Case Report

Mesenchymal stem cells in inflammatory microenvironment promotes cancer cell migration and epithelialmesenchymal transition through osteopontin

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ABSTRACT:

Backgrounds: Mesenchymal stem cells (MSCs) provide potential regenerative effects on chronic kidney disease (CKD) due to their paracrine signaling with cell tropic and anti-inflammation properties. However, in CKD patients combined with renal cell carcinoma (RCC), the roles of MSCs in inflammatory or tumors' microenvironment are still controversial. Methods & Results: To evaluate the real characteristics of MSCs in inflammatory microenvironment, we first detected the human MSC secretome by cytokine array after MSCs were incubated with or without inflammatory cytokines (IL-1β or TNF-α). The array data showed that, compared to control MSCs, osteopontin (OPN) were significantly increased after MSCs were incubated with inflammatory cytokines. Furthermore, OPN mRNA level and protein secretion were confirmed by quantitative real-time PCR and ELISA respectively. We further collected MSC condition medium (MSC-CM) after inflammatory cytokine treatments to test the effects of MSC-CM as well as OPN alone on RCC migration. MSC-CM and OPN alone facilitated RCC migration by Boydon chamber assay. The epithelial-mesenchymal transition (EMT) of RCC was significantly promoted by MSC-CM and OPN alone since the reduction of E-cadherin and increase of Snail and vimentin. Using OPN-specific antibody to neutralize OPN in MSC-CM would attenuate the RCC migration and EMT that were stimulated by whole MSC-CM. Moreover, the activities of cancer-associated fibroblasts (CAF) were enhanced by treating CAF with MSC-CM and OPN alone. Conclusion & Significance: In this study, we demonstrated that OPN secreted by MSCs would promote cancer cell migration, EMT progression and CAF activation while MSCs were incubated in an inflammatory microenvironment. We hope that this study will provide another consideration of MSC application in kidney regeneration while CKD patients combined with RCC.

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