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Characterization of the Diabetic Foot Ulcer Microenvironment by Assessment of Wound Fluid Cytokines, Chemokines and Soluble Receptors

Löffler M[1,2], Schmohl M[3], Schneiderhan-Marra N[3], Joos T[3], Königsrainer A[1], Beckert S[1]
[1]Department of General, Visceral and Transplant Surgery, University of Tuebingen/ Germany, [2]Department of Immunology, University of Tuebingen/ Germany and [3]Natural and Medical Sciences Institute (NMI) at the University of Tuebingen, Reutlingen/ Germany

Introduction: In diabetic foot ulcers, markers of chronic inflammation have been shown predictive for non-healing, supporting the impact of the local wound microenvironment on successful tissue repair. In this study we aimed to characterize the local wound microenvironment by measuring mediators of inflammation such as cytokines, chemokines and soluble receptors. **Methods:** Consecutive diabetic foot ulcer patients without clinical signs of soft-tissue infection were enrolled at the Department of Surgery, University of Tuebingen, Germany. Wound fluid was obtained by superficial wound swabbing and subsequent centrifugation. Cytokines and soluble receptors were assessed by bead-based sandwich immunoassays. In case detection limits were reached, the respective values were assigned. Results are presented as median [min-max]. **Results:** Samples were obtained from 20 patients with a median age of 70 years [29-83]. Median wound size was 8,7 cm^2 [0,19-132,3]. Non-palpable pulses were present in 52% and probing to bone was positive in 54% of patients. Multiplexed immunoassay analysis revealed the following amounts of cytokines and chemokines: IL-17 54 pg/ml [<14-986], IFNγ <2,8 pg/ml [<2,8-104], IL-8 >100 ng/ml [58,1->100], TNFα 557,3 pg/ml [68,9-7071], IP10 5,6 pg/ml [<2,7-3200], IL-1ß 21,7 ng/ml [0,3->100], IL-1α 5,2 ng/ml [0,6-672], IL-6 89,6 ng/ml [1,6->100], MIP-1ß 1,9 ng/ml [0,03-7,9], MCP-1 2,3 ng/ml [0,06-26,8], IL-5 5,7 pg/ml [0,3-256], TARC 23,7 pg/ml [<9,9-1142], TSLP <3,4 pg/ml [<3,4-21,3], IL-12p70 <22,7 pg/ml [<22,7-1725], IL-10 47,9 pg/ml [<1,6-520], IL-4 <6,7 pg/ml [<6,7-449], IL-13 <172 pg/ml [not detected], Eotaxin <84,4 pg/ml [84,4-2044], IL-1ra >100 ng/ml [27,3->100]. Measuring a panel of eight different soluble receptors and cell adhesion molecules, the following amounts were detected: VCAM 12,9 ng/ml [0,13->160], IL-2Ra 0,60 ng/ml [<0,13-17], gp130 39,1 ng/ml [8,6-53,4], TNFRI14,4 ng/ml [0,9->18], TNFRII >120 ng/ml [3,7->120], E-Selectin 9,9 ng/ml [<2,7-79,8], ICAM1 11,6 ng/ml [1,4->320], Fas 171,2 ng/ml [0,57->400]. **Conclusions:** Wound fluid obtained from diabetic foot ulcers was characterized as a rich source of cytokines, chemokines and soluble receptors. Since persistent inflammation is intricately connected with the local micro-milieu, at least some of the detected analytes might evolve as helpful prognostic biomarkers for estimating chances of healing in the future.