Int J Hematol (2014) 99:217–218
DOI 10.1007/s12185-014-1526-x

Guest Editorial: peripheral T-cell lymphomas: progress is not "peripheral", but "central"

Masaki Yasukawa

Received: 23 January 2014 / Accepted: 26 January 2014 / Published online: 7 February 2014

Peripheral T-cell lymphomas (PTCLs) are heterogeneous neoplasms of mature T cells and represent 10–15 % of all lymphoid malignancies. In the 1970s, when it was first realized that non-Hodgkin lymphoma cells were derived from either T cells, B cells, or NK cells, T-cell lymphomas were recognized as a separate clinicopathological entity of lymphoid malignancies. Although various methodologies for the classification of lymphomas have been developed, PTCLs have been often regarded as "orphan diseases", reflecting the difficulties encountered in their classification, diagnosis, and treatment.

Understanding the immune system is helpful in categorizing T-cell malignancies. The innate immune system including NK cells and γδ T cells plays an important role in defense against the microbes. Extranodal NK/T-cell lymphoma, nasal type, is an aggressive disease, often with destructive midline lesions. Most cases of this disease are NK-cell-derived. Normal γδ T cells in the spleen, thymus, and intestinal epithelia express Vγ1. Hepatosplenic T-cell lymphoma shows preferential expression of Vγ1, suggesting that this lymphoma is derived from normal splenic γδ T cells. On the other hand, the adaptive immune system, also known as the acquired immune system, is composed of highly specialized immune cells. This system is highly adaptable because of the rearrangement of T-cell receptor genes. Effector T cells include various kinds of T cells, and functional counterparts of these T-cell subsets have been recognized among the PTCLs.

M. Yasukawa (✉)
Department of Hematology, Clinical Immunology, and Infectious Diseases, Ehime University Graduate School of Medicine, Toon, Ehime 791-0295, Japan
e-mail: yasukawa@m.ehime-u.ac.jp

One of the characteristics of PTCLs is the different geographic distribution. For example, adult T-cell leukemia/lymphoma (ATLL) is most prevalent in Japan and the Caribbean basin, and EB virus-related extranodal NK/T-cell lymphoma of the nasal type is most prevalent in Hong Kong and Central America. On the other hand, angioimmunoblastic T-cell lymphoma (AITL) and enteropathy-associated T-cell lymphoma are overrepresented in Europe. Since the causes for the different geographic distributions of T-cell lymphomas are only partially understood, the epidemiology of this malignancy is an interesting issue.

PTCLs have traditionally been treated much like diffuse large B-cell lymphomas. A large meta-analysis of the patients with PTCLs treated with CHOP or CHOP-like regimens reported the significantly inferior outcomes compared to patients with B-cell lymphomas. Recently, new agents have gained regulatory approval for the treatment of relapsed/refractory cutaneous T-cell lymphoma and PTCLs. These new agents, together with recent advances in both combination chemotherapy and transplant strategies, promise to improve the outcome of PTCLs.

The 4th Japanese Society of Hematology International Symposium was held on May 24 and 25, 2013, in Matsuyama city, Japan. In this symposium, 9 invited speakers presented and discussed recent advances relating to the pathogenesis, classification, and treatment of PTCLs. This issue includes four excellent review articles focusing on PTCLs written by the guest speakers of the 4th Japanese Society of Hematology International Symposium.

Piccaluga, Tabanelli, and Pileri review the molecular genetics of PTCLs based on their own study and data from the literature [1]. Recent high-throughput technologies have contributed to a detailed understanding of the molecular pathogenesis of malignancies. In particular, gene expression profiling has clarified the borders between the

various kinds of PTCLs. Besides improving the diagnosis of lymphomas, molecular studies have provided the rationale for the use of novel drugs in the setting of PTCLs, such as ALK inhibitors in ALK^+ anaplastic large cell lymphoma (ALCL), anti-angiogenetic drugs in AITL, and tyrosine-kinase inhibitors in PTCL/NOS, and ALK^+ and ALK^- ALCLs.

PTCLs are endemic to Asia. Park and Ko review the epidemiologic data of PTCLs in Asia, together with recent progress in the pathology of PTCLs compared with the WHO 2008 classification [2]. Although the etiology of PTCLs is mainly unknown, several risk factors, including genetic factors, abnormal immunity, environmental factors and infectious causes such as HTLV-1 and EB virus have been proposed.

ATLL is a unique T-cell malignancy associated with the human retrovirus, HTLV-1. ATLL seems to be a prototype of oncogenic virus-mediated malignancies, and previous studies have provided valuable information for understanding the mechanisms of leukemogenesis. Ohshima, Niino, and Karube review the histopathology of ATLL, focusing on the microenvironment of nodal lesions [3]. This review clearly shows that the microenvironment plays an important role in the pathogenesis of ATLL as well as other types of malignant lymphoma.

Given the disappointing outcomes for PTCLs, numerous attempts have been made to improve upon CHOP chemotherapy. Intlekofer and Younes review current progress in mechanism-based therapy for PTCLs [4]. Recent advances in biology and genetics have resulted in the identification of distinct molecular lesions within and across histological subtypes of PTCLs. Therefore, an individualized mechanistic and biomarker-driven treatment approach is expected.

Although there are still many mysteries in the world of PTCL, recent basic and clinical studies have made steady progress in clarifying lymphomagenesis and developing novel therapies for this disease. As an editor of the Progress in Hematology in this issue, I believe these reviews would be valuable for readers wishing to grasp the recent advances in PTCLs.

References

1. Piccaluga PP, Tabanelli V, Pileri SA. Molecular genetics of peripheral T-cell lymphomas. Int J Hematol. 2014 (this issue).
2. Park S, Ko YH. Peripheral T-cell lymphoma in Asia. Int J Hematol. 2014 (this issue).
3. Ohshima K, Niino D, Karube K. Microenvironment of adult T-cell leukemia/lymphoma-associated nodal lesions. Int J Hematol. 2014 (this issue).
4. Intlekofer AM, Younes A. From empiric to mechanism-based therapy for peripheral T cell lymphoma. Int J Hematol. 2014 (this issue).