BMP-7 IS INCREASED IN ENDOTHELIAL BUT NOT IN VASCULAR SMOOTH MUSCLE CELLS OF EPIGASTRIC ARTERIES IN DIALYSIS PATIENTS WITH RADIOLOGICALY VISIBLE CALCIFICATIONS

Basic-Jukic Nikolina, *Gulin Marijana, Hudolin Tvrtko, Coric Marijana, Jelakovic Bojan, Katalinic Lea, Kastelan Zeljko, Kes Petar
Department of nephrology, arterial hypertension, dialysis and transplantation, University hospital centre Zagreb, Zagreb, *General hospital Sibenik, Sibenik, **CROATIA**

Introduction

Vascular calcification (VC), in which vascular smooth muscle cells (SMC) undergo transformation into osteoblast-like cells is closely related to cardiovascular events in chronic kidney disease (CKD). Over the recent years, several factors were demonstrated to be involved in process of VC. However, the cellular mechanisms responsible have yet to be fully explained. Bone morphogenetic protein-7 (BMP-7) has been proposed to play an inhibitory role in vascular calcification, but was not found to be associated with outcomes in recent human experiments. Additionaly, its inhibitory effect has not been fully elucidated.

Patients and methods

Seventy-nine patients undergoing renal transplantation from which epigastric artery samples were taken at the time of surgery, were included in this study. BMP-7 was detected by immunohistochemistry. Immunoreactivity in endothelial (BMP-7e) and media smooth muscle cells (BMP-7m) was assessed by grading (0 - 3) and the results were expressed as percentage of positive cells (negative < 10 %, 10-49 %– grade 1, 50-74%– grade 2, and more than 75 %– grade – 3). Microvascular calcification was assessed by the von Kossa staining method. Pelvic X-rays were used to determine presence of macrovascular calcifications which were classified as present or absent.

Results

Patients' characteristics are presented in Table 1. Glomerulonephritis (40%) was the most common cause of CKD. Four patients had type II diabetes and 8% had history of cardiovascular diseases. Vascular calcifications determined by X-rays at the time of transplantation were significantly associated with age, smoking, hyperlipoproteinemia, and dialysis vintage, but not with sevelamer or calcium carbonate therapy.

Patients with BMP7e grade 3 staining had 18 times higher odds for X-rays visible vascular calcifications compared to patients without BMP-7e expression after adjustment for other variables. BMP-7m expression had no statistically significant correlations with other variables. Von Kossa staining was not associated with either BMP7 staining in endothelium or media of epigastric artery, or with other parameters.

Characteristic (n=79)	Value
Age	51 ± 14 years
Gender	60% male
Dialysis vintage	2.8 years (range, 1-4)
History of cardiovascular disease	8%
Radiologically visible vascular calcifications	59%
MM	3 (range, 1-5)
Senstitisation	2 patients (6 and 12%)
Deceased donor	78

Table 1. Patients' characteristics.

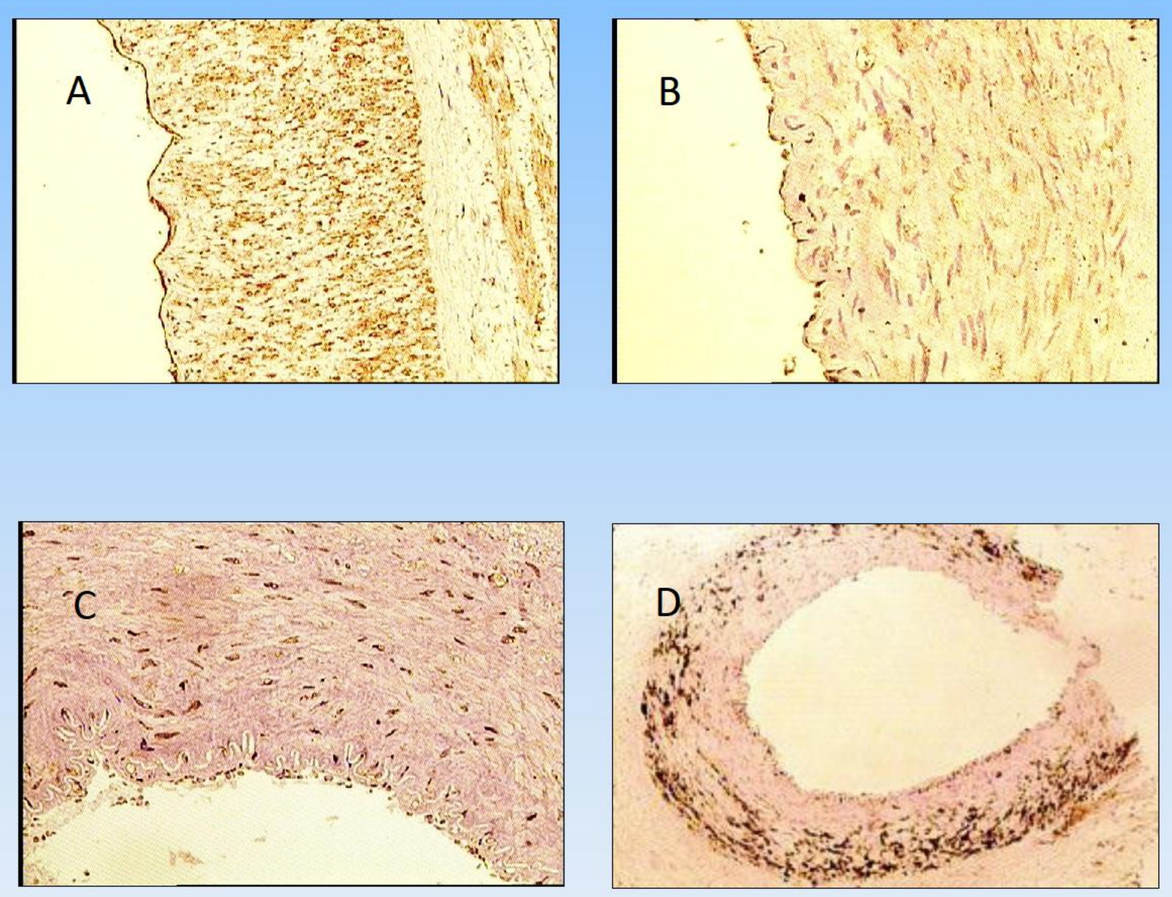

Figure 1. Immunohistochemistry. A, BMP-7 strongly positive in endothelial cells; B, BMP-7 positive in vascular smooth muscle cells; C, BMP-7 negative staining; D, diffuse punctate staining in media layer of artery wall (von Kossa staining)

Conclusion

We observed a marked BMP-7 overexpression in endothelial, but not media SMC cells of epigastric arteries of patients with radiologicaly visible vascular calcifications. We postulate that increased BMP-7e expression might be result of attempt to protect blood vessels and to reduce VC. However, this speculation has to be tested in future investigations.

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