head and neck cancer

INDUCTION OF CD44 VARIANT 9-EXPRESSING CANCER STEM CELLS ATTENUATES THE EFFICACY OF CHEMORADIOSELECTION AND WORSENS THE PROGNOSIS OF PATIENTS WITH ADVANCED HEAD AND NECK CANCER

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Aim: At our institute, a chemoradioselection strategy has been used to select patients for organ preservation on the basis of response to an initial 30-40 Gy concurrent chemoradiotherapy (CCRT). Patients with a favorable response (i.e., chemoradioselected; CRS) have demonstrated better outcomes than those with an unfavorable response (i.e., nonchemoradioselected; N-CRS). Successful targeting of molecules that attenuate the efficacy of chemoradioselection may improve results. Thus, the aim of this study was to evaluate the association of a novel cancer stem cell (CSC) marker, CD44 variant 9 (CD44v9), with cellular refractoriness to chemoradioselection in advanced head and neck squamous cell carcinoma (HNSCC).

Methods: Through a medical chart search, 102 patients with advanced HNSCC treated with chemoradioselection from 1997 to 2008 were enrolled. According to our algorithm, 30 patients were CRS following induction CCRT and 72 patients were N-CRS. Using the conventional immunohistochemical technique, biopsy specimens and surgically removed tumor specimens were immunostained with the anti-CD44v9 specific antibodies.

Results: The intrinsic expression levels of CD44v9 in the biopsy specimens did not correlate with the chemoradioselection and patient survival. However, in N-CRS patients, the CD44v9-positive group demonstrated significantly (p = 0.008) worse prognosis, than the CD44v9-negative group. Multivariate analyses demonstrated that among 5 candidate factors (T, N, stage, response to CCRT, and CD44v9), CD44v9 positivity alone was significantly correlated with the poor prognosis (HR: 3.140, 95% CI: 1.230-8.017, p = 0.0167). Furthermore, the survival rate of the CD44v9-induced group was significantly (p = 0.04) worse than the CD44v9-non-induced group.

Conclusions: CRT-induced CD44v9-expressing CSCs appear to be a major hurdle to chemoradioselection. The addition of an xCT (a coupling molecule of CD44v9) inhibitor (e.g., sulfasalazine) to chemoradioselection may provide a new approach for clinically feasible CSC-targeted therapy in HNSCC, improving the efficacy of chemoradioselection and consequent organ preservation and survival.

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