The Calcitonin Receptor Protects Against Bone Loss And Excessive Inflammation In Collagen Antibody-Induced Arthritis

Trauma / Shoulder & Upper Arm Trauma / Miscellaneous

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Background
The chondroprotective and anti-resorptive role of calcitonin (CT) plays an essential role in healthy bone and joint homeostasis. CT derived from eel or salmon has been used successfully to improve bone lesions and alleviate pain in patients suffering from rheumatoid arthritis (RA) and osteoarthritis. While the bone sparing mechanism of action behind telest CT has been attributed to the inhibition of osteoclastogenesis and cartilage degradation, the role of endogenous CT in inflammatory joint diseases remains elusive.

Objectives
The objectives of this study were to determine the roles of endogenous CT on inflammation and cartilage and bone metabolism in antibody-mediated arthritis.

Study Design & Methods
Collagen II-antibody-induced arthritis (CAIA) was induced in wild type (WT) and CT receptor-deficient (Calc–/–) mice, while control (CTRL) animals received phosphate-buffered saline. Animals were monitored over 10 and 48 days with daily assessments of a semiquantitative arthritis score. Joint inflammation, cartilage degradation, and bone erosions were assessed by histology, gene expression analysis, and μ-computed tomography.

Results
WT CAIA and Calc–/– CAIA mice developed full arthritic phenotypes with no differences between groups for clinical indices. Congruently, acute signs of histological inflammation and cartilage degradation were present in both groups, yet more pronounced in Calc–/– CAIA mice. While the expression of TNF-α and CD80 was induced in both groups, TGF-β, IL-1β, CD14, CD68, CCL-2 and SPHK1 were only upregulated in Calc–/– CAIA mice compared to CTRL animals during the acute inflammatory phase. Further, bone volume, bone density, bone surface and trabecular number were all decreased in Calc–/– CAIA mice while this substantial bone loss was not noted for WT CAIA animals after 48 days.

Conclusions
This study displays the protective role of endogenous CT against excessive joint inflammation, cartilage degradation and concomitant systemic bone degradation in a murine antibody-based arthritis model. While teleost CT has been used as a protective agent against bone erosions in RA patients, we hereby demonstrate the importance of intact endogenous CT signaling for the containment of inflammation and maintenance and restoration of bone integrity during arthritis.