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652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Patterns of CS1 Expression on Natural Killer Cells and Correlated Factors in Plasma Cell Dyscrasias

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Abstract

Background CS1 is overexpressed on myeloma cells, making it a promising target for immunotherapy in plasma cell dyscrasias (PCDs). However, monoclonal antibody (mAb) targeting CS1 showed limited efficacy when used alone. In addition, few clinical data of anti-CS1 chimeric antigen receptor T cell (CAR-T) have been published to date, suggesting that there may be some barriers to CS1-targeted immunotherapy. From previous studies, CS1 is expressed on some normal lymphocytes and plays an immunomodulatory role, and NK cells in particular play an important role in CS1-mediated immunity against MM. However, there are few studies on CS1 expression by NK cells in patients with plasma cell disease. Therefore, we investigated the expression of CS1 on NK cells, normal lymphocytes, and plasma cells in plasma cell dyscrasias and examined factors related to the CS1 expression level of NK cells and its relationship to survival.

Methods Between January 2018 and September 2019, a retrospective analysis was performed in 236 patients with multiple myeloma (MM) and 30 patients with other PCDs, including systemic light chain amyloidosis (AL), monoclonal gammopathy of undetermined significance (MGUS), POEMS syndrome, and monoclonal gammopathy of renal significance (MGRS). CS1 expression levels in NK cells, lymphocytes, and monoclonal plasma cells were assessed in patients with plasma cell dyscrasias. Membrane-bound CS1 of these three cell types was measured by multiparameter flow cytometry. Associations of CS1 expression with clinical and laboratory features were determined by univariate and multivariate analyses. Correlations between CS1 expression and survival were computed using the Cox proportional hazards regression and by plotting Kaplan-Meier survival plots.

Results When subgroups of MM and other PCDs were compared, there were no significant differences in CS1 expression in lymphocytes and NK cells alone. MM Patients had significantly higher CS1 expression levels in monoclonal plasma cells than other PCDs patients. In both MM and other PCDs patients, CS1 expression was significantly higher on monoclonal plasma cells than on NK cells and lymphocytes. There was a significant correlation between CS1 expression of monoclonal plasma cells ($r = 0.60$; $P < 0.001$) and that of NK cells ($r = 0.79$; $P < 0.001$) on univariate and multivariate analysis(Figure 1). Factors such as cytogenetic abnormalities, disease progression, or survival were not associated with CS1 expression level on NK cells. Neither CS1 expression level of monoclonal plasma cells nor that of NK cells was an independent predictor of patient survival.

Conclusion We demonstrated that CS1 expression level in NK cells is consistent in plasma cell dyscrasias. CS1 expression in NK cells positively correlates with that in clonal plasma cells. This positive correlation may have implications for the development of immunotherapy targeting CS1.

Disclosures No relevant conflicts of interest to declare.

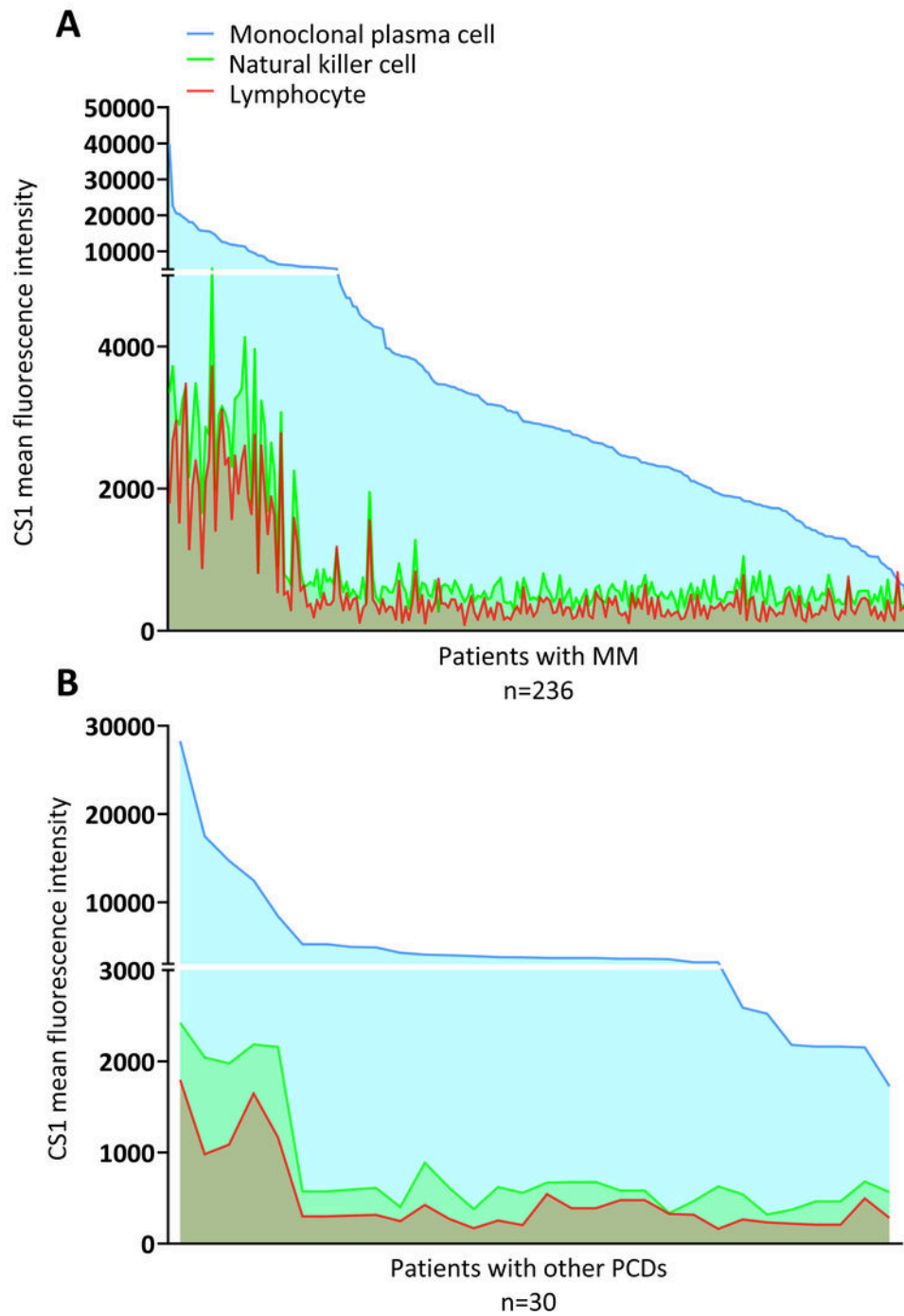## Figure 1. Expression of CS1 in the three cell subtypes

Figure 1

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