AB003. Increased myeloid dendritic cells and TNF-α expression predicts poor response to hydroxycoloquine in cutaneous lupus erythematosus

Majid Zeidi[1,2], Hee Joo Kim[1,2,3], Krisha Desai[1,2], Rachel Lim[1], Victoria P. Werth[1,2]

[1]Corporal Michael J. Crescenz VAMC, Philadelphia, PA, USA; [2]Department of Dermatology, University of Pennsylvania, Philadelphia, PA, USA; [3]Department of Dermatology, Gil Medical Center, Gachon University College of Medicine, Incheon, Korea

Background: Although antimalarials are the primary treatment for cutaneous lupus erythematosus (CLE), not all patients are equally responsive. We investigated whether different inflammatory cell population and cytokine profiles in lesional CLE skin could affect the antimalarial responsiveness, and if hydroxychloroquine (HCQ) and quinacrine (QC) differentially suppress inflammatory cytokines.

Methods: CLE patients were grouped according to their response to antimalarials (HCQ *vs.* HCQ + QC). Inflammatory cell composition of plasmacytoid dendritic cells (pDCs), myeloid dendritic cells (mDCs), neutrophils, and macrophages, and gene expression of type I interferon (IFN) signatures and tumor necrosis factor (TNF) α were evaluated in CLE lesions. The suppressive effects of antimalarials on toll like receptor (TLR)-mediated production of inflammatory cytokines (IFN-α, TNF-α, and IL-6) and NF-κB phosphorylation were evaluated on peripheral blood mononuclear cells (PBMCs) isolated from CLE patients.

Results: Among inflammatory cells, only mDCs were significantly increased in the HCQ + QC group compared to HCQ group. Gene expression of type I IFN signatures, including LYE, OAS1, OASL, ISG15, and MX1, was significantly upregulated in HCQ group, whereas TNF-α level was higher in the HCQ + QC group. HCQ and QC had differential suppressive effects on cytokine production and NF-κB phosphorylation. QC inhibited TNF-α and IL-6 more profoundly than HCQ did, while both QC and HCQ inhibited IFN-α from TLR-stimulated PBMCs. QC also suppressed phospho-NF-kB p65 more than HCQ.

Conclusions: Increased numbers of mDCs with higher TNF-α expression might contribute to HCQ-refractoriness and a better response to QC. Differential suppressive effects of HCQ and QC could also affect antimalarial responses in CLE patients

Keywords: Cutaneous LE; hydroxychloroquine; clinical response biomarkers

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