) and bone remodeling during the healing process.

Short term use of prednisone, in association with betamethasone and omalizumab, maybe consequently to a local oral traumatic event could induce bone exposure and a sequestrum release.

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OSTEONECROSIS OF THE JAW ASSOCIATED TO PEMBROLIZUMAB: A CASE REPORT

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Background. Medication related osteonecrosis of the jaw (MRONJ) is a potential adverse outcome associated to the treatment with antiresorptive agents and antiangiogenic medications. In the literature, some cases of MRONJ have been described in association to Immune Checkpoint Inhibitors in cancer therapy, including ipilimumab, nivolumab and pembrolizumab. Pembrolizumab is a humanized monoclonal antibody directed against Programmed cell death protein 1 (PD-1) and represents the treatment of choice for metastatic non-small-cell lung cancer (NSCLC), due to its efficacy in extending both progression-free survival and overall survival. We describe a case of MRONJ associated to Pembrolizumab to enhance awareness and provide better guidance for dental treatment in the context of cancer patients undergoing pembrolizumab therapy.

Patients and methods. In September 2023, a 69-year-old male patient was referred to the Unit of Dentistry and Oral Surgery of the University of Pisa for the development of a painful mucosal lesion. Medical history was significant for hypothyroidism, depressive syndrome and metastasizing NSCLC. The patient did not have documented allergies, occasionally smoked cigars and did not report alcohol consumption. The patient was under medication with levitaceram and levothyroxine, and had received a total of ten infusions of pembrolizumab (administered four times a week) for the treatment of NSCLC. The patient complained the presence of pain in the right maxillary region at the level of the edentulous alveolar crest.

Clinical examination revealed the presence of a fistula along with suppuration, persisting for longer than 8 weeks and involving the maxillary buccal gingiva at the level of the missing element teeth 1.2, 1.3. This area was tender and painful to palpation.

Computed tomography revealed a moth-eaten radiolucent pattern, in the absence of bone sequestrum. According to the MRONJ classification of the Italian Society of Oral Medicine and Pathology, this case was a stage 2b.

Results. After MRONJ diagnosis, conservative treatment was performed and involved one session of professional oral hygiene with reinforcement of domestic oral hygiene maneuvers and prescription of 2% chlorhexidine mouthwash to be used twice daily for 14 days. Medical treatment with amoxicillin 1g/day and metronidazole 750 mg/day was prescribed for 14 days. The patient was clinically re-evaluated after two weeks. There were no signs of complete healing at this stage, only stabilization of necrosis and symptoms improvement. Surgical intervention was then scheduled, and involved local resection, soft tissue debridement, and curettage. Any residual sequestra were removed to ensure healing by first intention. The resection margins were extended until obtaining spontaneously bleeding bone. Lesion fragments were sampled and sent for histology. Follow-up was performed at 1 week, 1 month, and 3 months after surgery. Complete healing with resolution was observed.

Conclusions. This is the fourth case described in the literature reporting ONJ onset following the treatment with Pembrolizumab. The symbiotic relationship between the immune system and osteoclasts is considered the reasoning for the occurrence of immunotherapy-related ONJ. Given the promising potential of Immune Checkpoint Inhibitors in managing metastatic malignancies, it appears relevant to include oral cavity screening in patients scheduled for treatment with these medications.

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DENOSUMAB-RELATED ONJ IN METASTATIC LUNG CANCER: A CASE REPORT AND LITERATURE REVIEW

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Background. Medication-related osteonecrosis of the jaw (MRONJ) during or after bisphosphonate (BFs) treatment is well known in literature.

However, there are few cases reported related to the use of other pharmaceutical agents, such as Denosumab.

In 2010, the US Food and Drug Administration approved the clinical use of Denosumab (Xgeva) for the prevention of skeletal-related events (SREs) in patients with metastatic bone cancer.

This report highlights the importance of a proper management of a Xgeva-related ONJ, providing a comprehensive review of related cases to investigate the relationships between risk factors and clinical manifestations.

A comparative analysis with BFs-ONJ is then carried out in relation to differences in terms of incidence, risk factors and treatment.

Patients and methods. A patient with lung cancer, treated with subcutaneous injections of Denosumab (Xgeva), was referred to the oral surgery department at the "G. d'Annunzio" University in Chieti (Unich). The patient developed an osteolytic lesion involving the first quadrant.

A "drug holiday" from Denosumab was prescribed, along with antiseptic and antibiotic therapy prior to the surgical treatment.

The lesion was exposed and necrotic bone removed until bleeding margins were reached.

A strict follow-up was established and, after the complete healing of the tissues, the drug was reintroduced.

Results. In the reported case, Denosumab-related ONJ had a similar clinical manifestation to BFs-ONJ.

The treatment, conducted following the SICMF-SIPMO's guidelines, led to the complete healing of the lesion and no recurrence was observed during the follow-up.

Although the overall frequency of Denosumab-related ONJ was low, such a condition has a huge impact on the patient's quality of life.

Dose regimen and frequency of assumption are critical factors to be considered for a comprehensive analysis of such results.

Conclusions. Medical and dental practitioners must recognize the importance of Xgeva when assessing the patient's risk and planning treatment.

ONJ treatment by surgical intervention must be carefully evaluated.

Due to its favorable pharmacodynamics, the temporary discontinuation of the drug should be considered and concerted by clinicians and prescribing specialists in order to foster the healing process.

Personalized risk assessment and a multidisciplinary approach are essential for optimizing patient outcomes. Managing risks and treatments in accordance with current guidelines is mandatory to maximize the effectiveness of procedures and improve overall patient well-being.

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OSTEONECROSIS OF THE JAWS IN A PATIENT UNDER TREATMENT BY GUSELKUMAB: A NEW ETIOLOGICAL FACTOR FOR ONJ?

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Background. Guselkumab is a human monoclonal antibody that specifically inhibits IL-23 by binding the cytokine's p19 subunit.

Inhibition of upstream IL-23 signaling reduces downstream production of cytokines with established (TNFα) or emerging (IL-17 family) roles in inflammatory conditions such as psoriasis. It has also been postulated that IL-23 blockade, by trans-differentiating Th17 lymphocytes (probably central effector cells in psoriasis) into T-regulatory cells or Th1 cell populations, interrupts Th17 pathways that contribute to the chronic inflammation underlying the pathophysiology of many immune-mediated diseases, including inflammatory arthritis, psoriatic arthritis, and psoriasis. This drug seems to be efficacious and it seems to provide an acceptable benefit-risk profile in patients with active psoriatic arthritis who are naive to treatment with biologics.

