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Role of inflammation in the pathogenesis of chronic renal damage in renovascular hypertension

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Abstract

Renovascular disease (RVD) is an important cause of end stage renal disease and conveys a significant risk of mortality. Optimal management of patients with RVD and renovascular hypertension (RVH) is a matter of considerable controversy, as recent studies have failed to show that percutaneous transluminal angioplasty improves renal outcome in patients with RVH. Both local and systemic inflammation has been linked to morbidity and mortality in patients with RVH. Mechanisms underlying this association have not been adequately defined. We have established a murine model of RVH employing placement of a tetrafluoroethylene cuff on the right renal artery. In vivo imaging studies demonstrate that renal blood flow is reduced by 70% in this model. The right kidney maintains its size for approximately one week. By histopathologic analysis, there are minimal alterations in the stenotic kidney (STK) at 3 days following surgery. After one week, the STK develops progressive atrophy, a process that is associated with the influx of CD3+ T cells and F4/80+ macrophages. By qPCR analysis, CCL2 (MCP-1) is rapidly (within 3 days) induced, prior to the influx of inflammatory cells. CCL2 expression was increased after 7 days in infiltrating CD90+ T cells and CD11b+ macrophages isolated from renal cortex by immunomagnetic separation. Inhibition of CCL2 signaling by RS-102895 prevented T cell and macrophage infiltration into the STK and significantly reduced renal atrophy. We conclude that CCL2 may provide a therapeutic target for preventing inflammation and development of atrophy in RVH.

Biography

Joseph P. Grande received his M.D. and Ph.D. degrees from the University of Chicago and post-doctoral training at the University of Michigan. He is currently a Professor of Laboratory Medicine and Pathology at Mayo Clinic and has over 20 years experience as a clinical and experimental renal pathologist. He has published more than 200 manuscripts on basic, clinical, and translational studies related to progression of renal and vascular disease.