Inflammation, Angiotensin II, and Hypertension

To the Editor:

In a recent article, Liao et al.1 used mice lacking the CC chemokine receptor 2 (CCR2) to test the hypothesis that CCR2 activation plays an important role in the renal damage induced by angiotensin infusions. In their elegant article, it was also shown that CCR2−/− mice and CCR2+/− mice developed similar elevations of blood pressure despite significantly different levels of oxidative stress and tubulointerstitial inflammation. The authors concluded that CCR2, oxidative stress, and renal inflammation play an important role in the development of hypertensive nephropathy but not in hypertension.

Although the conclusions of the article are logical, they apply to conditions characterized by a high level of circulating angiotensin II. The experiments of Liao et al.1 were done during angiotensin infusion, and the potent hemodynamic actions of circulating angiotensin II make it unlikely that any modification of other contributing factors would result in a significant amelioration of hypertension.

Interestingly, however, the infusion of angiotensin II can also cause salt-sensitive hypertension after the infusion is stopped. In this setting, the salt-sensitive hypertension has been shown to be attributed to the induction of renal microvascular disease, tubulointerstitial inflammation, and the generation of local oxidative stress and intrarenal angiotensin II.2 The triad of renal inflammation, oxidative stress, and local angiotensin II production is interlacing and interdependent.3 Under these conditions, immunosuppression with mycophenolate does prevent inflammation and hypertension, although this same treatment has no effect on blood pressure during the infusion of angiotensin II.2 Salt-sensitive hypertension is, of course, a condition characterized by low plasma renin and high renal angiotensin II.4 Several studies from us and others have demonstrated that immune suppressive drug therapy is associated with improvement of hypertension, oxidative stress, and intrarenal angiotensin II activity in the Dahl salt-sensitive rat, in the spontaneously hypertensive rat, and in practically all of the experimental models of salt-dependent hypertension and in humans with grade I essential hypertension (reviewed in Reference 5). Thus, whereas inflammation may not have a role in blood pressure in animals during the infusion of pharmacological doses of angiotensin II, the evidence is mounting that intrarenal inflammation has a central role in the pathogenesis of salt-sensitive hypertension.

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