The aim of this communication is to present and discuss a possible role of Guselkumab in the development of ONJ in a 67-year-old patient

Patients and methods. A 67-year-old man had been on treatment with Guselkumab for psoriatic arthritis for 14 months. Past medical history was negative for other diseases. The assumption of bisphosphonates or antiresorptive drugs was not reported. In September 2023, the patient was referred to the Dentistry Department for the assessment of a suspected bone exposure in correspondence of maxillary incisor region. The patient had undergone the extraction of the left maxillary central incisor in July 2023.

Results. Clinical intraoral examination revealed the presence of necrotic bone exposure in the region of the left maxillary central incisor.

Panoramic and CT scan radiograph confirmed the presence of an irregularly healed post-extraction socket of tooth 21, with a small area of necrotic bone that was classified as MRONJ stage 1. A surgical intervention of bone sequestrectomy under local anesthesia was proposed. Following the patient's acceptance and informed consent, under local anesthesia, a necrotic bone sequestrectomy together with curettage was performed. Reabsorbable sutures were placed. Postoperative healing was uneventful. At 3 months follow up, no bone exposure or necrotic bone could be appreciated.

Conclusions. The present case could represent and describe a possible new etiological factor for Medication related osteonecrosis of the jaws. Further studies are needed to investigate the possible relationship between Guselkumab and ONJ.

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TRUST THE SYMPTOMS: CASE REPORT OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW DURING TREATMENT WITH ZOLEDRONATE AND OSIMERTINIB

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Background. Medication-related osteonecrosis of the jaw (MRONJ) is a severe adverse drug reaction, consisting of progressive bone destruction in the maxillofacial region of patients (Pts) treated with either antiresorptives, mainly denosumab and zoledronic acid (ZA), or antiangiogenic drugs. Also Tyrosine kinase inhibitor (TKI)-induced ONJ has been reported. The clinical presentation is an exposed bone or presence of an intraoral or extraoral fistula persisting for more than 8 weeks. However, a large multicenter European study showed that up to a quarter of Pts with MRONJ remain undiagnosed because their symptoms do not conform to the traditional case definition and 24% MRONJ could not be diagnosed because of non-visible necrotic bone.

Patients and methods. We reported a case of MRONJ associated with ZA and Osimertinib, a third generation TKI with initial diagnostic difficulty due to the lack of bone exposure for the first months.

Results. A 73-year-old caucasian female patient was diagnosed in September 2020 with EGFR mutated (ex 21) non-small cell lung cancer (NSCLC) with bone metastasis. She started a first-line treatment with Osimertinib from September 2020 and concomitant ZA. An oral examination and a Maxillofacial computed tomography scan (MFCTs) were performed before starting ZA. After 20 months of treatment, she felt persistent periauricular pain and paresthesia irradiated to the right mandibula without swelling. She discontinued ZA from June 2022, was treated with analgesics and was referred to the Department of Oral and Maxillofacial Surgery for assessment. Clinical examination, orthopantomography and MFCTs excluded signs of MRONJ. In September 2022 for persistence of gingival and mandibular pain, the patient underwent treatment with antibiotic therapy. In November 2022, oral examination showed a mucous fistula in the right retromolar trigone without any bone exposure. She was treated conservatively and performed a Dentalscan Cone Beam which revealed sequestrum. In January 2023 the patient presented bone exposure, compromised dental implants and anesthesia of the inferior alveolar nerve region. She underwent surgical debridement of the necrotic bone removal of dental implants and mandibular osteoplasty. Histopathological analysis of the bone biopsy confirmed a diagnosis of MRONJ.

Conclusions. Combination of TKI with ZA has been reported to increase the risk of MRONJ, dental consultation is important both prior to and during treatments to better prevent the risk and choose the therapeutic strategy. Despite a correct prevention, our patient had suffered from prime symptoms after 20 months of treatment and another 8 months before a visible bone exposure with a negative impact on quality of life. Non-exposed MRONJ are not so rare and are challenging, multidisciplinary consultation is necessary to give the best care for these pts.

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THE "STRANGE" CASE OF ONJ OCCURRING AFTER A SINGLE 60 MG DOSE OF DENOSUMAB, IN A PATIENT PREVIOUSLY TREATED WITH ZOLEDRONATE

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Background. Osteonecrosis of the jaw (ONJ) is a serious complication of treatment with bone modifying agents (BMA), commonly used in the clinical practice to prevent skeletal-related events (SREs) in patients with bone metastases[1]. The risk of developing ONJ in patients receiving BMA for osteoporosis is much lower, ranging from 0.01% to 0.06%[2], although several predisposing local and systemic factor may promote this phenomenon[3].

Case description. We report the case of a class III obese (BMI 43.72 Kg/m^2) 64-year-old woman, who came to our Institution in 2022, attending the "Osteoncology" outpatient clinic. In 2006, the patient had received a diagnosis of a left T2N0M0 breast cancer (ER$^+$, PgR$^+$, Her2$^-$), for which she had undergone conservative surgery and irradiation (QUART), followed by adjuvant chemotherapy and hormone treatment with Tamoxifen for 5 years. In 2012, a bone scan had revealed bone metastases in the hip and ribs, for which she had started aromatase inhibitors (stopped after 5 years) and 4 mg zoledronate, received every 4 weeks for 2 years. After that, the patient had discontinued regular oncological follow-up.

In 2018, she was diagnosed with acute myocardial infarction, complicated by ventricular septal rupture, that was successfully surgically repaired.

In 2022, the patient experienced a pathological fracture at the right femur, after which a whole-body CT and a bone scan were performed. No new distant lesions were identified by the CT, while the bone scan showed a moderate uptake of 99mTc in the site of fracture. A severe osteoporosis was revealed by Dual-Energy X-Ray Absorptiometry. The patient underwent orthopedic surgery, during which a biopsy of the femoral lesion was performed; surprisingly, histological examination of the sample described the absence of tumor cells. Blood tests showed mild hypercalcemia and increased PTH levels, for which the patient was referred to an Endocrinologist. Following this consultation, a Sestamibi parathyroid scan was performed that revealed a right parathyroid adenoma. The patient was then referred to a General Surgeon but her risk of intra-/post-operative complications was defined "high", due to her cardiac comorbidities; as a consequence, the patient refused the proposed surgery.

A conservative therapeutic approach was thus proposed, including treatment with 6-monthly 60 mg denosumab, after orthopantomogram (OPT) and dental visit that excluded contraindications to the BMA. The patient received her first dose of denosumab in April 2023 but, two months later, she complained severe pain in the right half of the mandible; an OPT and a CT scan were performed, revealing the onset of a stage I ONJ.

