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Decreased osteocyte viability in multiple myeloma patients: osteolytic bone lesions, apoptosis and their potential role in bone remodeling alterations

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Osteocytes seem to regulate bone remodelling by different manners including apoptosis. A reduction of osteocyte viability (OC-V) was shown in osteoporotic bone. Osteolysis/osteoporosis, induced by multiple myeloma (MM), are characterized by severely imbalanced uncoupled bone remodelling due to increased osteoclastogenesis and suppressed osteoblast differentiation occurring close to MM cell infiltration. The aim of this study is to investigate the eventual involvement of osteocytes in bone remodelling alterations occurring in MM patients. Iliac crest biopsies were taken from 34 patients with MM (52% of which displayed osteolytic bone lesions), 10 with monoclonal gammopathy of uncertain significance (MGUS) and 10 without haematological malignancies/osteoporosis/metabolic bone diseases. Viable osteocytes and degenerated or apoptotic osteocytes/empty lacunae were evaluated on 500 lacunae per histological section. Significant reductions of OC-V in MM patients were found compared to healthy controls, whereas not statistical significance in OC-V was observed between MM and MGUS. Death osteocytes/empty lacunae number was significantly increased in MM vs. controls but not as compared to MGUS. Concerning the skeletal involvement, in MM patients either OC-V percentage was significantly lower in osteolytic vs. non-osteolytic patients or the number of dead osteocytes/empty lacunae was higher in osteolytic vs. non-osteolytic patients. Monolayers were also performed of human preosteocytes incubated with/without conditioned media (CM) taken from human myeloma cell lines (HMCLs) or co-cultured with them, and TEM observations showed dead cells in those monolayers treated with HMCL-CM or co-cultured with HMCLs as compared to non treated cells. In CM of preosteocytes co-cultured with HMCLs significantly increased CD14+-derived osteoclastogenesis occurs, evaluated by TRAP staining and pit-forming assay. Our data demonstrate that MM bone is characterized by reduction of OC-V; the increase of osteocyte death (apoptosis/degeneration) in relation to the presence of bone lesions may represent a triggering event to osteoclast recruitment.