CHRONIC KIDNEY DISEASE. BONE DISEASE

EXPRESSION OF OSTEOCYTES MARKERS IN VESSELS FROM CHRONIC KIDNEY DISEASE RATS WITH VASCULAR CALCIFICATION

Sarah-Kim Bisson¹, Sylvain Picard², Roth-Visal Ung², Mohsen Agharazii², Richard Lariviere² and Fabrice Mac-Way³

¹CHU de Québec Research Center, l’Hôtel-Dieu de Québec Hospital, Biochemistry, Quebec, QC, Canada, ²CHU de Quebec Research Center, l’Hôpital-Universitaire de Québec Hospital, Medicine, Quebec, QC, Canada, ³CHU de Québec Research Center, l’Hôpital-Universitaire de Québec Hospital, Medicine, Quebec, QC, Canada

Introduction and Aims: Bone and mineral disorders affect every patients with chronic kidney disease (CKD) and contribute to the burden of fractures and cardiovascular disease. Bone disorders have been associated with vascular calcification in CKD but the mechanisms underlying this bone-vessels axis anomalies are poorly understood. Vascular calcification is a tightly regulated process involving the transdifferentiation of vascular smooth muscle cells (VSMC) into "osteoblast-like" cells. We hypothesized that during this process of transdifferentiation, VSMC will acquire an "osteocyte-like" phenotype. The aim of this study is to determine if calcified vessels from CKD rats express osteocytic markers.

Methods: CKD is induced by 5/6 nephrectomy in Wistar rats and vascular calcification is induced by high calcium, phosphate and vitamin D supplementation. These rats were compared to CKD rats fed with a normal diet and control rats fed with either a normal diet or high calcium, phosphate and vitamin D supplementation. Thoracic aortas were harvested at sacrifices 4 weeks after 5/6 nephrectomy. The markers of vascular remodeling and osteogenic differentiation were analyzed by qPCR (RunX2, BMP-2, α-SMA) and immunofluorescence (osteocalcin) on thoracic aortas. The expression of sclerostin, dentin matrix acidic phosphoprotein-1 (DMP-1) and FGF-23 (osteocytic markers) in addition to Dickkopf related protein 1 (DKK1) were performed on the thoracic aortas by immunofluorescence and western-blot. Serum levels of sclerostin were determined at sacrifices.

Results: Only CKD rats given a high calcium, phosphate and vitamin D supplementation developed vascular calcification. Serum levels of sclerostin was elevated only in rats who developed vascular calcification. In the thoracic aortas, the genes coding for RunX2 and BMP-2 and the expression of osteocalcin were significantly increased in CKD rats with vascular calcification while α-SMA was significantly reduced. These results confirmed the process of transdifferentiation into "osteoblasts-like" cells. Sclerostin, DMP-1, FGF-23 and DKK1 were highly expressed in areas of calcification from thoracic aortas.

Conclusions: In this study, we show that there is upregulation of osteocytic markers such as sclerostin and DMP-1 in calcified vessels from CKD rats. These findings confirm the central role of bone metabolism in the development of vascular calcification and the major role of osteocytes in bone-vessels axis anomalies in CKD.