Activation of human mast cells by aggregated IgG through FcγRI: additive effects of C3a.

Human mast cells (huMC) increase surface expression of FcγRI (CD64) in response to IFNγ. Subsequent receptor aggregation of FcγRI using CD64-specific F(ab′)(2) or antibody directed against FcγRI-bound IgG results in cell activation. Human mast cells may be observed degranulating in inflammation associated with autoimmune disease and where IFNγ is produced. We sought to determine if human mast cells cultured in IFNγ would degranulate in response to aggregated IgG, what mediators might be generated (i.e., cytokines and eicosanoids), and whether C3a might enhance such activation. Activation of IFNγ-treated huMC sensitized with 1 μg/ml aggregated IgG(1) resulted in 15-30% degranulation (β-hexosaminidase release), which was half-maximal by 7.5 min; no degranulation was observed using heat-generated aggregates of IgG(2), IgG(3), or IgG(4). Activation using aggregated IgG(1) led to PGD(2) and LTC(4) generation as well as enhanced IL-3, IL-13, GM-CSF, and TNFα production. Preincubation of cells with F(ab′)(2) from CD64-specific clone 10.1 reduced aggregated IgG(1)-mediated β-hexosaminidase release by 38% while degranulation was unaffected by blocking FcγRII with F(ab′)(2)-specific antibody (clone 7.3). Simultaneous activation of huMC via aggregated IgG and C3a led to additive degranulation. These data support a mechanism by
which mast cells may contribute to the inflammatory component in fibrosis, vasculitis, and arthritis.