Denosumab was discontinued and the ONJ was managed by a medical and conservative approach, until complete healing. Due to her high risk of fracture, in October 2023 she received the second dose of denosumab, undergoing close dental follow-up that, to date, has not revealed relapse of the ONJ nor new lesions.

Conclusions. Multidisciplinary management of patients treated with BMA is necessary to stratify their risk of ONJ and set-up appropriate follow-up. Early diagnosis of ONJ could avoid surgical therapeutic management, especially in patients at high risk of complications.

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Reports linked to particular clinical aspects/
Report legati ad aspetti clinici particolari

SURGICAL MANAGEMENT OF MRONJ WITH THE USE OF HUMAN AMNIOTIC MEMBRANE (hAM): TWO CASE REPORTS

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Background. The human amniotic membrane (hAM) has several beneficial effects, including low immunogenicity, anti-inflammatory, antifibrotic, antimicrobial and analgesic properties. It's also a source of stem cells and growth factors that promote tissue regeneration. hAM acts as a barrier with suitable mechanical properties such as permeability, stability, elasticity, and resorbability, which help prevent the proliferation of fibrous tissue and promote early neovascularization at the surgical site. In oral surgery, hAM stimulates healing and facilitates the proliferation and differentiation of epithelial cells in the oral mucosa leading to its regeneration. At the Oral Surgery Unit of the C.I.R. Dental School of Turin, we are conducting a pilot-study to test the use of cryopreserved hAM for patients with stage 2-3 MRONJ.

Patients and methods. A 49-year-old female patient with breast cancer with bone metastases treated with Zoledronic Acid from January 2013 to January 2014, in supportive therapy with Denosumab from January 2014 to today was treated for recurrence of MRONJ in quadrant IV. The patient undergoes sequestrectomy surgery, carrying out osteoplasty of the necrotic bone with piezosurgery and positioning the hAM on the treated bone, after a first surgical failure.

An 84-year-old female patient with breast cancer with bone metastases, treated with Denosumab since August 2022 was treated for MRONJ of the II quadrant. The patient undergoes sequestrectomy surgery, carrying out osteoplasty of the necrotic bone with piezosurgery and positioning the hAM on the treated bone.

Results. Patients were enrolled in a regular follow-up schedule, which consisted of visits on the following post-intervention days:

- 7 days (suture removal); - 14 days, - 1 month, - 2 months. At each follow-up visit, the primary endpoint was determined through a clinical evaluation of bone reexposure and the extent of wound healing.

Secondary endpoints were evaluated at each follow-up visit:

- signs of inflammation, (presence of local erythema, easily hemorrhagic surgical site...);
- infection, (presence of purulent discharge, abscess, or cellulitis).

In Patient 1 partial bone reexposure was reported 1 week after surgery. The treated lesions had partial bone reexposure (less than one-third relative to preoperatively) located on the anterior part of the wound.

14 days after surgery, the posterior mandibular part had healed correctly, but the bone was still reexposed in the anterior mandibular part. The patient remained asymptomatic.

After 1 month, the whole surgical site was almost completely reepithelialized. After 2 months, the patient was completely pain-free, the surgical site was clean, and no adverse effect was noticed.

In Patient 2 a hematoma was reported 1 week after surgery. 14 days after surgery, the whole surgical site was almost completely reepithelialized.

After 1 month, the whole surgical site was almost completely reepithelialized. After 2 months, the patient was completely pain-free, the surgical site was clean, and no adverse effect was noticed.

The patients will be re-evaluated at 6 months with new radiographic imaging.

Conclusions. It is known that hAM is being used in oral surgery, but there is insufficient clinical evidence to prove its superiority over traditional surgery in this field. Nevertheless, hAM shows potential as a viable alternative for MRONJ surgical treatment. Further studies are required to ascertain the effectiveness of hAMSC-based therapy in treating bone diseases. Despite the limitations of a case report, our pilot study provides preliminary data that is encouraging with regards to the use of hAM in the surgical treatment of MRONJ.

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MEDICATION-RELATED OSTEONECROSIS OF THE JAW (MRONJ) AFTER A SINGLE DOSE OF DENOSUMAB IN A CANCER PATIENT: A CASE REPORT

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Background. Medication-related osteonecrosis of the jaw (MRONJ) is an adverse event associated with drugs classified as bone-modifying agents (BMAs), specifically antiresorptive and/or antiangiogenic medications, administered particularly to oncologic and osteometabolic patients. The first antiresorptive medications linked to MRONJ are bisphosphonates (BP) and denosumab (DNB). BPs exhibit prolonged bone persistence due to a half-life of approximately ten years, and the risk of MRONJ tends to increase with the duration of treatment. Conversely, DNB has a short half-life of about 32 days, with effects on bone resorption that gradually decrease within six months after discontinuation of administration; the duration of treatment does not appear to influence the risk of MRONJ. This paper reports a case of medication-related osteonecrosis of the jaw (MRONJ) after one administration of X-geva® (120 mg Denosumab).

Patients and methods. A 70-year-old man with pulmonary carcinoma and bone metastases undergoing Denosumab therapy presented to the Unit of Oral Medicine with Dentistry for Fragile Patients (AOUP "Paolo Giaccone" of Palermo) for pain of with the fourth quadrant from seven days.

The patient had treated with a single dose of X-geva® (Denosumab 120 mg) one month before. No other medications were reported. No alterations were detected during the extraoral examination. The patient wore an ill-fitting removable resin prosthesis in the lower arch and at the intraoral examination revealed the presence of an ulcerated lesion of edentulous ridge of the fourth quadrant. The lesion appeared bleeding upon probing. Radiographic examinations, including orthopantomography and subsequently cone-beam computed tomography (CBCT), revealed an area of bone rarefaction with a "ground glass" in the fourth quadrant. The findings confirmed diagnosis of MRONJ. With positive opinion of the patient's oncologist and after informed consent of the patient, a surgical sequestrectomy was performed by piezosurgery. The patient underwent a combined therapy with 0.2% chlorhexidine mouthwash and antibiotic prophylaxis with amoxicillin with clavulanic acid (1 g/day) and metronidazole (500 mg/day), starting from the day before the surgery and for six days after. The denture didn't be worn until complete osteo-mucosal healing and only after well fitted and comfortable relining.

