

Activation of anti-inflammatory cell pathways in skin ulcers upon photodynamic therapy

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This study was aimed at assessing the variations in skin histology in ulcers caused by chronic venous insufficiency of the lower extremities, upon photodynamic therapy (PDT). The study was approved by the ethical committee of Azienda Sanitaria Firenze. Patient assessment included clinical history, physical examination and echo-Doppler sonography. Four to five sessions of photodynamic therapy (20% 5-aminolevulinic acid gel application followed by 3 min irradiation at 630 nm, total 180 J/cm²) were administered to 15 patients refractory to previous conventional treatments. Skin biopsies were embedded in freezing tissue medium and quick frozen. Cryosections were post fixed in cold acetone. Sections from each case were stained with hematoxylin and eosin or labelled with primary antibodies against the following antigens: MHC-II class, DC-SIGN, CD68, CD163, BDCA2, CD4, CD25, TNF alpha. In some instances avidin and Ulex europaeus lectin were used to tag mast cells and vessels respectively. Upon treatment, MHC-II signal intensity per positive cell and TNF alpha signal in mast cells increased, as well as the numbers of CD68 positive/CD163 positive cells (M2 macrophages), BDCA2 positive (plasmacytoid dendritic) cells and CD4 positive/CD25 positive (Treg) lymphocytes number. Diffuse tissue TGF beta positivity also increased. DC-SIGN positive cells decreased in number. Mast cells were found in proximity of dendritic cells and of vessels; plasmacytoid dendritic cells were found in proximity of T reg cells. Clinically, mild decrease in ulcer size and granulation at ulcer borders were observed. Therefore treatment apparently led to the activation of cells and of intercellular communication pathways possibly down-regulating the inflammatory response. The same treatment had been shown to increase mast cell expression of basic fibroblast growth factor and fibroblast number (1), potentially responsible for increased production of extracellular matrix. Both types of effects could be synergistically beneficial for ulcer repair.

This work was supported by the Italian Ministry of Education, MIUR FIRB 2010 and MIUR PRIN-2009; University and Research, Ente Cassa di Risparmio di Firenze (Grant n. 3681 year 2012) and Foemina Foundation.

References

- [1] Corsi A., Lecci P.P., Bacci S., Cappugi P., Pimpinelli N. (2016) Early activation of fibroblasts during PDT treatment in leg ulcers. *G. Ital. Dermatol. Venereol.* 151: 223-229.

Keywords

Dendritic cells; mast cells; photodynamic therapy; PDT; T cells.