Review of: "Italian Position Paper (SIPMO-SICMF) on Medication-Related Osteonecrosis of the Jaw (MRONJ)"

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The Italian Position Paper provided by the SIPMO and the SICMF on Medication-Related Osteonecrosis of the Jaw (MRONJ) gives a comprehensive overview on the current literature on disease classification, diagnostics and therapy. The Reviewer supports the main aspects of the position paper. Some minor points can be discussed:

Introduction

The introduction gives a good overview of the emergence of MRONJ as a new disease associated with the increasing use of antiresorptive agents. However, the chronologic development of understanding MRONJ initially as “Bisphosphonate related osteonecrosis”, later as “Antiresorptive related osteonecrosis” including the RANKL antibody Denosumab and finally as “Medication related osteonecrosis of the jaw” (MRONJ) could be explained more precise by the authors.

Regarding the Epidemiology section the Reviewer considers it as critical to state a “limited expected survival” for patients with metastatic disease or Multiple Myeloma. Modern oncologic treatment including Bisphosphonates can enable long “survival times” for these patients turning the malignant disease into a chronic condition.

MRONJ diagnosis

The authors of the SIPMO-SICMF Position Paper give a good overview of the diagnostic measures for MRONJ. However, it can be made clearer that the key clinical symptom is the exposure of bone, presence of fistula or local infection.

According to the Reviewer, it is not necessary to screen for MRONJ using any aperitive diagnostics including 3D x-ray. MRONJ screening should be performed using clinical examinations with thorough dental examination including orthopantomograms. 3D-imaging is applied if there is a clinical suspicion for MRONJ and therapy is planned.

As therapy of MRONJ is mainly based on clinical parameters, the Reviewer supports the AAOMS staging system. The SIPMO-SICMF staging is a viable alternative for MRONJ staging that should be internationally accepted.

Risk factors

Tyrosine kinase inhibitors and mTOR inhibitors should not be subsumed under antiangiogenetic agents as it is performed by the SIPMO-SICMF Position Paper authors.

Dental Management

The Reviewer agrees that implant placement in patients with malignant disease and high potency intravenous Bisphosphonate treatment is very critical. However, it is difficult to formulate a general contraindication. The German treatment guideline is less strict in this regard and is weighing the risk of the prosthesis pressure points against the risk of implantation [1].

Surgical Management of MRONJ

Generally, the Reviewer agrees with the presented treatment algorithm. However, the stage-related surgical algorithm of MRONJ treatment presented in Table 7 differs from the clinical concept that is applied by the Maxillofacial Surgery Department of the Reviewer: In cases of clinically apparent MRONJ (exposed bone over 8 weeks) [2] the following procedure is favored by the Reviewer: Surgical exposure of the necrotic bone, freshening of the wound edges in the area of fistulas or exposed bone, careful local removal of sequestrated or avascular bone until sufficient bleeding is visible. Thorough soft tissue closure applying local soft tissue flaps and using resorbable stiches [3].

As MRONJ needs to be considered a condition that is affecting the whole jaw bone, a segmental resection and reconstruction, as it is suggested as standard therapy in Stage 2 diffuse ONJ in the SIPMO-SICMF Position Paper, should be avoided if possible according to the Reviewer. Segmental resections, especially involving the continuity of the mandible, should only be applied if no local surgical treatment option is feasible.

The authors of the SIPMO-SICMF Position Paper could be more precise regarding their recommendation on “segmental resection + bone reconstruction when indicated”. Which kind of reconstructions are suggested for which kinds of defects? The Reviewer favors microvascular reconstruction using free fibula flaps if bone continuity has to be discontinued and the paitient is suitable for this procedure.

Additionally, the Reviewer disagrees on the necessity to distinguish in the treatment algorithm depending on the antiresorptive agent (Bisphosphonates vs. Denosumab) and on the underlaying disease (malignant disease vs. osteoporosis). Of course, it is understood that the different underlaying diseases influence the risk of osteonecrosis development. However, in the clinical practice, according to the Reviewer, the treatment of MRONJ is only depending on the clinical extend of the necrosis. To better assess the clinical extend of necrosis, the analysis of preoperative CT scans is helpful.

A further aspect that could be discussed by the authors of the SIPMO-SICMF Position Paper is the postoperative use of nasogastric feeding tubes. According to the Reviewer, it is a clinically helpful measure to apply a nasogastric feeding tube for 5 days to facilitate initial would healing.

Aftercare

The authors of the SIPMO-SICMF Position Paper could include further recommendations on the prevention and aftercare of patients receiving antiresorptive or antiangiogenetic treatment or that have already presented with MRONJ [4].

Literature

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