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Editorial

Mantle cell lymphoma: a model for risk-adapted treatment approach

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Mantle cell lymphoma (MCL) is a rare but unique subtype of non-Hodgkin B-cell lymphoma that is molecularly characterized by the chromosomal translocation, t(11;14)(q13;q32) leading to the aberrant expression of cyclin D1, although a few cases are positive for cyclin D2 or D3 without expression of cyclin D1 [1, 2]. In the current issue of the **Blood Research**, Kang *et al.* reported the results of nationwide retrospective analysis regarding clinical features and treatment outcomes of 131 patients with MCL [3]. This is one of the largest series focused on MCL, especially in Asian patients. In the study, they summarized clinical features and treatment outcomes of MCL and validated the prognostic value of simplified MIPI (Mantle cell lymphoma International Prognostic Index) in Korean MCL patients. Although many studies about other subtypes of lymphomas in Korea including retrospective analyses as well as clinical trials have been reported, there are just a few studies regarding Korean MCL patients. One of the reasons for the lack of studies is the relatively low incidence of MCL because it accounts only for 2% of B-cell lymphomas in Korea [4]. However, peculiar clinical characteristics of MCL different from other subtypes of non-Hodgkin lymphoma might be another reason. First of all, MCL occurs more commonly in elderly patients, and the majority cases of MCL initially follow indolent clinical course without symptoms. Although MCL responds to conventional chemotherapy regimens, the duration of response is relatively shorter than other subtypes, and repeated relapses ultimately lead to death in MCL. This extremely low curability of MCL with conventional chemotherapy has leaded to "watch and wait" strategy for asymptomatic patients or elderly patients similar to the treatment strategy for indolent lymphomas. However, some patients initially present as aggressive disease and need immediate intensive treatments. As a result, there is a wide spectrum of clinical behaviors and various treatment approaches in MCL [1, 5]. This heterogeneity associated with MCL might have made it hard to study.

Owing to lengthy asymptomatic indolent period, MCL patients are commonly diagnosed with advanced stage disease after their extent of disease increased up to the state of producing significant symptoms. Thus, patients might have extensive lymphadenopathy, bone marrow invasion, splenomegaly, and frequent involvement of gastrointestinal tract at diagnosis, and almost all patients finally require treatments during their clinical course [6]. Therefore, the risk-stratification for MCL patients is mandatory for the determination of treatment strategy. As Kang *et al.* reported its prognostic value, the simplified MIPI incorporating age, performance status, serum lactate dehydrogenase level, and white blood cell count, can predict the survival outcome for patients with MCL [7]. Thus, the risk-adapted treatment approach according to the simplified MIPI might help physicians decide their treatment for MCL patients. As various initial treatment options became available in Korea from intensive treatments such as hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose cytarabine

and methotrexate plus rituximab (R-hyper-CVAD) to standard chemotherapy regimens such as rituximab-CHOP and bendamustine-rituximab (BR), the risk-adapted application of treatment might lead to better survival outcome for MCL patients than that of this retrospective analysis. Especially, considering elderly patients might be more vulnerable to anthracycline-containing chemotherapy-related toxicity, bendamustine in combination with rituximab can be more appropriate for elderly frail patients with MCL. Indeed, the phase III trial comparing BR with R-CHOP demonstrated that BR had a similar response rate to R-CHOP, but BR had less hematologic toxicity as well as significantly lower progression rate than R-CHOP [8]. Furthermore, newer drugs such as Bruton's tyrosine kinase inhibitor (Ibrutinib) and PI3K inhibitor (Idelalisib) might become a useful treatment option for salvage as well as upfront treatment setting considering their promising outcomes in relapsed or refractory MCL patients [9, 10]. Taken together, this report contributes valuable information for the management of MCL patients through a nationwide retrospective analysis of large number of patients with MCL in Korea. A prospective study should be warranted in the near future to overcome the limits of this retrospective study.

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