BACKGROUND: The oral cavity is an anatomical structure characterized by the juxtaposition of soft and hard tissues, and is continuously threatened by the external environment and foreign materials. Diseases and disorders caused by oral microorganisms are very common, particularly dental caries, periodontitis and halitosis. Oral diseases can also arise from drugs or antiresorptive-antiangiogenic treatments. Osteonecrosis of the jaw (ONJ) is a complication related to many drugs, notoriously aminobisphosphonate (BP) but also antiresorptives and anti-angiogenetics. Several cases of denosumab-related ONJ have been reported in the literature, and the overall incidence is similar to that for BP-related ONJ. It is known that, concomitant administration of two or more of these drugs increases considerably the risk of onset and severity of ONJ.

We describe a case report of early onset ONJ in oncologic patient treated with denosumab and bevacizumab, with negative anamnesis for BP administration.

METHODS: In March 2015, a 58-year-old female patient was referred to our department for pain and swelling of upper left maxilla. Patient reported the following anamnestic data: in 2010, for the diagnosis of breast cancer, she was underwent to right quadrantectomy surgery and radiant treatment; she was treated with monthly subcutaneous injections of 120 mg denosumab (eight doses from April 2014 to November 2014) and bevacizumab (five doses from August 2014 to November 2014); she had no history head and neck radiotherapy and BP administration. One trigger (local risk factor for ONJ) has been recognized: extractions of maxillary left second premolar and first molar have been performed few months before. Intraoral examination showed a painful area of bone exposure in the left posterior maxilla and erythematous soft tissue with purulent discharge and swelling was detected. After OPT and CBCT scans, bone necrosis was classified as stage II, according to Bedogni et al. Systemic antibiotic (ampicillin/sublactam intramuscularly twice daily for 8 days and metronidazole (off-label use) 250 mg orally twice daily for 8 days), local antiseptics (chlorhexidine 0.2% mouth rinses and 0.5% chlorhexidine gel) were administered. The patient was referred to Oral and Maxillofacial surgery for surgical management.

CONCLUSIONS: Early onset ONJ is more hazardous in oncologic patients, especially in regard to dental aspects, may be established in the future. Further studies are needed to test if the suspension of the administration of drugs could lead to higher percentage of improvement and/or healing in patients treated through Zoledronic acid combined with antiresorptive-antiangiogenic drugs or antiresorptive-antiangiogenic drugs only.
CONCLUSION: Overexpression of NNMT in HSC-2 OSCC cell line significantly increases cell growth. The effect on the antiapoptotic survivin ΔEx3 isoform seems to suggest a possible involvement of NNMT in the proliferation and tumorigenic capacity of OSCC cells.

Prognostic value of mitochondrial DNA analysis in patients with secondary oral squamous cell carcinoma

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BACKGROUND: In head and neck oncology a novel classification of the secondary tumors was recently proposed on the basis of the mucosal phylogenetically related, suggesting a genetically altered mucosal field. Second neoplastic lesions can be classified as: Second Primary Tumors (SPTs) independent from the index tumor at the molecular level, Local Recurrences (LRs) or metastases that are instead related to the primary tumor and "second field-tumors" (SFTs), derived from the same genetically altered mucosal field as the primary tumor. The distinction between LR, SPT and SFT is not a simply problem of classification but may influence prognosis and the choice of treatment. mtDNA (D-loop) sequence analysis was proposed in previous studies as a reliable method for establishing the clonal relationship between two neoplastic manifestations. In the present study mtDNA D-loop analysis was applied in a group of consecutive patients experiencing a second loco-regional neoplastic manifestation after surgical resection of a primary Oral Squamous Cell Carcinoma (OSCC). The purpose was to evaluate differences in terms of survival rate between LRs, SPTs and SFTs.

METHODS: The study population consisted of 24 patients who experienced a second neoplastic lesion after a surgical resection of a primary OSCC. 21/24 (87.5%) were limited to the oral cavity whereas 3/24 (12.5%) presented a neck lymph node metastasis (LMN) as secondary event. mtDNA D-loop analysis was performed by deep sequencing and phylogenetic clusterization in all index OSCCs, in all secondary events and in respective normal mucosa. Disease-free survival endpoints was defined as the duration between the appearance of second neoplastic lesion and dead of disease or last follow-up visit.

RESULTS: mtDNA analysis showed 7/24 second neoplastic events (31.1%) phylogenetically related to index OSCC, and 17/24 cases (68.9%) phylogenetically independent. The genetic distinction of secondary tumours in LR, SPT and SFT was acquired on the basis of the phylogenetic relationship between normal mucosa of index OSCC and normal mucosa of secondary OSCC. All 7 clonal paired tumours showed respective normal mucosa phylogenetically related, suggesting a genetic diagnosis of LR. Among non clonal patients 3 out of 17 presented respective normal mucosa phylogenetically related, suggesting a genetic diagnosis of SPT whereas in remaining 14 out of 17 non clonal paired lesions also the respective normal mucosa resulted phylogenetically distant entities suggesting the presence of an altered mucosal field and a genetic diagnosis of SFT. The presence of an altered mucosal field in non clonal patients resulted a variable significantly related with a better survival rate (p<.05), indeed 2/17 (11.8%) SFTs events failed as compared to 5/7 LR, (71.4%) and 3/3 SPTs (100%).