Brucella abortus infection drives rapid macrophage disappearance reaction from the peritoneal cavity

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Brucella is a facultative intracellular pathogenic bacterium responsible for brucellosis, a worldwide re-emerging zoonotic disease affecting wildlife and livestock. The pathogenesis of brucellosis is linked to the ability of Brucella to survive and replicate inside host cells via several virulence factors. Brucella LPS, its major virulence factor, displays properties distinct from those of enterobacterial LPSs and plays critical roles in modulating innate and adaptive immune responses. We previously demonstrated that wild-type B. melitensis (Bm-wt) LPS exhibited a poor stimulatory effect on dendritic cells in vitro and in vivo in contrast to modified LPS with a defective outer core purified from Brucella carrying a mutated wadC gene (Bm-wadC), which efficiently potentiated mouse and human dendritic cell activation and T cell proliferation. The immunomodulatory properties of Bm-wt, Bm-wadC mutant and E. coli LPS on various myeloid cells were studied in vivo inside peritoneal cavity. Bm-wt LPS significantly triggered transient disappearance and weak Th1 polarization of large peritoneal macrophages (LPM). Concomitantly, Bm-wt LPS favored massive peritoneal influx of monocytes and neutrophils at early time-points post-injection. Both macrophage migration and granulocyte recruitment by Bm-wt LPS occurred via a TLR4-independent pathway. In contrast, Bm-wadC LPS drove a TLR4-dependent M1 polarization of LPM and a strong Th1 cytokine profile comparable to that elicited by E. coli LPS, the prototypical endotoxin. Intriguingly, both Bm-wadC and E. coli LPSs showed a delayed effect on macrophage migration and granulocyte recruitment. In a mouse model of infection, B. abortus also caused transient disappearance of LPM and peritoneal influx of monocytes and neutrophils during the acute phase of infection. Altogether, our findings revealed a novel peculiar property of Brucella LPS, which through triggering migration of weakly polarized macrophages and early monocyte and granulocyte recruitment in vivo, may facilitate dissemination and survival of bacteria at the onset of infection.

Keywords : LPS, Brucella, macrophage disappearance, peritoneal cavity
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