Analysis of the correlation between HLA phenotype and prognosis of non-small cell lung cancer patients in Japan

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Background: Lung cancer is one of the most common malignant disease and its incidence and mortality continue to increase worldwide. The prognosis for patients with non-small cell lung cancer (NSCLC) remains extremely poor, thus the analysis of genetic and epigenetic alterations in the pathogenesis of lung cancer has extensively researched recently. The present study was undertaken to investigate the correlation between HLA phenotype and the prognosis of patients with NSCLC.

Methods: We reviewed the medical records of 695 NSCLC patients who underwent surgical resection from January 1996 to December 2005 at University of Occupational and Environmental Health and Kitakyushu municipal medical center. Serological typing of HLA class I was performed using a microcytotoxicity test of lymphocytes or PCR-sequence-specific oligonucleotides (PCR-SSO). The correlation between HLA phenotypes and clinicopathological features was analyzed. The survival curves were calculated by the Kaplan-Meier method, and then the comparison of the survival curves was carried out using Log-rank test. Multivariate analysis was performed by Cox’s proportional hazard model.

Results: The frequency of HLA-A11 in patients with NSCLC was higher, whereas the frequencies of B13 and B51 were lower as compared with the control population of each HLA phenotype. The 3-year and 5-year overall survival rate of the 695 patients underwent complete resection was 71.1% and 64.9%. The 3-year and 5-year disease free survival rate (DFI) of entire patients was 62.4% and 54.4%. The correlation between the prognosis (overall survival or DFI) and each HLA class I phenotype was analyzed in these patients. The 5-year overall survival rate was 73.6% in HLA-A2 positive patients (A2(+) (n=156) and 83.0% in HLA-A2 negative patients (A2(-) (n=249) at stage I. The 5-year DFI was 65.7% in A2(+) and 75.4% in A2(-) at stage I. HLA-A2(+) group at stage I showed the unfavorable prognosis significantly than A2(-) group both in overall survival (p < 0.05) and DFI (p < 0.05). The 5-year overall survival rate was 38.8% in A24(+) (n=181) and 56.8% in A24(-) (n=109) at stage II and III. Although there was no significant difference at stage I between HLA-A24(+) and HLA-A24(-) groups, HLA-A24(+) group at stage II and III showed poorer prognosis than HLA-A24(-) group in overall survival significantly (p = 0.01). Multivariate analysis was demonstrated that HLA-A2 was the independent unfavorable factor that affected overall survival.

Conclusions: Expression of HLA-A2 was considered as one of the unfavorable prognostic factors in NSCLC patients at stage I. HLA-A24(+) group also showed significant unfavorable prognosis at stage II and III. These results suggested that HLA-A2 and HLA-A24 were the prognostic factors in NSCLC patients.