Bisphosphonate-Related osteonecrosis of the jaws in patients affected by osteometabolic diseases: a serial case analysis

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Introduction. The bisphosphonates are the most commonly prescribed antiresorptive drugs for the treatment of metabolic disorders. However, there are several adverse effects associated with oral bisphosphonates including the bisphosphonate related osteonecrosis of the jaw (BRONJ). Several risk factors drug-related, local and sistemic factors have been linked to BRONJ. A more recent report described an absolute risk ranging from 0.46 to 0.99% among patients receiving oral bisphosphonates. In this paper, the osteonecrosis of the jaw associated with oral BP therapy in patients affected by osteometabolic disorders was reviewed in order to renew the current knowledge.
Materials and methods. Were observed 12 in 55 patients affected by metabolic diseases (36 cases of BRONJ in total observed), between 2010 and 2013, and treated with oral NBP. The patients were referred to our hospital for diagnosis and surgical treatment. Each patient was clinically examined and a detailed medical history was raised. The majority (8/12) were prescribed alendronate, 2 oral ibandronic acid; 1 risendronic acid; in 8 patients, the osteoporosis was associated with systemic risk factors as Diabete, Rheumatic disease, Hypothyroidism, Hepatitis C Virus Infection and supportive therapy (steroids and antiangiogenetic drugs). In 10 cases the duration of oral BP therapy exceeded 5 years (>5 -10 aa.) prior to BRONJ diagnosis. The total of patients with concerning symptoms, received maxillofacial imaging (8 panoramic radiography; 1 computed tomography; 2 CBCT in the context of clinical care). The retrospective review of the clinical and surgical stage of BRONJ, was performed according to SIPMO - 2013 recommendations. Of the 12 patients, 8 cases were stage 1, 3 cases were stage 2 and 1 cases was stage 3. The surgical treatments were: 8 debridements, 3 marginal bony resections and 1 segmental bony resection.

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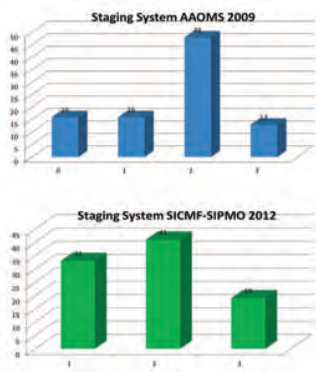
What happens to the BRONJ patients when re-classified according to the novel SICMF-SIPMO recommendations? Our experience



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Background. Since 2009, according to the American Association of Oral and Maxillofacial Surgeons staging system (AAOMS-SS), Bisphosphonate Related Osteonecrosis of the Jaw (BRONJ) has been defined by the presence of bone exposition; in absence of this condition, patients presenting other unspecific clinical and/or radiological signs of disease were classified into the "stage 0". In 2012, the Italian Society of Maxillo-Facial Surgery (SICMF) and the Italian Society of Oral Pathology and Medicine (SIPMO) redefined BRONJ, as an adverse drug event, with several clinical forms (exposed and not-exposed), and updated the staging system, abolishing the stage 0. Aim of this study was to re-classify BRONJ cases in order to define the most adequate managements accordingly.

Method. A retrospective database analysis of BRONJ cases observed at the Sector of Oral Medicine-University of Palermo from 2005 to 2012 was performed. A total of 93 patients (M: 27; F: 66; mean age ± SD 69 ±7yy), previously classified according 2009 AAOMS-SS (stages 0, 1, 2 and 3), were reclassified according 2012 SICMF-SIPMO staging system (SS-SS) [stage 1 (focal); 2 (diffuse) and 3 (complicated)].
Results. In our sample, BRONJ AAOMS staging was the following: "stage 0" 16/93 (17.2%); "stage 1" 16/93 (17.2%); "stage 2" 48/93 (51.6%) and "stage 3" 13/93 (14%). On the basis of the novel SS-SS, distribution of cases were: "stage 1" 33/93 (35.5%); "stage 2" 41/93 (44.1%) and "stage 3" 19/93 (20.4%). Of the 16 cases "stage 0", 6/16 (37.5%) has become "stage 1"; 6/16 (37.5%) "stage 2" and 4/16 (25%) "stage 3", respectively.
Conclusion. After the re-classification, a large quote of BRONJ cases, previously underestimated as stage 0, were properly diagnosed as diffuse-complicated cases. According to our experience, the updated staging system provide important clinical benefits, such as anticipating BRONJ diagnosis, performing therapies earlier and adequate to the correct staging, in order to increase treatment effectiveness.

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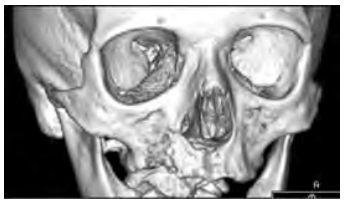
ONJ (osteonecrosis of jaw) in breast cancer patients: effect of preventive measures in a mono institutional experience



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Background. Breast cancer incidence was 114 cases on 100.000/year.
Bone is the most frequent site of metastases (mts) from breast and the presence of Skeletal Related Events (SRE) increases morbidity. The treatment is based on chemotherapy, endocrine therapy, radiotherapy and recently also target therapy agents (trastuzumab, lapatinib, bevacizumab, everolimus). These therapies are frequently associated with antiresorptive agents, such as Bisphosphonates (BPs), including Pamidronate, Zoledronic Acid, Ibandronate, or an anti-RANKL agent, Denosumab. All these agents are able to reduce the risk of SRE and to delay SRE onset. However they are associated with adverse events, including Osteonecrosis of Jaw (ONJ) that can occur in 1.1-9.9 % of breast cancer pts. Preventive (risk reduction) measures before BP and Denosumab treatment (dental visit, dental RX, eventual teeth extractions, dental and denture care) have been recommended.
Materials and methods. We reviewed all breast cancer patients affected by bone mts observed by our team at the Oncology Unit in years 2005-2013. They were classified as: a) Hystoric group (pts already under BP treatment on 2005); b) Prevention group (pts undergoing preventive measures before BP therapy start); c) Screening group (pts treated with BP, not receiving prevention due to several reasons, on years 2006-2013).
Results. We followed 168 pts treated with BPs and/or Denosumab. ONJ was observed in 10/168 pts (5.9%). In the Historic group we observed ONJ in 6/60 pts (10%); in the Screening group in 3/24 pts (12.5%); in the Prevention group in 1/84 (1.2%).
Conclusions. The preventive measures can minimize the rate of ONJ and could potentially reduce the impact on Quality of Life in case of ONJ onset. Breast cancer pts that start BP and Denosumab without pre-treatment assessment (due to clinical emergency, etc.) are at higher ONJ risk. Our experience data reinforce the literature recommendations about implementing preventive protocols.

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