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Editorial

Soluble syndecan-1 (CD138): is it useful as a prognostic factor in Korean patients with multiple myeloma?

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Multiple myeloma (MM) is a malignant hematological neoplasia of plasma cells. The clinical manifestations of MM are heterogeneous and include monoclonal immunoglobulin production, hypogammaglobulinemia, impaired hematopoiesis, osteolytic bone disease, hypercalcemia, and renal dysfunction. Recently, novel agents such as thalidomide, lenalidomide, and bortezomib were introduced for the treatment of MM; treatment with these agents can effectively control both relapsed and newly diagnosed diseases and thereby improve survival.

Patients with MM show heterogeneous outcomes, which range from a relatively indolent course with a lengthy survival period to a more aggressive disease course with dismal prognosis. Therefore, identification of these subgroups of patients has great clinical significance. Several factors related to the disease or the patient's status have been shown to influence the disease course in MM. The Durie-Salmon staging system was previously used for clinical staging, and currently, the International Staging System (ISS), which uses laboratory factors such as serum albumin and beta-2-microglobulin levels, is commonly applied as a tool for standardized risk assessment [1]. Recently, new genetic risk stratifications have been proposed by several groups. The Mayo stratification, which is based on the results of plasma cell fluorescence *in situ* hybridization (FISH), metaphase cytogenetics, and plasma cell labeling index (PCLI), is a commonly cited representative system; the developers of this system have framed the mSMART (Mayo Stratification of Myeloma and Risk-Adapted Therapy) consensus guideline as a risk-adapted approach [2]. In the risk stratification, the high-risk group shows del17p, t(4;14), and t(14;16) in FISH, deletion 13 and hypodiploidy in metaphase cytogenetics, and PCLI ≥3%. Flow cytometric analysis of immunophenotypic markers such as CD19, CD27, CD28, CD45, CD56, and CD117 has become a useful tool for the diagnosis and monitoring of disease in cases of monoclonal gammopathies [3]. Some biological parameters related to myeloma cells, such as hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), intercellular carboxy-terminal telopeptide of type I collagen (ICTP), procollagen type I N-terminal propeptide (PINP), osteoprotegerin (OPG), and syndecan-1/CD138, have also been reported to play some roles in the diagnosis, staging, and prognosis of MM [4].

Syndecan-1 (CD138) is a transmembrane heparan sulfate-bearing proteoglycan expressed on the surface of both normal and malignant plasma cells; this molecule regulates the adhesion, migration, and growth of myeloma cells. Syndecan-1 is actively shed from the surface of myeloma cells into human plasma. In an *in vivo* model, soluble syndecan-1 is known to actively promote growth and dissemination of myelomas [5]. Clinically, the serum level of syndecan-1 is correlated with a high percentage of plasma cells in the bone marrow, disease stage, and serum M-component concentration; therefore, soluble syndecan-1 level has been shown to be an independent prognostic factor in myeloma [6]. Syndecan-1 expression has been known to be an important prognostic factor in other tumors [7].

Kim et al. [8] analyzed soluble syndecan-1 levels in Korean patients with MM at the time of diagnosis and during therapy to evaluate the effect of soluble syndecan-1 on the therapeutic response and prognosis. Because the annual in-

cidence of MM in Korea has increased steadily by 30 times over the past 30 years, MM has become one of the major hematologic disorders in Korea, and the study performed by Kim et al. may have additional significance in the light of the epidemic aspect in Korea [9]. Although the median level of soluble syndecan-1 in patients with MM was higher than that in normal controls, the sensitivity of soluble syndecan-1 levels in indicating MM was 75%. Kim et al. suggested that soluble syndecan-1 does not have adequate diagnostic value in Korean patients with MM. Consistent with the previous reports, soluble syndecan-1 levels correlated with disease stage, percentage of plasma cells in the bone marrow, β2-microglobulin level, serum M-component concentration, and creatinine level. High soluble syndecan-1 levels were associated with poor survival in the patients, although the association did not show any statistical significance. The major reason for the absence of significance in Korean patients with MM was the limited number of patients enrolled in that study. However, Kim et al. suggested that soluble syndecan-1 was a feasible prognostic factor in Korean patients with MM, as in the case of Western patients [6].

Although the ISS is commonly used for clinical staging in patients with MM, several groups have tried to develop better prognostic factors that include the cytogenetic and FISH findings, the levels of biologic markers, and the results of gene-expression profiling. Among these, the representative tailed models for MM are microarray-based predictive models that use the gene expression data in Arkansas and the mSMART consensus guideline, which is a risk-adapted approach based on the Mayo stratification [2, 10]. Large-scale multicenter studies will be required to identify the prognostic model that is most suitable for predicting better clinical outcomes in the Korean patients.

REFERENCES

1. Greipp PR, San Miguel J, Durie BG, et al. International staging system for multiple myeloma. J Clin Oncol 2005;23:3412-20.
2. Kumar SK, Mikhael JR, Buadi FK, et al. Management of newly diagnosed symptomatic multiple myeloma: updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) consensus guidelines. Mayo Clin Proc 2009;84:1095-110.
3. Raja KR, Kovarova L, Hajek R. Review of phenotypic markers used in flow cytometric analysis of MGUS and MM, and applicability of flow cytometry in other plasma cell disorders. Br J Haematol 2010;149:334-51.
4. Scudla V, Pika T, Budikova M, et al. The importance of serum levels of selected biological parameters in the diagnosis, staging and prognosis of multiple myeloma. Neoplasma 2010;57:102-10.
5. Yang Y, Yaccoby S, Liu W, et al. Soluble syndecan-1 promotes growth of myeloma tumors in vivo. Blood 2002;100:610-7.
6. Seidel C, Sundan A, Hjorth M, et al. Serum syndecan-1: a new independent prognostic marker in multiple myeloma. Blood 2000;95:388-92.
7. Oguri K, Okayama M. Can syndecan-1 become a prognostic factor in solid tumors? J Gastroenterol 2004;39:197-9.
8. Kim JM, Lee JA, Cho IS, Ihm CH. Soluble syndecan-1 at diagnosis and during follow up of multiple myeloma: a single institution study. Korean J Hematol 2010;45:115-9.
9. Lee JH, Lee DS, Lee JJ, et al. Multiple myeloma in Korea: past, present, and future perspectives. Experience of the Korean multiple myeloma working party. Int J Hematol 2010;92:52-7.
10. Zhou Y, Barlogie B, Shaughnessy JD Jr. The molecular characterization and clinical management of multiple myeloma in the post-genome era. Leukemia 2009;23:1941-56.