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A Link Between Bone Marrow Angiogenesis and Pathological Subchondral Bone Resorption in Carrageenan-Induced Experimental Inflammatory Arthritis (CgA).

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Previously, our laboratory has demonstrated that the integrity of subchondral bone plate is severely compromised as a result of osteoclast-mediated bone resorption in an experimental animal model of carrageenan-induced arthritis (CgA) of the rabbit knee. In addition to bone destruction, CgA is characterized by cartilage degradation, synovial proliferation (pannus formation) and angiogenesis. Although, angiogenesis is an essential element of invasive synovium, and activated endothelial cells are abundant at pannus-induced bone erosion sites, it has not been shown whether angiogenesis occurs at a site remote from pannus. Taken together with our knowledge that bone marrow alterations occur in CgA, which includes an increase in hematopoiesis in the proximity of inflamed joints, abnormal monocyte and lymphocyte populations and T cell component, we asked whether intraosseous inflammatory state drives bone marrow angiogenesis which may contribute to subchondral bone damage. This work describes the extent of angiogenesis in the bone marrow as a result of chronic inflammation and how it relates to subchondral bone destruction as it occurs in CgA. This study employed CgA model of the rabbit knee. Carrageenan (0.3 ml of 1% in saline) was used to induce arthritis in female adult NZW rabbits by ten intra-articular injections into the tibiofemoral joint over 49 days. To assess the degree of bone marrow angiogenesis in CgA Vs. normal untreated controls, blood vessels were detected on 5µm 4% paraformaldehyde-fixed paraffin-embedded sections by immunohistochemical staining of endothelial cells with goat anti-human von Willebrand factor (vWf) affinity-purified antibody (Enzyme Research Laboratories, South Bend, Indiana, USA). Analysis of our results, based on gross observations, shows a marked increase in bone marrow angiogenesis as defined by vWf-stained endothelial cells, which are associated with the elevated levels of bone marrow cellularity in CgA, replacing mostly adipose tissue present in untreated controls. The extent of observed CgA-induced bone marrow angiogenesis mirrors the subchondral bone destruction in these specimens. This finding suggests that chronic inflammation may be a driving force for bone marrow angiogenesis, thus implicating a possible codependency between these two processes, which may contribute to an observed subchondral bone destruction in CgA. To establish this inflammation-angiogenesis codependency in CgA model, further work is required in order to correlate levels of pro-inflammatory cytokines, pro-angiogenic factors, and bone marrow angiogenesis with subchondral bone destruction.