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食道癌における術前血清中 IL-1β・IL-6 の予後因子としての意義と展望

(Preoperative high levels of IL-1ß and IL-6 are significant poor prognostic factors in patients with esophageal cancer)

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Abstract

Recent studies have indicated that the Th1/Th2 balance of the immune system in patients with malignant tumors is important in relation to the tumor invasion and the patients' clinical prognosis. We evaluated various cytokines in patients with esophageal cancers to elucidate the relationship between the Th1/Th2 balance and the patients' prognosis.

Various serum cytokines of preoperative 98 patients, who subsequently underwent radical esophagectomy in our institute between September 2005 and December 2006, were quantitatively measured by Cytometric Bead Array (CBA) system. The cytokines include Th1/Th2 balance related 14 cytokines—IL-1α, IL-1ß, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12p70, IL-13, IL-17A, INFγ and IgE. Multivariable analysis was performed using the Cox proportional hazard model. The survival rates based on CRP values were analyzed by the Kaplan-Meier method. Eight clinical pathological factors of the tumors, which are regarded as relevant prognostic factors —diameter, histological type, invasion type, vascular invasion, venous invasion, depth of the invation (T factor), regional lymph nodal status (N factor) and intramural metastasis (IM)— and the 14 cytokines were evaluated by the multivariable analysis.

The multivariable analysis showed that T factors ($p = 0.001$), N factors ($p = 0.002$), IL-1ß ($p = 0.003$) and IL-6 ($p = 0.021$) were significantly related to the worse prognosis. The two cytokines are known as inflammatory cytokines and they theoretically induce the production of acute inflammatory proteins, including C-reactive protein (CRP). We hereby evaluated the preoperative serum CRP values of the same patients. By means of ROC analysis (Youden index), the cut off value of the serum CRP was determined as 0.25 mg/dl and the survival rates were analyzed by the Kaplan-Meier method. The high CRP group (CRP≧0.25 mg/dl) showed significantly poorer prognosis than low CRP group (<0.25 mg/dl) ($p = 0.027$; Log-rank test).

Out study showed that the inflammatory cytokines, IL-1ß and IL-6, are significant prognostic factors of the patients with esophageal cancers and the Th1/Th2 balance in the patients of poorer prognosis may be shifted toward Th2-dominant side.