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Highlights: Focus on Diffuse Large B-Cell Lymphoma

Commentary

Diffuse Large B-Cell Lymphoma in 2016

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In this issue of the Journal of Clinical and Experimental Hematopathology, four review articles for diffuse large B-cell lymphoma (DLBCL) are included. As all of the readers know, DLBCL is the largest subtype of malignant lymphoma all over the world, both in Eastern and Western countries.[1] It is a heterogeneous disease entity derived from different cell of origin (COO), symbolically germinal center B-cell (GCB) and activated B-cell-like (ABC) subtypes.[2]

The GCB/ABC categorization represents not only the gene expression, but also many lymphoma characteristics including gene alteration and drug sensitivities. In this era of high throughput genetic analysis, numerous gene alterations have been identified in DLBCL. The pattern of gene mutations is much different in GCB and ABC subtypes. A review by Dobashi concisely summarized the current perception of genetic alteration of DLBCL by the next-generation sequencing techniques including whole genome, whole exome, and whole transcriptome sequencing.[3] Alterations of chromatin remodeling genes are predominantly found in GCB subtype of DLBCL. On the other hand, gene mutations of B-cell receptor (BCR) signaling and the NF-κB pathway are more frequently found in ABC subtype of DLBCL. Identification of such genetic events is particularly important in consideration of molecular pathogenesis of DLBCL by the COO, and further architecture of molecular targeted therapy for each pathway.[4]

With regard to the treatment of DLBCL, an inclusion of CD20 antibody rituximab to combination chemotherapy has improved the response and survival.[5] Currently, R-CHOP regimen is regarded as a standard, which produce long-term survival rate of 60% for DLBCL. Since then, several novel challenges have been conducted to improve the prognosis of DLBCL, such as dose-adjusted EPOCH-R[6] or R-ACVBP.[7] Both regimens included etoposide in addition to anthracycline, vinca alkaloid and alkylator. Miyazaki has summarized the progress of treatment of DLBCL, and further trials to overcome R-CHOP by these novel regimens in relation to the GCB/ABC COO.[8] The article also touches on the significance of CD5 expression in DLBCL.

After the introduction of rituximab to the treatment of DLBCL, an altered expression of CD20 antigen has become a curious and important issue. The loss of CD20 antigen after the treatment with rituximab was reported to induce rituximab resistance, but the mechanisms are heterogeneous.[9] The review article by Tomita focuses on this issue, and have summarized the molecular mechanisms of CD20-negative phenotype.[10]

High-dose chemotherapy with autologous stem cell transplantation (HDC/ASCT) is an important option for the treatment of DLBCL, particularly for those with relapsed or refractory disease.[11] On the other hand, the significance of HDT/ASCT in upfront setting is changing with the established use of rituximab.[12,13] Kondo reviewed the history and current status of HDT/ASCT for DLBCL.[14] The position of HDC/ASCT may further shift according to the future application of novel molecular-targeted agents.

I, as an editor of the Journal of Clinical and Experimental Hematopathology, believe that readers well recognize the updated information of DLBCL through these four review series. Hopefully, readers have new insights in the future directions on the management and research of DLBCL.

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