

LOW RECRUITMENT OF IMMUNE CELLS AND PRESERVED EXPRESSION OF CYTOKINES AND GROWTH FACTORS IN THE MARGIN OF DIABETIC FOOT ULCERS

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Aim: We examined by immunohistochemistry infiltrating cells phenotype and expression pattern of adhesion molecule on leukocytes, dermal fibroblasts and endothelial cells as well as the expression of various cytokines, chemotactic and growth factors and their receptors in the margin of diabetic foot ulcers and in normal nondiabetic foot skin.

Results: Although there was accumulation of granulocytes on the surface and superficial layers of granulation tissue, rare perivascular granulocyte infiltrates in the dermis were seen. Moreover, lack of macrophage and CD3+ T cell infiltrates was observed. In contrast, there was increased intensity of CD1a staining of Langerhans' cells in the epidermis and papillary dermis ($P < 0.05$). Fibroblasts revealed increased presence in the ulcer margins compared with normal skin ($P < 0.05$). Skin endothelial cells expressed stronger von Willebrand factor (f.VIII) and E-selectin compared with normal skin ($P < 0.05$). Our study found significantly elevated expression of transforming growth factor β 1 (TGF- β 1) and type I TGF- β receptors (TGF β RI), granulocyte macrophage colony stimulating factor (GM-CSF), and epidermal growth factor (EGF) in KC in the ulcer margin ($p < 0.05$). Significantly increased expression of monocyte chemotactic protein-1 (MCP1), GM-CSF, CXCR1, and TGF β RI and decreased expression of interleukin (IL) -10, IL-15 and TGF β 1 were observed in ulcer dermal EC ($p < 0.05$). There was a lack of up-regulation of IL8, CCR2A, IL10 receptor, GM-CSF receptor, platelet-derived growth factors and their receptors, VEGF and its type II receptor, EGF receptor, insulin-like growth factor-1, and nitric oxide synthase (NOS)-2 in both KC and EC cells in the ulcer. Finally, there was a lack of upregulation of IL10, IL15 in KC and of EGF, basic fibroblast growth factor and NOS-3 in EC in the ulcer margins.

Conclusion: Our study provides evidence that, lack of upregulation of some angiogenic and leukocyte chemotactic factors may account for a poor formation of granulation tissue and chronicity of ulcer epithelialization.