Centers of Advanced Medicine
Center for Medical Science of Fatigue

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General Summary

The Jikei Center for Medical Science of Fatigue (JCMSF) was established in 2014 with support from the Ministry of Education, Culture, Sports, Science and Technology-Supported Program for the Strategic Research Foundation at Private Universities. The JCMSF is aimed at contributing to human welfare through developing novel methods for the diagnosis, prevention, and care of fatigue-related diseases. For this aim, our research focuses on the mechanisms of fatigue and fatigue-related diseases.

Resulting from stress or insomnia — whether related to work or not — fatigue is something that everyone experiences. Long-term fatigue can cause cardiovascular dysfunction, such mental disorders as depression, and occupational sudden death (*karoshi*). Fatigue is, therefore, a major social problem. Physiological fatigue can be recovered from with rest. In contrast, pathological fatigue persists for 3 months or more and greatly affects quality of life. Because pathological fatigue requires therapeutic interventions, it must be distinguished from physiological fatigue. Levels of human herpesvirus (HHV)-6 and HHV-7 DNA in saliva increase with training and decrease with rest, suggesting their usefulness as biomarkers of physiological fatigue and cancer-related fatigue (CRF).

Research Activities

Clinical significance of CRF in patients with multiple myeloma

An adverse event in patients with multiple myeloma — treated with cytotoxic agents, proteasome inhibitors, and such immunomodulatory drugs as bortezomib, lenalidomide, and thalidomide — is CRF. The aims of our study were to prospectively analyze the clinical significance of CRF and to evaluate the cumulative incidence of CRF and the survival rates of 16 patients with multiple myeloma who were treated with proteasome inhibitors and immunomodulatory drugs. Reactivation of salivary HHV-6 and HHV-7 was analyzed with the real-time quantitative polymerase chain reaction. The CRF was evaluated with a visual analog scale. The subjects of this study were 11 patients with newly diagnosed multiple myeloma and 5 patients with relapsed or refractory multiple myeloma. The cumulative incidence of CRF was 54.9%. The incidence of CRF was not associated with the type of treatment. The cumulative incidence of reactivation for HHV-6 was 73.1% and for HHV-7 was 45.6%. However, the reactivation of HHV-6 and HHV-7 was not related to CRF. Overall survival and progression-free survival among patients with newly diagnosed multiple myeloma were significantly shorter for those with CRF than for those without CRF. In conclusion, CRF is a major symptom in patients with multiple myeloma and predicts shorter overall survival and progression-free survival in patients with a new diagnosis.

Attenuation of human herpesvirus 6B reactivation by aging

Objective: Little research has evaluated HHV-6B infection in healthy adults, and the prevalence rates in different age groups have remained unclear. Therefore, the major objectives of this study were to evaluate the seroprevalence of HHV-6 antibodies in working people and to examine the effect of aging on seroprevalence. Also, because HHV-6B is reactivated in saliva, another objective was to investigate an association between age and HHV-6B reactivation based on measured salivary levels of HHV-6 DNA.

Methods: Our subjects were 77 ordinary office workers who underwent a health checkup. In this population, we measured anti-HHV-6 antibody titers with enzyme-linked immunosorbent assay and measured salivary HHV-6 DNA levels. In addition to examining an association with age, we examined associations with body mass index, smoking habit, and alcohol consumption as confounding factors.

Results: The seropositivity of HHV-6 antibodies decreased significantly in subjects 50 years and older, and age was significantly negatively correlated with anti-HHV-6 antibody titers. Age and salivary HHV-6 DNA levels were also significantly negatively correlated, but no significant correlations with other factors was found.

Conclusions: Our results suggest that HHV-6B reactivation is attenuated by aging. Thus, HHV-6 antibodies steadily decrease in the body with aging.