EXPERT'S COMMENT

Peripheral T-cell lymphoma (PTCL) is a heterogeneous group of mature T-cell lymphoma with a generally poor prognosis. A recent study reported the 5-year cumulative incidence of central nerve system (CNS) relapse to be approximately 2% in PTCL, not otherwise specified (PTCL-NOS), which is the most common subtype of PTCL.[1] The outcome after CNS relapse was poor, with a median survival time within 2 months. Several clinical findings, such as increased serum lactate dehydrogenase and presence of extranodal involvement, have been identified as risk factors for CNS relapse in PTCL.[1-3]

In this issue of the Journal of Clinical and Experimental Hematopathology, Shimazu *et al*. describe a case of PTCL-NOS that demonstrated CNS relapse during treatment. The patient presented with systemic lymphadenopathy accompanying lymphoma involvement in the bone marrow (BM), peripheral blood (PB) and skin. Although the lymph node (LN) swelling decreased after CHOP therapy as a first treatment, the lymphoma cells increased in the PB. The patient therefore received salvage therapy. The lymphoma cells in LN and PB markedly decreased after the second therapy, but the patient died of lymphoma after CNS relapse as an intradural extramedullary tumor.

The current case report presents the challenging situation for CNS relapse in PTCL. According to the latest National Comprehensive Cancer Network guidelines, CNS prophylaxis is recommended only for adult T-cell leukemia/lymphoma (ATLL) among PTCL subtypes. ATLL and a part of PTCL-NOS cases share clinical, pathological and genomic features.[4-6] From this standpoint, CNS prophylaxis may be also recommended in some PTCL-NOS cases. Indeed, the patient in the current report had CCR4 expression, which is frequently observed in ATLL. The relapse manifestations in this case suggest the existence of multiple subclones, which are also observed in ATLL and PTCL-NOS.[5-7] Taken together, the clinicopathological findings in the current case are similar to those of ATLL even though human T-cell leukemia virus was absent in this case.[8]

A previous study revealed that CCR7 plays a key role in CNS involvement in T-cell acute lymphoblastic leukemia/lymphoma (LBL).[9] Gain-of-function mutations of CCR7 have been identified in ATLL and PTCL-NOS.[10,11] In addition, ITGA6 and its pathway were reported to be associated with CNS involvement in LBL cases, and PI3Kδ inhibitor is a promising drug for such involvement.[12] The clinical findings, including CNS relapse related to CCR7 and ITGA6 status in PTCL cases, are of interest as their expression and/or genomic alterations may have potential as predictive markers for CNS relapse and involvement. As several studies, including the current case report, found that CNS involvement is closely related to a poor clinical outcome of PTCL,[1-3] further studies are required to prevent and treat this condition. We now have multiple agents for PTCL. Clinical trials and analyses of patients based on the trials will be beneficial for PTCL patients in the future.

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