

Concentrations and activities of metalloproteinases-2 and -9 and their inhibitors (TIMPS) in oncocytoma and clear cell renal cell carcinoma

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Due to its asymptomatic clinical course, the majority of kidney tumors are discovered co-incidentally during abdominal imaging performed for unrelated diagnostic reasons. One of the strategies to improve this situation is the identification of biomarkers in serum or urine samples whose levels are sensitive to detect tumor forms and to monitor disease progression. Several tumor markers have been tested in the past, but there are no definitive biomarkers available for such purpose. Among protein markers, metalloproteinase -2 (MMP-2) and -9 (MMP-9), and their inhibitors (TIMP-2 and TIMP-1) have the potential to represent candidate to improve diagnosis and follow-up surveillance. In fact, these molecules are often linked to the malignant phenotype of tumor cells. We measured the activity and concentrations of MMP-2 and MMP-9 and the concentrations of their inhibitors in sera and urine from patients with kidney tumors. Of these patients, 16 had clear cell renal carcinoma (ccRCC) and 4 had oncocytoma. Sera and urine samples of 53 healthy subjects were used as control. To investigate the gelatinolytic activity present in the serum and in concentrate urine, substrate gel zymography was performed. In the sera of all patients, the gels revealed the existence of lytic band at 72 kDa (MMP-2) at 92, 130 and 240 kDa (MMP-9). MMP-9 activity was slightly enhanced in sera from ccRCC compared with oncocytoma patients. Serum MMP-2 activity was similar in ccRCC and in oncocytoma patients. In the urine, 2 oncocytoma patients and 3 of ccRCC patients showed gelatinolytic activity, whereas MMPs could not be detected in the concentrate urine of healthy subjects. The most abundant lytic activity was at 92 kDa, whereas MMP-2 was present in lesser quantities. By enzyme linked immunoassay (ELISA), MMP-2 was detected in all the sera of the control group (range 475- 798 ng/ml, mean \pm SD 522 \pm 140), as well as TIMP-2 (range 33-188, ng/ml, mean \pm SD 55 \pm 28), while MMP-9 and TIMP-1 were undetectable being at or below the sensitivity of the assay. We established the cut-off value by the mean + 2 SD and we considered 802 ng/ml for MMP-2 and 111 ng/ml for TIMP-2. MMP-2 values were positive in three oncocytoma patients and in 12/16 (75%) of ccRCC patients. TIMP-2 values were positive in all oncocytoma, and in 15/16 (94%) of ccRCC patients. Since serum MMP-9 and serum TIMP-1 were undetectable in all healthy subjects, we considered all pathological specimens positive as all samples possessed serum MMP-9 and serum TIMP-1 values higher than the sensitivity of the assay (assay sensitivity has been calculated by two standard deviations above the zero dose binding of 80 determinations and was 0.8 ng/ml for MMP-9 and 1.51 for TIMP-1). Considering the average value of each molecule we observed that MMP-2 and TIMP-2 and TIMP-1 are similar in oncocytoma and ccRCC patients, while MMP-9 is 2-fold higher in ccRCC patients compared with oncocytoma. With regard to urine specimens, the four molecules were undetectable in all normal individuals and in few pathological subjects. The urinary level is lesser than that of the sera. The average value of MMP-2, MMP-9, and TIMP-2 of the positive urine specimens are similar in oncocytoma and ccRCC patients; while the average value of TIMP-1 is higher in ccRCC patients compared with oncocytoma. Statistical analysis of the data did not reveal any correlation between tumor grade or stage and the expression levels of the molecules examined.

Biography

Angelina Di Carlo Graduated in Biology and she is specialized in Microbiology and General Pathology. Angelina Di Carlo is a Full professor of Clinical Pathology at "Sapienza" University of Rome, Italy and also President of Degree Course of Nursing, "Sapienza" University of Rome, Italy. Her research fields are Mechanisms of endocrine system regulation, Role of cAMP on growth and differentiation of cell, Evaluation of diagnostic and prognostic significance of biomarker in tissue and in biological fluids of human neoplasias, Identification and characterization of antigens and/or receptors of membranes, Recombinant immunotoxin: protein genetically modified for anti-tumor therapy, and Matrix metallo proteinases (MMPs) expression in biological fluids of subjects with neoplasias

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