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Potentiation of liposome-induced complement activation by surface-bound albumin

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Abstract

Large anionic multilamellar liposomes containing 71% membrane cholesterol (MLV) caused complement (C) activation in human serum in vitro, as reflected in significant rises in S protein-bound terminal complex (SC5b-9) and C3a-desarg levels. Increasing the albumin content in serum by 1^4 g/100 ml led to 50^100% further increase in MLV-induced C activation, while higher amounts of exogenous human serum albumin (HSA) gradually lost the capability to potentiate liposomal C activation. HSA alone had no influence on SC5b-9 formation at any level below 12%. Complement activation by liposomes and the potentiating effect of supplemental HSA were greatly reduced or eliminated in the absence of C1q or in the presence of 10 mM EGTA/2.5 mM Mg2, pointing to the involvement of the classical pathway. Potentiation of C activation by supplemental HSA was not unique to MLV-induced activation, as deposition of HSA on the membrane of `Centricon' ultrafiltration units also potentiated the C-activating effect of the polycarbonate membrane. Fatty acid (FA) or nonmonomeric protein contamination in HSA were unlikely to be playing a role in the described effects, as 96% pure, FA-rich (Buminate) and 99% pure, FA-free HSA had identical effects on liposomal C activation. While highlighting a new modulatory mechanism on liposomal C activation, the above data raise the possibility that deposition of extravasated HSA at sites of tissue injury may serve a hitherto unrecognized proinflammatory function. ß 2002 Elsevier Science B.V. All rights reserved.

Keywords: Serum albumin; Liposome; Complement; Inflammation; Phospholipid bilayer; Polycarbonate membrane; Natural antibody

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