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201.GRANULOCYTES, MONOCYTES, AND MACROPHAGES

Macrophage Immune Checkpoint for Immunotherapy of Osteosarcoma

Jin Kyung Suh, MD PhD[1], *Jun Ah Lee, MD PhD*[1], *Yunmi Ko, PhD*[1], *Meerim Park*[2], *Hyeon Jin Park*[1]

[1] Department of Pediatrics, Center for Pediatric Cancer, National Cancer Center, Goyang, Korea, Republic of (South)
[2] Department of Pediatrics, Center for Pediatric Cancer, National Cancer Center, Goyang, South Korea

Purpose: Macrophages account for the majority of immune cells infiltrated in sarcoma tissues. CD47 is a "don't eat me" signal expressed on the cell surface. We tested a feasibility of CD47, a macrophage immune checkpoint, for immunotherapy of osteosarcoma.
Methods: Twenty-four biopsy samples of osteosarcoma patients younger than 20 years were retrospectively analyzed for CD47 protein expression by immunohistochemistry. Relationships between CD47 expression and clinicopathologic characteristics were evaluated. Two osteosarcoma cell lines, KHOS/NP and MG63, were analyzed for CD47 expression by western blotting and flowcytometry. Efficacies of CD47 antibody (B6-H12) on the phagocytic activity of M1-type macrophages, differentiated from peripheral blood monocytes, were evaluated.
Results: CD47 protein was expressed in 5 (20.8%) samples and in three osteosarcoma cell lines. Positive staining for CD47 was related to the presence of metastasis at diagnosis (P=0.04). Patients with tumors stained positive for CD47 tended to be older than those with tumors stained negative (16.5±6.2 years vs. 15.7±3.0 years, P=0.07). However, sex, tumor size, histologic response to preoperative chemotherapy were not associated with CD47 protein expression.
Influence of CD47 antibody (B6-H12) on cell viability varied between KHOS/NP and MG63 cells. Phagocytic activity of M1-type macrophage on osteosarcoma cells was higher in cells pretreated with CD47 antibody, compared to cells not treated (4.52% vs. 2.02%). However, CD47 antibody pretreatment did not influence the viability of osteosarcoma cells.
Conclusion: The association between CD47 protein expression on biopsy tissues and clinical characteristics suggest a possibility of CD47 as a new target for immunotherapy of osteosarcoma. As we observed a discrepancy between phagocytic activity and cell viability, future studies needs to focus on coupling the macrophage phagocytosis and effector T cell function.

Disclosures No relevant conflicts of interest to declare.

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