Processing-dependent and -independent pathways for recognition of iodinated contrast media by specific human T cells

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BACKGROUND: One to three percent of patients exposed to intravenously injected iodinated contrast media (CM) develop delayed hypersensitivity reactions. Positive patch test reactions, immunohistological findings, and CM-specific proliferation of T cells in vitro suggest a pathogenetic role for T cells. We have previously demonstrated that CM-specific T cell clones (TCCs) show a broad range of cross-reactivity to different CM. However, the mechanism of specific CM recognition by T cell receptors (TCRs) has not been analysed so far.

OBJECTIVE: To determine how T cells specifically recognize CM. METHODS: CM-specific TCCs were generated from human blood of three CM-allergic patients and a specific TCR was transfected into a mouse T cell hybridoma. Functional analysis such as proliferation assays, IL-2 secretion assays, and calcium influx experiments were performed using irradiated, glutaraldehyde-fixed, CM-pre-incubated, human leucocyte antigen (HLA)-DR-matched or -mismatched antigen-presenting cells (APCs), and HLA-blocking antibodies.

RESULTS: We identified two mechanisms of T cell stimulation: some TCCs and the transfectant reacted to CM independent of uptake by APCs because proliferation/IL-2 secretion occurred in the presence of glutaraldehyde-fixed APCs, and intracellular calcium increased within seconds after drug addition. Other TCCs required functional APCs, compatible with uptake and presentation of CM on MHC-class II molecules, as implied by three findings: (1) glutaraldehyde fixation of APCs abrogated presentation; (2) CM could not be washed away from CM-pre-incubated APCs; and (3) the optimal pulsing time was 10-20 h. Because allogeneic, MHC-matched, CM-pulsed APCs could induce proliferative responses as well, the ability of CM uptake and presentation is not unique to APCs from patients with CM-induced delayed hypersensitivity.

CONCLUSION: Our data suggest that CM may be stimulatory for T cells either by direct binding to the MHC-TCR complex or by binding after uptake and processing by APCs. This questions the assumed inert nature of CM.

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