

The Role of Bevacizumab in the Management of Head and Neck Squamous Cell Carcinoma Patients

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Introduction

Angiogenesis is a crucial step in tumor growth and metastasis. Clinical association of tumor vascularity with tumor aggressiveness has been clearly demonstrated in a wide variety of tumor types including head and neck squamous cell carcinoma (HNSCC) [1]. Thus, determination of microvessel density in tumor tissue can be useful in estimation of prognosis. Inhibition of angiogenesis can repress the growth rate of tumor cells, and also induce apoptosis due to reduced nutrition and oxygen supply to the tumors. Vascular endothelial growth factor (VEGF), which is a major element for many angiogenic processes, binds VEGF receptor (VEGFR) to stimulate endothelial cell proliferation and migration [2,3]. Thus, determination of microvessel density in tumor tissue can be useful as a predictive factor for the effectiveness of bevacizumab in chemoradiotherapeutic strategies.

The Role of Bevacizumab in Treatment by Chemoradiotherapy in HNSCC

The humanized monoclonal antibody bevacizumab binds VEGF preventing VEGF from binding to VEGFR; as a result, bevacizumab exhibits an antitumor effect. Although bevacizumab alone has only a modest anti-tumor effect, various studies have reported the efficacy of combination bevacizumab and chemoradiotherapy [4,5].

The Role of Bevacizumab in Treatment for Radiation Necrosis in HNSCC

Radionecrosis is a major complication of radiotherapy. Although its incidence is small at approximately 1% [6,7]. It is predicted to increase with increasing use of concomitant chemoradiotherapy. The clinical manifestation of radionecrosis of HNSCC patients, includes hoarseness of voice, difficulty with oral intake, pharyngeal pain, dyspnea owing to mucosal edema, skin fistula, and more. Recently, one possible mechanism of its pathogenesis is thought to be the role of VEGF. Although classically characterized as an angiogenic factor, VEGF also potentiates capillary permeability [8]. Nonoguchi et al. showed overexpression of VEGF in resected radiation necrosis lesions [9]. Furthermore, degree of radiation injury has been correlated with amount of VEGF expression [10]. Moreover, Levin et al. indicated that bevacizumab is a treatment option in patients who suffer from radiation necrosis secondary to treatment of head, neck and brain cancers [11]. We previously reported a case of a 67-year-old Japanese man who presented with a condition extremely difficult to diagnose differentially as radionecrosis or tumor recurrence after chemoradiotherapy for hypopharyngeal cancer [12]. Although tumor recurrence was suspected from clinical conditions and computed

tomography findings, pathological analysis revealed no evidence of tumor recurrence, and successful therapy with steroids and antibiotics reduced the mucosa edema. Bevacizumab may be considered a treatment option of radiation necrosis in cases of unsuccessful therapy with steroids and antibiotics, and appropriate medical imaging studies, including MRI and PET scans are not helpful in excluding tumor recurrence.

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