Results. Clinical healing was achieved at 15 days, and the patient was subsequently monitored clinically and radiologically at 30, 45, and 90 days post-intervention without any signs or symptoms of recurrence of MRONJ.

Conclusions. This clinical case reports occurrence of MRONJ related to Xgeva® (Denosumab 120 mg) after a single administration.

The cancer patient, exposed to medications with risk of developing osteonecrosis of the jaw, necessitates a pre-administration preventive strategy. Among known risk factors, it is imperative to warrant well-fitted denture. This imperative for vigilant monitoring aims to prevent potential complications while simultaneously ensuring a significant enhancement in the quality of life for the cancer patient.

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CHALLENGES OF LONG-TERM BISPHOSPHONATE THERAPY: A CASE OF MRONJ WITH MANDIBULAR FRACTURE IN OSTEOMETABOLIC PATIENT

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Background. First-line pharmacotherapy for osteoporosis involves Bone-modifying Agents (BMA) therapy, typically comprising bisphosphonates (BPs). Prolonged BPs use can result in serious complications, notably medication-related osteonecrosis of the jaw (MRONJ). Pathologic mandibular fractures (PMF) are the most serious complications of MRONJ that may have significant consequences. While osteometabolic patients generally face a lower risk of MRONJ compared to cancer patients, there is a potential for a gradient in MRONJ risk over time. Specifically, osteometabolic patients who have been using BPs for more than 3 years, especially those lacking preventive care for dental-periodontal diseases, are at a heightened risk, as extended duration of BP intake and local dento-alveolar conditions are recognized risk factors for MRONJ. While the number of reported PMF cases due to MRONJ is limited, there is only sparse data available regarding its incidence, with reported rates ranging from 2.9% to 3.8%. Moreover, there is a lack of information on the incidence of MRONJ-related PMF in osteometabolic patients treated exclusively with BP. However, as MRONJ tends to progress over a long time in osteoporotic patients, it is reasonable to anticipate that proactive dental prevention measures may reduce the incidence of MRONJ-related PMF. Considering the significant impact of this complication on patients' quality of life, further research is warranted.

Patient and methods. A 75-year-old male patient presented to the Unit of Oral Medicine with Dentistry for Fragile Patients (AOUP "Paolo Giaccone" of Palermo) in January 2023 with complaints of pain localized to the region of tooth 3.7, which had been extracted in August 2022. No details were available regarding the surgical and pharmacological protocol that had been employed for the dental extraction. The patient had a longstanding history of osteoporosis and had been undergoing treatment with alendronate (70 mg weekly) for 15 years. Notably, the patient was a non-smoker and did not utilize dental prostheses. Radiographic assessment, including panoramic radiography (OPT) performed in December 2023 after the onset of the patient's reported symptoms, followed by cone-beam computed tomography (CBCT) in January 2024, was conducted by the patient before the visit and presented during the consultation. These examinations revealed distinctive radiographic features including non-healed bone of the post-extraction alveolar socket of tooth 3.7, an irregular appearance in the left mandibular angle region, and complete discontinuity of the basal cortical bone. Clinical examination revealed swelling localized to the left mandibular angle region, exhibiting tenderness on palpation. Intraoral examination disclosed the presence of exposed bone in the region corresponding to the extracted tooth 3.7, accompanied by purulent suppuration.

Results. Clinical and radiographic examinations confirmed a complicated stage 3 symptomatic MRONJ diagnosis according to SIPMO-SICMF classification, with the PMF also categorized at MRONJ stage 3 in AAOMS clinical staging. Following the diagnostic findings, the patient was promptly started on a therapeutic regimen comprising topical antiseptics and systemic antibiotic therapy, with the anticipation of continued therapeutic management under the supervision of the Plastic Surgery Unit at the same institution.

Conclusions. This report underscores the importance of primary (pre- and during BMA therapy) and secondary preventive strategies to mitigate complications linked to long-term bisphosphonate therapy, especially in elderly patients, aiming to prevent the development of MRONJ and to make its early diagnosis.

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A STORY OF RECHALLANGE: CASE REPORT OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW DURING TREATMENT WITH DENOSUMAB

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Background. Bone metastases (BM) are responsible for high morbidity and limit the quality of life (QoL) of patients. Treatment of BM from solid tumors often includes the use of bone antiresorptive agents (BA) beside tumor-directed specific treatment. Denosumab (DmB), a receptor activator of nuclear factor kappa-B ligand (RANK-L), is a BA that exists as a fully humanized antibody against RANK-L. By inhibiting osteoclast function and associated bone resorption, it is effective in reducing BM skeletal-related events (SREs). However, medical-related osteonecrosis of the jaw (MRONJ) is a rare yet severe and treatment-limiting adverse event. The question of whether and how DmB can be rechallenged after a MRONJ remains a topic of ongoing discussion.

Patients and methods. We reported a case of MRONJ linked to DmB in a breast cancer patient. Despite potential treatment-related risks, DmB was rechallenged.

Results. A 77-year-old caucasian female patient, initially diagnosed with breast cancer in 2005, experienced a BM relapse in 2018. She initiated first line therapy with Palbociclib, Letrozole and concurrent subcutaneous DmB in September 2018. Given the stable skeletal disease (SD), DmB was suspended after 24 months of treatment. After ten months of DmB suspension and bone SD, a computed tomography (CT) scan showed skeletal progressive disease (PD), leading to the reintroduction of DmB in July 2021. Eleven months later, the patient developed MRONJ; thus, DmB injections were halted. Following an attempt with conservative therapy, the patient underwent surgical debridement in March 2023. DmB remained discontinued for 16 months. In September 2023, upon experiencing uncontrolled pain, later confirmed by a staging CT scan to be caused by skeletal PD, DmB rechallenge was thoroughly discussed with a dental specialist and the patient. In the process of evaluating whether to rechallenge DmB, careful consideration was given to the risks and benefits of continuing treatment, as well as determining the frequency of oral check-ups in the context of confirmed skeletal PD.

The patient has currently been undergoing DmB rechallenge for 7 months, with regular dentistry follow-ups, no signs of MRONJ relapse and a good BM control.

Conclusions. The possible reintroduction of BA after MRONJ is a matter of debate and should be taken into consideration prioritizing its benefits on BM and QoL. To optimize bone health management and minimize the risk of complications, a multidisciplinary, patient-centered approach is essential, involving consultations with dental specialists.

