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CORRESPONDENCE

Not All Aggressive Adult T-Cell Leukemia/Lymphoma Subtypes Are Created Equal

TO THE EDITOR: In a recent article, Katsuya et al[1] presented what is probably the largest study to evaluate prognostic factors in patients with adult T-cell leukemia/lymphoma (ATLL) to date; the study included more than 800 patients. The proposed prognostic index (PI), called ATL-PI by the authors, consists of five adverse variables: stage III/IV, Eastern Cooperative Oncology Group performance status 0-1, age > 70 years, serum albumin level < 3.5 g/dL, and soluble interleukin-2 receptor level > 20,000 U/mL. According to the risk category, patients with high-, intermediate-, and low-risk disease experienced a median overall survival time of 4.6, 7, and 16.2 months, respectively.

ATLL is a rare type of peripheral T-cell lymphoma (PTCL) that develops in individuals with a chronic infection by the human T-lymphotrophic virus type I. The epidemiology of ATLL, not surprisingly, mimics that of human T-lymphotrophic virus type I and affects individuals living in specific geographic regions such as Japan, the Caribbean, Central and South America, Northern Africa, and the Middle East. Clinically, ATLL has at least four variants: acute (leukemic), lymphomatous, smoldering, and chronic. Classically, the acute and lymphomatous subtypes have been associated with a worse prognosis.

However, there are specific distinctions between the acute and lymphomatous subtypes of ATLL. First, few studies have shown genetic and pathophysiologic heterogeneity within the aggressive variants of ATLL. Oshiro et al[2] performed comparative genomic hybridization and polymerase chain reaction studies in 17 patients with acute ATLL and 49 patients with lymphomatous ATLL; gains were demonstrated at chromosomes 1, 2, 4, and 7 and losses were shown at chromosomes 10, 13, 16, and 18 in acute ATLL, whereas lymphomatous ATLL showed gains at chromosome 3. In a study by Nakagawa et al,[3] patients with a diagnosis of PTCL, unspecified, who carried genomic instability had shared genetic features (identified by comparative genomic hybridization) and similar survival rates compared with patients with lymphomatous ATLL. Second, according to the Shimoyama classification, acute ATLL is characterized by a predominant leukemic component, whereas lymphomatous ATLL presents mainly with lymphadenopathy without lymphocytosis; this represents a clinical difference.[4] Third, with regard to therapy, a patient-level meta-analysis that included more than 200 patients showed that only leukemic ATLL benefits from zidovudine and interferon therapy.[5] Finally, several studies have also shown that the survival time varies between ATLL subtypes; acute ATLL has a shorter median overall survival than lymphomatous ATLL.[5-7]

In a recent study,[6] we were able to demonstrate that acute and lymphomatous ATLL had distinct, almost exclusive, prognostic factors. Our study included 81 patients with aggressive ATLL, and in a multivariate analysis we could identify that low albumin levels and the presence of B symptoms were adverse prognostic factors in lymphomatous ATLL, whereas high β_2-microglobulin was adverse in acute ATLL. Furthermore, in a study from the International PTCL Project that included 126 patients with ATLL, the International Prognostic Index was a predictor of survival only in lymphomatous but not in acute ATLL.[8] A study from Japan also found almost exclusive prognostic factors for acute and lymphomatous ATLL, although with a smaller sample.[9]

In conclusion, we believe that there are biologic, genomic, molecular, and clinical differences between acute and lymphomatous ATLL that could also be reflected in distinct prognostic factors and survival. It would have been of extreme interest to evaluate the ATL-PI separately for patients with acute versus lymphomatous ATLL.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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