Pathological Significance of HuR Expression in Bladder Cancer: Correlation with Cell Proliferation and Angiogenesis

Introduction and Objective: The control of mRNA stability is an important mechanism controlling gene expression. HuR is well-known to regulate stability of m-RNA and it is reported to regulate cell proliferation and angiogenesis in various pathological. Actually, there were several reports that HuR expression positively associated with malignant aggressiveness and served as a prognostic factor of poor clinical outcome. However, clinical and pathological significance of HuR in patients with bladder cancer is still unclear. The main objective is to clear its clinical significance, and prognostic roles, and predictive value for survival in patients with bladder cancer. In addition, we also investigated relationships between its expression and cancer cell proliferation and angiogenesis.
Materials and Methods: All expressions were examined by immunohistochemical technique in 122 formalin-fixed specimens. HuR expression was evaluated in cytoplasmic and nuclear staining separately. Cell proliferation, angiogenesis and lymphangiogenesis were measured by percent of Ki-67-positive cell (proliferation index, PI) and CD34-stained vessels (Microvessel density, MVD).
Results: In normal urothelial cells, 90% (18/20) were judged as high nuclear expression, in contrast, only 5% was judged as high cytoplasmic expression. On the other hand, in bladder cancer cells, 88 (72.1%) and 31 specimens (25.4%) showed high expression of nucleus and cytoplasm, respectively. Nuclear HuR expression bears no significant relation to pathological features; however, cytoplasmic HuR expression was positively associated with pT stage and grade ($p<0.001$). Cytoplasmic HuR expression also correlated to PI and MVD. High expression of HuR in cytoplasm is significant predictor for metastasis and cause-specific survival, and it was identified as a prognostic correlative factor for metastasis (hazard ratio = 4.75, 95% CI = 1.78 – 12.75, $P = 0.028$) in multivariate analysis model including pathological features.
Conclusions: Our results demonstrated that cytoplasmic HuR was speculated to play important roles of cell proliferation, progression, and survival of bladder cancer patients. In addition, these pathological roles are regulated by angiogenesis.