Altered bone microarchitecture and gene expression profile due to calcium deficiency in a mouse model of myeloma

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Résumé en anglais	It is not clear why patients with an indolent form of multiple myeloma (MM) develop into an aggressive form with poor prognostic. We investigated the effect of a dietary calcium deficiency on tumor growth, osteolysis and gene expression in the 5T2MM murine model. Two groups of C57BL/KaLwRij mice received 5T2MM cells and started a diet with normal (0.8%; "normal-Ca-MM") or low calcium content (0.05%; "low-Ca-MM"). Two control groups (without 5T2MM cells) received either a normal or low calcium diet (normal-Ca and low-Ca groups). Tumor growth, osteolysis and marrow gene expression of the Wnt pathway, RANKL and MIP-1α were monitored at 6, 8 and 10 weeks (w) after cell injection. In low-Ca mice, serum level of PTH was higher after 10w; microCT showed trabecular bone loss and decrease of cortical thickness at the tibia. A higher M-protein level was evidenced at 10w and 4 mice developed paraplegia at 8/9w in low-Ca-MM group only. Numerous cortical perforations of the tibia were observed in MM groups with a marked decrease in cortical thickness in low-Ca-MM. At 6w, osteoclast number from the endosteum was significantly higher in low-Ca-MM compared to normal-Ca MM. This observation was not found at 8 and 10w. MicroCT of the lumbar vertebrae showed dramatic bone destruction in the low-Ca-MM group. qPCR revealed no difference in RANKL expression whereas differences were obtained in the expression of Lrp5/Lrp6 and MIP-1α from 6w. A low calcium diet induced higher bone destruction in the tibia and vertebra associated with an earlier decrease in bone formation level and a higher increase in bone resorption level at early time in the MM development.
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