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POST-SURGICAL FRACTURES OF THE JAWS IN MRONJ: A RESTROSPECTIVE STUDY ON 255 LESIONS

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Background. Maxillary and mandibular fractures can occur in advanced medication-related osteonecrosis of the Jaws (MRONJ) or can be complications of the lesions' surgical treatment. This retrospective study aims to show fractures occurred after the surgical treatment in patients with MRONJ referred to the Complex Unit of Odontostomatology of the Aldo Moro University of Bari from 2010 to 2023.

Patients and methods. The authors analyzed their institutional database of MRONJ and included all patients who developed jaw's fractures after the surgical treatment during the study period. These fractures did not require other surgical treatment, but only functional rest. The authors excluded patients that got lost in follow-up and patients with follow-up lower than six months. All patients underwent the same authors' protocol: detailed medical and pharmacological history, clinical examination, panoramic radiogram, and multi-slice computed tomography with 3D reconstruction of the facial skull. Before surgery, the authors established a one-to-six-month drug holiday depending on drugs administer in agreement with the specialists. All oncologic patients underwent surgery during the chemotherapy-free period. The preoperative antibiotic therapy consisted in three consecutive cycles of 1 g of ceftriaxone and 1 g of metronidazole per day for six days with a drug-free period of ten days after each cycle. After surgery, all patients repeated at least one cycle of antibiotic therapy. The patients underwent clinical follow-up monthly; in addition, the patients underwent panoramic radiograms every three months and computed tomography every six months. After the healing of the surgical wound, if necessary, the patients resumed the antiresorptive and anti-angiogenic therapies. During the follow-up period, the patients who developed fractures underwent panoramic radiograms to evaluate fracture type and then monthly to control bone healing and other lesions.

Results. During the study period, 217 patients with 255 MRONJ came to the authors' attention; considering the inclusion and exclusion criteria authors included five oncologic patients with six mandibular both stage III MRONJ and fractures occurred after surgical treatment; two men with prostatic cancer and three women, two with breast cancer and one with myeloma. Three also received intravenous denosumab every twenty-eight days; two patients received intravenous zoledronate every twenty-eight days. All these patients with MRONJ III stage underwent extensive bone resection and a histopathological exam. All six fractures were below masseter and they occurred in a period ranging from one to three months after surgery. All cases were favorable fractures healed in two months with bone callus. The patients did not develop further MRONJs.

Conclusions. According to this study, fractures are uncommon events that occur most frequently in the mandible of oncologic patients with stage III MRONJ during the postoperative follow-up period. In addition, they have a good prognosis because fractures are below masseter.

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METASTASES OCCURRING WITHIN MRONJ LESIONS IN ONCOLOGIC PATIENTS: A RETROSPECTIVE STUDY ON AN UNCOMMON HISTOLOGICAL FINDING

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Background. In oncologic patients, medication-related osteonecrosis of the jaws (MRONJ) can occur because of the antiresorptive and antiangiogenic therapies, such as Zoledronate, Clodronate, Denosumab, and Bevacizumab. Anyway, several tumors show a tendency to metastasize in the jaws, thus inducing lesions resembling MRONJ clinically and radiologically. Therefore, the current study aims to investigate the presence of bone metastases in MRONJ lesions.

Methods. The authors carried out the retrospective study using the institutional database of MRONJ referred to the unit of Odontostomatology of the Aldo Moro University of Bari. The authors included oncologic patients who received concomitant histological diagnoses of metastases and MRONJ considering the study period from 2004 to 2023. All patients underwent clinical examination, panoramic radiogram, multi-slice computed tomography with 3D reconstruction of the facial skull, and anesthesiologic assessment before surgery. The preoperative antibiotic therapy involved three consecutive cycles of 1 g of ceftriaxone and 1 g of metronidazole per day for six days with a drug-free period of fifteen days after each cycle. Before surgery, the authors established a three-to-six-month drug holiday depending on drugs administer in agreement with the specialists. All oncologic patients underwent surgery during the chemotherapy-free period. The authors staged the MRONJ lesions according to both the dimensional staging system and SICMF-SIPMO staging system and treated stage I lesions with surgical debridement, stage II with open-access bone surgery, and stage III with extensive bone resection. The authors sent the resected bone samples for anatomopathological examination. When necessary, immunohistochemical examination was carried out considering patients primary tumor. The patients underwent clinical follow-up monthly; in addition, the patients underwent panoramic radiograms every three months and computed tomography every six months. The authors conducted descriptive statistical analysis considering all inclusion criteria and the follow-up.

Results. During the study period, 360 patients showing 455 MRONJ lesions came to the authors' attention. The authors included: seven women with metastatic ductal breast cancer, one woman with lung cancer and a man with prostatic cancer, with a mean age of 55,0 ± 19,9 years. They had eleven lesions that contained metastases of cancers occurred in the molar region of the mandible; four lesion was stage II, six was stage III, and one developed a stage III in the postoperative site of a previous stage I. All patients received multiple antiresorptive drug therapies with denosumab, clodronate or zoledronate; two patients also received trastuzumab. The mean follow-up period was 28.0 ± 6.9 months, and one patient developed a fracture after surgical treatment that healed after a year.

Conclusions. The authors' experience suggests that metastases within MRONJ lesions are uncommon occurrences in oncologic patients. The histological examination of the resected bone is mandatory to achieve the diagnosis and to menage other therapeutic strategies for patients.

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NON-SURGICAL MANAGEMENT OF STAGE I MRONJ: A CASE REPORT TREATED ONLY BY MEDICAL AND LOW- LEVEL LASER THERAPY

