Journal of clinical and experimental hematopathology
Vol. 57 No.3, 85-86, 2017

Highlights: Focus on T/NK-Cell Lymphoma

Commentary

Topics on the molecular pathogenesis and therapeutic approaches for T/NK-cell lymphoma

Motoko Yamaguchi

Keywords: T-cell lymphoma, NK/T-cell lymphoma

T/NK-cell lymphoma is a heterogeneous group of lymphomas characterized by distinct clinicopathological and molecular features. In the revised fourth edition of the World Health Organization (WHO) classification of lymphoma, approximately 30 disease entities of mature T/NK-cell lymphoma are listed.[1] The frequency of some T/NK-cell lymphoma entities varies geographically, with high incidences of extranodal NK/T-cell lymphoma, nasal type (ENKL) in East Asia and Latin America, and adult T-cell leukemia/lymphoma (ATL) in southwestern Japan. Next-generation sequencing has facilitated the discovery of novel genomic abnormalities in T/NK-cell lymphomas, and new treatment approaches targeting disease-specific molecular abnormalities have improved the prognosis of patients with some T/NK-cell lymphomas. This issue of the Journal of Clinical and Experimental Hematopathology contains four review articles on T/NK-cell lymphoma by experts in Japan.

Katsuya and Ishitsuka summarized their continuous work on developing prognostic models for ATL, and reviewed treatment approaches for ATL including the use of new agents.[2] Their recent work highlighted the potential risk of disease progression in patients with chronic and smoldering types of ATL.[3] Multidisciplinary treatment approaches, including antiviral therapy, chemotherapy with or without new agents and hematopoietic stem cell transplantation, are being evaluated for improved disease control of ATL.

Miyazaki and I reviewed pretreatment evaluation and treatments for ENKL, including the current treatment strategies in Japan.[4] There is considerable geographic variation in treatment approaches for ENKL. Next-generation therapies, such as concurrent chemoradiotherapy or L-asparaginase-containing chemotherapy, have improved the prognosis in patients with localized ENKL,[5] but there are unmet medical needs for patients with advanced or relapsed/refractory disease.

Fujisawa, Sakata-Yanagumoto and Chiba reviewed genetic features and treatments of angioimmunoblastic T-cell lymphoma (AITL).[6] In the revised fourth version of the WHO classification, AITL has been categorized in nodal lymphomas of follicular helper T-cell-origin. Next generation sequencing revealed recurrent mutations of *TET2*, *IDH2*, *DNMT3A* and *RHOA* in AITL,[7] and some of these gene mutations are also found in other hematological malignancies and solid cancers. According to the progress in the molecular understanding of AITL, the development of molecular-targeting treatment strategies for AITL just beginning.

Tsuyama, Takeuchi and colleagues provided a detailed review of the history, pathogenesis, clinical features, and treatments for anaplastic large cell lymphoma (ALCL).[8] ALCL is characterized by CD30 expression in tumor cells and is divided into two subtypes, ALK-positive and ALK-negative ALCL. ALK is well known as a molecular target in the treatment of non-small cell lung cancer,[9] and ALK inhibitors have been introduced in the treatment algorithm for lung cancer. Many clinical trials of ALK inhibitors, such as crizotinib, ceritinib and alectinib, for ALCL are ongoing.

I believe you will find this review series focused on T/NK-cell lymphomas informative and relevant.

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Department of Hematology and Oncology, Mie University Graduate School of Medicine, Tsu, Japan
Corresponding author: Motoko Yamaguchi, M.D., Ph.D., Department of Hematology and Oncology, Mie University Graduate School of Medicine 2-174 Edobashi, Tsu, Mie 514-8507, Japan. E-mail: myamaguchi@clin.medic.mie-u.ac.jp

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