GM-CSF is a pro-inflammatory cytokine in experimental vasculitis of medium and large arteries.

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Background: Giant Cell Arteritis (GCA) is a granulomatous vasculitis with tissue tropism for medium and large arteries. Macrophages are a key cellular component of the granulomatous infiltrates and contribute to the disease process through the production of cytokines, growth factors and tissue-injurious proteases. Lesional macrophages can fuse to form the typical giant cells, the namesakes of the disease. To which extent the number of macrophages in the vasculitic lesions affects the intensity of inflammation is unknown. We have tested whether granulocyte-macrophage colony-stimulating factor (GM-CSF), a soluble cytokine involved in the generation, the survival and the activation of macrophages has a role in exacerbating vascular inflammation. In a preclinical animal model of vasculitis, we have injected recombinant GM-CSF (rGM-CSF) or blocked GM-CSF activity by treating with Mavrilimumab (KPL-301, a monoclonal antibody, which inhibits the GM-CSF receptor-α.

Methods: Vasculitis was induced in human artery mouse chimeras by engrafting medium-sized human arteries and adoptively transferring peripheral blood mononuclear cells from patients with GCA. One group of mice received 50 µg of recombinant GM-CSF. Another group of mice was treated with control IgG or anti-GM-CSFRα antibody intraperitoneally over one week. Arteries were harvested and examined by Haemotoxylin & Eosin staining and tissue transcripts.

Results: Compared to treatment controls, recombinant GM-CSF intensified and KPL-301 reduced tissue inflammation in the arteries. The numbers of tissue-residing T cells doubled after rGM-CSF injection and was reduced by about 50% after treating with the blocking antibody. Changes in the density of inflammatory cells were accompanied by parallel changes in the tissue gene expression of IL-1β, IL-6 and IFN-γ. The tissue expressions of IL-17 and TNF-α transcripts were unaffected by either intervention.

Conclusions: We conclude that GM-CSF has a role as an inflammatory cytokine in medium vessel vasculitis. The density of inflammatory cells in the lesions appears to be GM-CSF dependent. The effect of GM-CSF seems selective, with IL-17 and TNFα being independent of GM-CSF signaling in this model.