Altered Host Immunity, Human T Lymphotropic Virus Type I Replication, and Risk of Adult T-Cell Leukemia/Lymphoma: A Prospective Analysis from the ATL Cohort Consortium

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MEETING ABSTRACT Open Access

Altered host immunity, human T lymphotropic virus type I replication, and risk of adult T-cell leukemia/lymphoma: a prospective analysis from the ATL Cohort Consortium

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Background

Adult T-cell leukemia/lymphoma (ATL) is a rare and often fatal outcome of infection with human T-lymphotropic virus type I (HTLV-I). Altered host immunity in HTLV-I carriers has been postulated as a risk factor for ATL, but is not well understood.

Methods

We prospectively examined well-validated serologic markers of HTLV-I pathogenesis and host immunity in 53 incident ATL cases and 150 carefully matched asymptomatic HTLV-I carriers from eight population-based studies in Japan, Jamaica, the United States and Brazil. We used multivariable conditional logistic regression, conditioned on the matching factors (cohort/race, age, sex, and sample collection year), to evaluate the biomarkers' associations with ATL in all subjects and by years (≤5, >5) from blood draw to ATL diagnosis.

Results

In the pooled population, above-median soluble interleukin-2-receptor-alpha levels (sIL2R, v. ≤ median; odds ratio (OR), 95% confidence interval (CI)=4.08, 1.47-11.29) and anti-Tax seropositivity (anti-Tax; OR, 95% CI=2.97, 1.15-7.67), which indicate T cell activation and HTLV-I replication, respectively, were independently associated with an increased ATL risk. Above-median total immunoglobulin E levels (v. ≤ median; OR, 95% CI=0.45, 0.19-1.06), which indicate type 2 (B cell) activation, predicted a lower ATL risk. The sIL2R and anti-Tax associations with ATL were stronger in samples collected ≤5 years pre-diagnosis.

Conclusions

The biomarker profile predictive of ATL risk suggests a role for heightened T cell activation and HTLV-I replication and diminished type 2 immunity in the etiology of ATL in HTLV-I carriers. Translation of these findings to clinical risk prediction or early ATL detection requires further investigation.

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