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Background. Medication-Related Osteonecrosis of the Jaw (MRONJ) is the most severe and debilitating side effect in patients treated or in treatment with anti-resorptive and anti-angiogenetic drugs for oncologic diseases or osteoporosis.
In literature, the treatment/management of low stage MRONJ is reported to be focused on infection control, pain reduction and prevention of progression and recurrences of necrotic bone formation. Low-Level Laser Therapy (LLLT) is one of the most successful adjuvant procedures promoting tissues healing also in the oral cavity. Authors report on a case of MRONJ in a patient with history of multiple myeloma receiving also Zoledronate, managed by non-surgical treatment which consisted in medical and LLLT therapy only. The aim of the study was focused on the effectiveness of LLLT on mucosal and residual bone healing as treatment strategy for early (low stage) MRONJ.
Patients and methods. In July 2023, an 81 years-old female patient referred to the Complex Unit of Odontostomatology of the University of Bari "Aldo Moro", complaining a gingival lesion characterized by pain, swallowing and pus discharge of one month duration. Patient was edentulous and her medical history revealed a recurrence of a stage III multiple myeloma treated with Deratumumab, Bortezomib and Zoledronate (11 i.v. infusions monthly, interrupted 15 days before referring to our observation for the suspicion of MRONJ). The intraoral examination revealed the presence of bone exposure in the I quadrant. Consequently, with the suspect of MRONJ, patient underwent panoramic radiogram and computed tomography to better define the necrotic area dimension and perform staging.
As lesion was classified as Stage I, according with American Association of Oral and Maxillofacial Surgeons, authors agreed for a non-surgical treatment protocol, starting with 3 cycles of antibiotic therapy (Ceftriaxone 1g daily I.M. and Metronidazole 250mg twice a day per os) for 7 days with a drug-free period of 10 days between each cycle and clinical follow-ups every month. In September 2023, at the end of antibiotic therapy, clinical follow-up revealed the absence of necrotic bone due to its spontaneous expulsion, as referred by the patient. Expulsed bone sample was sent for histological examination. Therefore, authors decided for a LLLT to better provide the mucosal and residual bone healing. LLLT was performed every 5 days with a Diode Laser (Wavelength 980nm-Lasotronix-Poland) in continuous emission at 1 Watt and with a dedicated handpiece for photo-biomodulation; lesion was irradiated for about 2 minutes in de-focalized modality. Patient underwent Laser Therapy until the complete healing of the tissues and is still under clinical and radiographic follow-ups every three months.
Results. Patient showed a complete clinical and radiographic healing of the soft and hard tissues after two months. No further therapies were necessary as confirmed by the final radiological investigations. No recurrence was observed in the following months during follow-up.
Conclusions. LLLT confirmed its effectiveness regarding pain and infections reduction in patients with low stage MRONJ, in particular with photo-biomodulation, hard and soft tissues show a rapid and complete healing. Eventually, with this treatment modality patients could avoid surgical procedures and it might be possible to improve their life conditions.

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MULTIDISCIPLINARY MANAGEMENT OF POST-EXTRACTION MRONJ IN A 74-YRS WOMAN WITH A HISTORY OF BREAST CANCER AND DENOSUMAB THERAPY

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Background. Medication-Related Osteonecrosis of the Jaw (MRONJ) is an uncommon but severe complication associated with the use of bone modifying agents (BMA), described as the progressive destruction and necrosis of the mandibular and maxillary bone[1]. This case report describes a multidisciplinary approach to the treatment of a case of maxillary osteonecrosis in a patient previously treated with Denosumab.

Case presentation. A 74-year-old female patient presented at the IRCCS San Raffaele Hospital's Oral Medicine and Oral Pathology Unit with a complex medical and pharmacological history. Diagnosed with stage IV breast cancer, her extensive treatment regimen included radiation, chemotherapy, and various targeted therapies. She underwent a tumorectomy in 2016 and was treated with Denosumab from February 2021 for bone and nodal stability, discontinued two months prior to her dental extraction in September 2022. At presentation in January 2023, the patient arrived with an ECOG Performance Status (PS) of 0, indicating full functionality without symptoms. She exhibited delayed healing at the post-extraction site of tooth 1.1, characterized by bone exposure without symptoms. Clinical examination and CBCT scan revealed necrosis of the alveolar process in the anterior upper maxillary region, staging at stage 1 according to AAOMS[2]. Subsequently, she underwent cycles of antimicrobial therapy and antiseptic mouth rinses in order to reduce the local infection risk. The surgical management under local anesthesia was complex due to the location and extension of the defect, and involved the debridment of the diseased area of the premaxilla and removal of necrotic bone from the alveolar ridge to the nasal spine and the incisive suture of the palatine process; primary closure of the defect was obtained. A comprehensive management plan was initiated, encompassing antibacterial and antiseptic therapies, along with meticulous home wound care. Regular follow-ups were scheduled to closely monitor the healing process and the effectiveness of the osteonecrosis treatment. The post-surgery strategy was tailored, focusing on wound care, antimicrobial administration, rehabilitation of the upper frontal arch and bone defect with a provisional prosthetic appliance and periodic evaluations of soft and bone tissue healing.

Conclusions. This case highlights the intricacies involved in treating patients with a history of extensive cancer therapy, emphasizing the impact of such treatments on oral health and the importance of the personalized, multidisciplinary approach in managing of the post-extractive complication. The seamless collaboration between oral medicine and oral surgery specialists was pivotal. This partnership, along with the meticulous implementation of a tailored treatment plan, including surgical intervention and thorough follow-up, was instrumental in navigating the patient's unique challenges. The success of this case demonstrates the effectiveness of combining diverse expertise, comprehensive patient evaluation, and continuous monitoring to ensure optimal healing and patient care. It underscores the need for heightened vigilance and specialized care in similar cases, where the patient's extensive medical history and medication use pose significant treatment challenges.

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METACHRONOUS SITES OF MRONJ DUE TO DIFFERENT DRUGS IN THE SAME PATIENT: A CASE REPORT

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Background. MRONJ is multicentric (with involvement of different sites of mandible and/or maxillary bones) in 10-30% of cases.

Multiple sites of MRONJ can be observed at time of first MRONJ diagnosis (synchronous) or during the follow up process (metachronous); multiple sites are observed clinically (*i.e.*, bone exposure, fistula, etc) or radiologically (above all by Computed Tomogrsphy, CT scan)[1,2]. Furthermore, MRONJ sometimes occurs in patients receiving more than one Bone Modifying Agent (BMA) in sequence: for example in patients receiving a different treatment after shifting from pamidronate to zoledronic acid (historical cases in cancer and myeloma patients), from zoledronic acid (4 mg monthly) to denosumab (120 mg monthly) for bone metastases or myeloma (after 2010), or from alendronate to denosumab (60 mg every 6 months) in osteoporosis patients.

We present a singular case of a patient showing two metachoronous sites of MRONJ, some years distant as diagnosis time, induced by two different drugs: monthly zoledronic acid 4 mg and monthly denosumab 120 mg.

Case report. In May 2014, a 54-year patient was referred by another hospital. He had received treatment including monthly zoledronic acid (4 mg every 4 weeks, for 4 years) due to bone metastases of prostate cancer. A CT was performed due to mandibular pain and MRONJ was diagnosed according to the Italian SIPMO-SICMF definition[1,2]. The site of MRONJ was right hemi-mandible (at site of a dental extraction, performed out of our centre, during the bisphosphonate treatment). The AAOMS stage was 0 (pain without bone exposure) and the SIPMO-SICMF stage was IIb (bone involvement at CT scan: diffuse osteosclerosis). After a short time, bone exposure with pus discharge appeared. Treatment of MRONJ included medical therapy and debridment. A bone fragment was spontaneously expelled months later. The patient did not undergo further visits at our centre.

