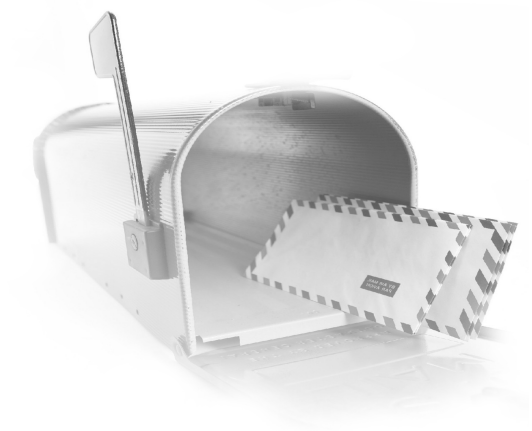

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Letter to the Editor

A controversial conclusion regarding primary extranodal diffuse large B-cell lymphoma

TO THE EDITOR: Recently, primary extranodal non-Hodgkin's lymphoma (NHL) has gained considerable attention. Many controversies are associated with primary extranodal NHL, mainly due to inadequate and contradictory literatures, and lack of uniformity in definition, clinicopathological characteristics, and clinical outcomes according to the involved sites. Jang et al. put forth prospects for further research to evaluate primary extranodal DLBCL [1]. Although they concluded that rituximab had no role in the treatment of primary extranodal DLBCL, their report included several limitations that were obstacles to achieve conclusive results.

The diversity in clinical presentation, morphology, immunophenotype, and genetic alterations strongly suggest that DLBCL belongs to a heterogeneous group of aggressive B-cell lymphomas. Extranodal disease is the predominant disease manifestation (incidence, about 40%) among DLBCL patients. Even in patients with stage I disease, 56% had extranodal DLBCL [2]. On the basis of the results of routine staging, the authors defined PENL (primary extranodal lymphoma) as a lymphoma with no or minor nodal involvement, along with a clinically dominant extranodal component. The definition of extranodal disease has been controversial, particularly in the presence of both nodal and extranodal manifestations. The designation of stage III and IV lymphomas as PENLs is debatable, since many clinicians consider only stage I and II presentations as primary extranodal disease [3]. For patients in the advanced stage of disease, this diagnostic approach may be inappropriate, because many extranodal lymphomas can disseminate and vice versa. In the above study, patients with stage III or IV disease constituted more than 50% of all subjects. Therefore, this definition for PENL inevitably introduces a selection bias.

The second controversial issue is the different prognosis according to the involved site. López-Guillermo et al. [4] reported that the clinical characteristics of nodal and extranodal DLBCLs were heterogeneous. Lymphomas arising from two specific sites [Waldeyer's ring (nodal) and gastrointestinal region (extranodal)] showed very favorable characteristics at diagnosis (e.g., early stage, absence of bone marrow involvement, normal serum LDH level, and low-risk IPI), whereas DLBCLs arising in the remaining areas (lymph nodes or other extranodal sites) presented with poorer diagnostic characteristics. In terms of response to therapy, risk of relapse and overall survival, both Waldeyer's ring and gastrointestinal lymphomas showed notably better outcomes than those shown by the other groups [4, 5]. Thus, not only the nodal or extranodal presentation, but also involvement of specific sites may be related to particular clinicobiological characteristics and disease outcomes. The authors did not provide detailed information about the involved sites and differences in patient's characteristics between the extranodal and nodal disease groups. Primary extranodal DLBCLs, according to the involved site, may be considered as different entities with different natural histories, therefore, inference from figures should be dealt with caution.

Therefore, further research using population-based studies is needed to achieve conclusive results for the diagnosis of primary extranodal DLBCL. Furthermore, the study of unresolved issues, including ambiguous definition, different clinicobiological characteristics, and gene profiles of primary extranodal DLBCL arising from different sites is warranted.

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Filler Photo

Garden of Children's Hospital, Boston S.W.Kwon