Blood Pressure Control: A Facelift for Macrophages?

To the Editor:

Machnik et al.1,2 recently demonstrated a new physiological role for macrophages in regulating salt-dependent volume and blood pressure by a vascular endothelial growth factor C–dependent buffering mechanism. In line with this work, they now extend their work demonstrating that the mononuclear phagocyte system depletion induces salt-sensitive hypertension in rats.1,2 These findings promote a new view on a protective role for macrophages in hypertension. Although cardiovascular inflammation has been widely evidenced to have detrimental effect on blood pressure and target organ damage,3 the common view needs to be differentiated, because macrophages in the lymphatic compartment seem to be protective with respect to salt-sensitive blood pressure regulation.

An important feature in this scenario is obviously the sodium homeostasis. The influence of sodium on blood pressure is not only restricted to models used by Machnik et al.1,2 but also influences other more general models of hypertension, such as the spontaneously hypertensive rat (SHR).4 Therefore, it is relevant to know whether the observed blood pressure effects after macrophage depletion in salt-sensitive models of hypertension are reproducible in models where macrophage action has been rather associated with deleterious effects.

In a preliminary study we used the same source and strategy to deplete macrophages in adult SHRs, as performed by Machnik et al.1 Age-matched liposome-treated SHRs and normotensive Wistar-Kyoto rats were used as controls (n = 5 each group), and macrophage depletion was confirmed by fluorescence-activated cell sorter analysis. In contrast to Machnik et al.1 we, furthermore, used radiotelemetry during the whole treatment period as the gold standard technique for blood pressure control in all of the groups. Despite appropriate macrophage depletion in clodronate-liposome–treated SHRs, we did not observe a similar blood pressure difference during the 2 weeks of intervention between clodronate-liposome– or control-liposome–treated SHRs (mean arterial pressure: 137.5 ± 4.4 versus 139.6 ± 3.9 mm Hg). Wistar-Kyoto rats receiving control liposomes had a blood pressure of 103.1 ± 3.9 mm Hg. Therefore, our preliminary data do not demonstrate that macrophage depletion has a detrimental blood pressure influence in a standard model of hypertension, which has also been demonstrated to be at least partially sodium dependent. Furthermore, protective cardiovascular effects of macrophage depletion need to be further investigated, because already several years ago colleagues of Machnik demonstrated the blood pressure–lowering effect of immunosuppressive treatment with mycophenolate mofetil in another hypertensive rat strain.3 Moreover, the group of Schiffrin4 demonstrated that osteopetrotic mice that miss macrophage colony-stimulating factor exhibit no blood pressure increase and reduced vascular inflammation during desoxycorticosterone acetate-salt intervention.

In our view, it will be highly interesting to differentiate the protective and deleterious (probably compartment-dependent) effects of macrophages on blood pressure and cardiovascular damage in the various types of hypertensive models. In this context, the work of Machnik et al.1 offers the basic understanding of protective macrophage effects that needs to be cautiously put in context with our common view of cardiovascular inflammatory processes.

Disclosures

None.

References

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