In 2022, after cancer disease progression, a new antiresorptive treatment was started by his oncologist and the patient received subcutaneous denosumab (120 mg every 4 weeks) for about one year.

In April 2023, he complained of pain at the left hemi-mandible; the oral exploration revealed spontaneous bone exposure with signs of infection; a CT scan showed diffuse osteosclerosis (extended to mandibular nerve canal). Consequently, a new metachronous site of MRONJ was diagnosed. The AAOMS stage was II, whereas it was staged as IIb according to the Italian staging system. The treatment included medical therapy and sequestrectomy. At the moment the patient is under strict follow-up.

Conclusions. Possible conclusions:

a. The sequence of "high dose" BMAs (*i.e.*, zoledronic acid and denosumab) is a potentially strong risk factor for MRONJ occurrence among long-surviving patients after a first MRONJ diagnosis, and patients receiving sequence of treatment should reserve careful attention in follow-up visits.

b. Metachronous MRONJ can be observed along time (even after years), due to long uptake of drugs in the bone tissue (as for zoledronic acid, but not for denosumab), or due to new triggers (infection episodes, trauma, etc.), or due to further treatment (resumption of the previous drug, or start of a new drug - as in this reported case).

c. MRONJ is a complex multifactorial disease, with potential different origins, both at first diagnosis and at occurrence of metachronous disease sites.

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TOOTH FRACTURE AS SENTINEL SIGN OF UNDERLYING MRONJ? CASE REPORT OF ATYPICAL DENOSUMAB-RELATED MRONJ IN A CANCER PATIENT

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Background. Tooth fracture is observed due to several reasons (e.g., jaw trauma, biting hard foods, gum chewing habit, periodontal disease, infection, aging, very severe teeth grinding, etc. – usually in deteriorated teeth) and is not included in the list of possible clinical signs of MRONJ (other than bone exposure or fistula)[1]. We present a case of a patient receiving monthly denosumab 120 mg complaining of unexplained maxillary pain and tooth fracture.

Case report. Female, 59-year old at presentation. Bone metastases from breast cancer were found in August 2020. Treatment of metastatic cancer included endocrine therapy and denosumab (120 mg subcutaneous, every 4 weeks) since October 2020, with a good oral health at the start of therapy. Denosumab was planned for at least two years, as indicated by recommendations of AIOM (Italian Medical Oncology Association). She had good response to endocrine treatment.

In July 2022, she started to complain of pain in right maxillary area; the pain increased after biting hard food, in September 2022. Her dentist did not find relevant problems.

In November 2022, as the pain persisted, she underwent a Cone Beam Computed Tomography at another private dental practice; the dentist did not reveal any relevant problem. Also an endoral Rx exam on March 2023 was negative.

In August 2023, a relative asked a phone opinion to a member of the MRONJ work group at Alessandria Hospital. Due to large treatment with "high dose" denosumab (33 months) and presence of a suspect symptom (pain), a Computed Tomography (CT) was indicated, according to MRONJ Italian recommendations (2020), that suggest a three-step process to draw or to negate a MRONJ diagnosis, underlining importance of adequate imaging evaluation, based on CT. Furthermore, bone scan scintigraphy was suggested.

The CT scan revealed diffuse osteosclerosis in several regions of jaws and a fracture of a dental element (14), in correspondence of the pain site. The bone scan showed a limited uptake at the right maxillary area (and no uptake in regions of known bone metastases). The case was classified as Stage 0 according to AAOMS and Stage Ib according to SIPMO-SICMF. Extraction of fractured tooth was performed and a control CT has been planned (after 6 months).

Discussion. According to The AAOMS definition of MRONJ - released by in 2007 and partially enlarged in 2014 (encompassing patients with fistula) - patients with suspected signs or symptoms but without bone exposure are left in a "limbo" named Stage 0. According to Italian recommendations, CT exam appears mandatory in any case of a patient "at risk" of MRONJ, in order to confirm or deny diagnosis of medication-related bone alterations. In the reported case, a delay of MRONJ diagnosis was induced by reduced awareness of the importance of drug history (high dose denosumab) and integration of clinical signs/symptoms (pain) with adequate imaging (CT). Furthermore, we reported an atypical sign (tooth fracture) and atypical symptom (cracked tooth syndrome, CTS) not usually listed in signs/symptoms of suspicion for MRONJ (together with most reported: tooth mobility, swelling, etc).

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Others/Altri

CHRONIC DIFFUSE SCLEROSING OSTEOMYELITIS: WHEN BISPHOSPHONATES ARE THE SOLUTION

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Aim. Chronic diffuse sclerosing osteomyelitis is a relatively rare and challenging condition because of its still unknown etiology and the lack of a standard treatment protocol.
Prevalence was found to be 1/200.000. Differential diagnosis includes Chronic Recurrent Multifocal Osteomyelitis, Paget's disease and Osteosclerotic dysplasia.

Methods. We present a case of a 44-year-old male patient which presented with swelling and pain at the jaw irradiating to the preauricular area, denying any trauma or significant medical history. Initial treatment with antibiotics and NSAIDs barely alleviated symptoms without any definitive resolution. Dental as well as gnathological causes were excluded.

Results. CT scans revealed osteosclerosis and endosteal reaction of the left mandible. Bone biopsy showed dystrophic bone tissue without dysplastic alterations. Bone scintigraphy highlighted an intense uptake. Blood count and bone turnover markers showed no alterations; C-reactive protein and erythrocyte sedimentation rate were slightly increased. Clinical and radiographic signs support a diagnosis of chronic diffuse sclerosing osteomyelitis.

Conclusions. Treatment options include both conservative and surgical approaches. The patient was treated with systemic antiresorptive therapy with a single injection of Aclasta (zoledronic acid 5mg intravenous) with complete remission of symptoms for 12 months. After 20 months, a second injection was administered.

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EFFICACY OF ADJUNCTIVE PDT IN THE TREATMENT OF A PARTICULAR PRESENTATION OF MRONJ: A CASE REPORT

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Background. Drug-related osteonecrosis of the jaw (MRONJ) is an adverse event in patients with osteometabolic and/or oncological disease treated with antiresorptive (pAR) drugs including anti-RANKL antibodies (e.g., denosumab) and nitrogen-containing bisphosphonates (N- BP; e.g., zoledronic acid), or angiogenesis inhibitors (AgI). We present a case of MRONJ in a patient suffering from systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) which resolved thanks to antibiotic therapy (AT) and photodynamic therapy (PDT).

