P51 Expression of DKK1 and LRP5 in renal cell carcinoma bone metastasis

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Introduction & Objectives: Canonical Wnt signaling (Wnt/β-catenin signaling) maintains the bone homeostasis by promoting the osteoblastic activities. The inhibitory factor, Dickkopf (DKK)1, enhances the bone resorption, especially in malignancies. The low density lipoprotein related protein (LRP) 5 is a component of membranous co-receptor of Wnt/β-catenin signaling and is also involved in serum low density lipoprotein cholestrol (LDL-C) level regulation. The clear cell renal cell carcinoma bone metastasis (ccRCC-BM) is characterized by osteolytic bone resorption. Whether and how Wnt/β-catenin signaling plays roles in regulating the invasion, metastasis and osteolytic process of ccRCC to bone remain unclear. This study investigated the expression of DKK1, LRP5 proteins in primary and metastatic lesions of RCC-BM. The therapeutic potential of Wnt/β-catenin signaling target medication was also evaluated.

Materials & Methods: Eleven ccRCC-BM patients with paired samples of primary and metastatic lesions were selected. ccRCC patients without any metastasis (ccRCC-only) were set as control. Slides of paraffin-embedded tissue underwent immunohistochemical staining with monoclonal anti-DKK1 antibody and polyclonal anti-LRP5 antibody. Semi-quantitatively scoring according to staining intensity was performed. The staining results in the renal tissue adjacent to RCC, the primary RCC lesions (with BM or without BM), and the RCC-BM lesions were recorded. The expression difference was analyzed by univariate analysis of variance (ANOVA).

Results: The expression of DKK1 was significantly different amid renal tissue adjacent to RCC, primary RCC and RCC-BM tissues ($p < 0.001$). The expression of DKK1 in primary RCC was significantly lower than that in renal tissue adjacent to RCC ($p<0.001$). No difference was found between ccRCC-BM group and ccRCC-only group. DKK1 expression in bone metastasis was significantly higher than that in primary tumor ($p < 0.001$). The expression of LRP5 in the primary tumor of ccRCC-BM group was significantly lower than that of adjacent renal tissue ($p<0.01$). Tendency of decreasing expression was found between primary lesion of ccRCC-BM group and primary lesion of ccRCC-only group ($p=0.073$). In bone metastasis, the expression of LRP5 protein was not significantly different from that in adjacent renal tissue and RCC primary lesion.

Conclusions: A "rebound" of DKK1 expression was found in bone metastasis lesions. Along with the decreasing LRP5 expression in primary lesions of RCC-BM patients, this suggests that the canonical Wnt signaling (Wnt/β-catenin signaling) is inhibited during the bone metastasis process in ccRCC. The overexpression of DKK1 and the down-regulation of LRP5 receptor are involved.