Bevacizumab-induced osteonecrosis of the jaw: A cause of concern

Sir,

Currently, skeletal related events (SREs) include pathologic fractures, spinal cord compression, hypercalcemia, and severe bone pain is common with multiple myeloma, breast, prostate and lung malignancy. SREs are treated with bisphosphonates (BPs) widely, and 1–18% patients have been reported with osteonecrosis that is called as BPs related osteonecrosis of the jaw (BRONJ).[1] Except BPs other recently reported pharmacological agents associated with osteonecrosis of the jaw (ONJ) are denosumab and bevacizumab. The antiangiogenic effects of BPs are of particular interest in regard to ONJ, due to the importance of neo-vascularization in wound healing. Dental extraction, bone invasive surgeries and mucosal trauma are risk factors for ONJ, healing after which requires the revascularization. It is possible that the interruption of the normal healing process increases the risk for ONJ. Angiogenesis and ONJ have also been linked by the case reports of ONJ occurring in patients treated with antitumor therapies targeting vascular endothelial growth factor (VEGF). Guarneri *et al*. provided an excellent presentation of the ONJ in patients treated with bevacizumab or sunitinib and the rationale for performing their analysis of bevacizumab in patients with locally recurrent or metastatic breast cancer (MBC).[2]

Vascular endothelial growth factor A is a potent proangiogenic growth factor that stimulates the proliferation, migration, and survival of endothelial cells. VEGF-A is one of the important proteins that is also expressed by tumor cells and is an important target of anticancer therapy.[3] Bevacizumab is a humanized anti-VEGF-A monoclonal IgG1 antibody (molecular weight, 149 kDa).[4] In combination with chemotherapy, it is approved for the treatment of advanced colorectal cancer, advanced nonsmall cell lung cancer, MBC and advanced renal cell cancer.[4] As a single agent, it can be used for second-line treatment of advanced glioblastoma multiforme. Further studies are being conducted in other solid tumors as well, indicative of the potential therapeutic benefit of bevacizumab in combination anticancer therapy.[5]

The overall incidence of ONJ with bevacizumab was 0.3% in the blinded phase of the two randomized trials and 0.4% in the single-arm study. There was trend toward increased ONJ incidence in patients who received BP therapy versus those with no BP exposure (0.9% vs. 0.2%, respectively, in

the pooled analysis of the randomized trials; 2.4% vs. 0%, respectively, in ATHENA). The 0.9–2.4% incidence seen in BP-exposed patients receiving bevacizumab is within the 1–6% range reported for BPs alone. Good oral hygiene, dental examination, and avoidance of invasive dental procedures remain important in patients receiving BPs, irrespective of bevacizumab administration.[5]

Osteonecrosis of the jaw is a serious complication in oncology setting, affecting patients who are already suffering from malignancy, gives the greater importance to critically evaluate patient's oral cavity with status of the dentition. If any treatment is needed, it should be according to risk-benefit ratio. Clear guidelines should be followed to critically evaluate the patient by proper history. Proper oral hygiene maintenance instruction, thorough dental evaluation and antibiotic prophylaxis should be practiced in patients receiving BPs to avoid BRONJ.

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