

ALTERED OSTEOGENIC PROPERTIES OF BONE MARROW STROMAL CELLS FROM MULTIPLE MYELOMA PATIENTS

S. Colucci¹, G. Brunetti¹, A. Oranger¹, G. Mori¹, R. Rizzi², S. Capalbo², V. Liso², M. Grano¹

¹ Department of Human Anatomy and Histology, University of Bari, Bari, Italy

² Hematology, University of Bari, Bari, Italy

Multiple myeloma (MM) is a B cell neoplasm characterized by clonal expansion of malignant plasma cells in the bone marrow (BM) with frequent occurrence of lytic bone disease. It results from an unbalanced bone turnover with enhanced resorption related to increased OC recruitment and activity and low bone formation. In particular, the reciprocal relationship between MM cells and OCs is known to be critical for the induction of osteoclastogenesis and the activation of bone resorption as well as the relationship between MM cells and OBs could be crucial to affect bone matrix formation, thus preventing lesion repair. Thus, we investigated the osteogenic properties of bone marrow stromal cells (BMSCs) collected from patients affected by MM. We demonstrated that, culturing BMSCs for 14 days in differentiating conditions, the induction of ALP expression at mRNA level and activity were completely absent in BMSCs from patients with multiple myeloma bone disease. Differently, ALP was weakly expressed in BMSCs from patients with multiple myeloma without osteolysis, and it was strongly evident in the controls. To further investigate the ability of BMSCs from multiple myeloma patients to differentiate toward the osteoblastic phenotype, the expression of collagen type I (COLL-I) and the formation of mineralized nodules were evaluated respect to BMSCs from the controls. Low basal mRNA levels of COLL-I were detected in BMSCs from multiple myeloma bone disease patients before the incubation with osteogenic medium. The mRNA levels were further reduced in these cells after 7 and 14 days of culture in differentiating conditions. In addition, no COLL-I expression was detected at protein levels in the BMSC lysates from the same patients. The mineralized nodule formation did not occur in BMSCs from multiple myeloma bone disease patients despite the incubation with osteogenic medium for 4 weeks. Differently, a substantial mineralization was detected in BMSCs from multiple myeloma patients without osteolytic lesions, and, as expected, significantly higher mineralization areas were detected in the controls as demonstrated by quantitative analysis of Von Kossa staining. In conclusion, our results demonstrated that the BMSCs from MM bone disease patients show a reduced capability to differentiate toward an osteoblastic phenotype.