Patients and methods. A 48-year-old patient comes to our attention with history of SLE and RA from several years treated with monoclonal antibodies (Tolicizumab) since 2015 and bisphosphonate for 24 months. The patient has been taking deltacortene 25 mg per day for 25 years. He has never undergone radiation therapy. On intraoral physical examination, a bony exposure of approximately 1,5 cm in diameter is found in the upper right hemimaxillary bone. In the lower arch, white reticular lesions attributable to SLE are observed. In addition, the patient is suffering from periodontitis. The patient underwent AT according to ministerial guidelines (amoxicillin + clavulanic acid and metronidazole), for 4 weeks during which the elements with a poor prognosis (mobility 3) were extracted.

Results. During the first week of AT, the bone exposure area was treated with PDT based on Curcumin + 3% hydrogen peroxide, activated by a diode lamp at 460 nm wavelength and 7 watts of power. 2 sessions of 5 minutes were performed. 1 week after PDT and 3 weeks after the start of AT there is a total re-epithelialization of the osteonecrotic area with a significant reduction in pain revealed by the patient.

Conclusions. In the literature, emerges that PDT is increasingly performed in combination with other therapeutic options with excellent clinical outcomes. The most important aspect at a clinical level is the absence of adverse effects, due to the ability of the photosensitizer to bind and induce apoptosis of only damaged cells. This is important in immunosuppressed patients who are undergoing other drug therapies, thus improving their lifestyle.

Randomized clinical trials should be conducted so that the benefit of PDT in the treatment of MRONJ can be demonstrated with a greater scientific basis.

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OSTEONECROSIS OF THE MAXILLARY AND ZYGOMATIC BONE AFTER SEVERE COVID-19 INFECTION: A CASE REPORT

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Introduction. The Sars-CoV2 (covid-19) is known to affect the respiratory system as a complication. However, some cases of involvement of the maxillofacial area have been reported in the literature, including osteonecrosis and osteomyelitis. It can either be the result of the pathogenic mechanism or therapy administered.

Case report. This article presents a case of osteonecrosis of the maxillary and zygomatic bone after severe Covid-19 infection in a 75-year-old man. He denied any intake of antiresorptive drugs or radiotherapy. The patient had type II diabetes mellitus and had undergone high-intensity care admission to the intensive care unit for respiratory failure in Sars-Cov-2 infection. During hospitalization, he received dexamethasone 8 mg daily for 36 days.

The case was treated with extensive hemi maxillary and zygomatic sequestrectomy combined with orbital-zygomatic-maxillary reconstruction with custom titanium mesh (T-mesh) using CAD/CAM technology designed by our team, under general anesthesia.

Discussion. Numerous factors have the potential to contribute to the initiation and progression of osteonecrosis of the jaw following a post-COVID-19 infection. The virus itself, leading to a hyperinflammatory state. Additionally, microvascular thromboses and a hypercoagulable state may further exacerbate the condition. Furthermore, medications employed for managing the hyperinflammatory syndrome and cytokine storm, specifically corticosteroids and biological drugs like monoclonal antibodies. Recent investigations into individuals who have recovered from COVID-19 reveal an elevated susceptibility to developing osteonecrosis when exposed to glucocorticoids. Some authors suggest the connection between COVID-19 and osteonecrosis, particularly in relation to corticosteroid usage as it could be in this case.

Conclusions. This article aims to raise awareness on rarer causes of osteonecrosis of the jaw, such as use of extensive corticosteroid treatment in COVID-19 patients. We believe it is important to take this into consideration for better management of diagnosis, treatment, and subsequent follow-up.Inizio modulo

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A SUCCESSFUL CASE OF SECONDARY PREVENTION OF MRONJ, STANDARZID BY DIALOGUE BETWEEN ONCOLOGISTS, DENTISTS AND DENTAL HYGIENISTS

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Background. Drug-related osteonecrosis of the jaw (MRONJ) is a potentially serious condition which may occur in patients receiving long-term antiresorptive medications (bisphosphonates and denosumab), often in combination with antiangiogenics, for treatment of oncological diseases and for osteoporosis, in the absence of head and neck radiotherapy. Removable dentures have been classified as a risk factor in the development of osteonecrosis of the jaws (ONJ), in fact they can cause microtraumas to the oral mucosa, furthermore, they can become a bacteriological niche for mostly fungal infections. Primary prevention, the main goal of which is the elimination of risk factors, is aimed at recovery and/or maintain good oral health and reduce the risk of developing pathologies conditions or any other adverse event. Secondary prevention is implemented in patients already undergoing treatment with drugs at risk of ONJ, in which it is necessary to intercept all clinical and radiological signs, primary and secondary, associated with the initial stages of the disease. The aim of this work is to document a primary and secondary prevention experience of a cancer patient with removable total dental prosthesis at risk of MRONJ.

Patients and methods. A 79-year-old female patient suffering from IgAK multiple myeloma was brought to our attention for a specialist dental examination preparatory to therapy with intravenous bisphosphonates (zolendronic acid). The patient with complete bimaxillary edentulism, wearing upper and lower removable prostheses, had no root residues on objective examination; the gingival tissues were moderately erythematous, the genial mucous membranes, the oral floor and the lingual belly were normal.

In addition to the clinical examination, the patient underwent a radiographic examination (Orthopantomography) which certified the absence of ongoing infectious-inflammatory processes and a readjustment and stabilization of the removable prostheses through resin relining which completed the preventive oral preparation for suitability of the start of antiresorptive therapy. The patient was asked for dental clearance at each administration of the drug (monthly) which led to intercepting the prodromes of the osteonecrotic complication at the fourth administration of the drug with evidence of jaw pain, appearance of ulcerations of the attached gingiva in various locations and evident signs of osteosclerosis to the CBCT exam.

All this led to an immediate suspension of zolendronic acid and consequent modification of the oncological therapy associated with careful monitoring (periodic dental specialist visits). We also suspended the use of the dentures for 2 weeks and prescribed rinsing with bicarbonate solution 3 times a day after careful oral hygiene of the mucous membranes and tongue.

Results. The secondary prevention protocol prepared made it possible to successfully prevent the appearance of necrosis phenomena of the jaw bones.

Conclusions. Dentists and dental hygienists, within a multiprofessional team, play a key role in the primary and secondary prevention of MRONJ. A standardized multidisciplinary approach is needed, which promotes a lasting dialogue between specialists involved in the management of patients at risk of MRONJ.

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