AUTOIMMUNE CONNECTIVE TISSUE DISEASES

CLINICO-PATHOLOGICAL CHARACTERIZATION OF PATIENTS WITH LOCALIZED SCLERODERMA AND RESPONSE TO UVA-1 PHOTOTHERAPY: IN VITRO AND IN VIVO SKIN MODELS.

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Introduction: Localized scleroderma (LS) is a rare autoimmune disorder characterized by an altered fibroblast function with excessive collagen production in cutaneous and subcutaneous tissues, reaching muscular fascia in its very rare deep variant, eosinophilic fasciitis (EF). Treatment is often delayed and frustrating, causing disfiguring scarring and reduced life quality. Though UVA-1 phototoherapy is currently recommended for limited and diffuse forms, we still do not know how this treatment acts on the sclerodermic tissue.

Objective: We aimed to evaluate the response to medium-dose UVA-1 phototherapy of a series of patients with either superficial (morphea) or deep (EF) LS, in order to obtain clinic-functional and laboratory correlates on lesional scleroderma fibroblasts.

Materials and Methods: Clinical and anamnestic data, before, during and after phototherapy were collected in order to detect possible predictive factors; the response to phototherapy treatment was evaluated and monitored through standardized lesion mapping, clinical-functional LS scores, DLQi questionnaires and high resolution ultrasound (HRUS); primary fibroblasts cell lines were obtained from lesional skin before and after phototherapy for testing the response in vitro UVA-1 irradiation and investigating the gene expression profiling of both pro-fibrotic/anti-fibrotic pathways.

Results: A total of 22 patients, 14 with morphea and 8 with EF (F:M=5:1, age~49yrs) were

enrolled: chronic micro-traumatism and BMI>26 resulted to be predisposing factors. HRUS demonstrated a significant reduction of dermal fibrotic band. In vitro UVA-1 irradiation showed: maintained cell viability for all administered doses (0.1/0.5/1/5j/cm2), reduced cell count and collagen production, contraction after high doses. Genetic profiling examination demonstrated: reduced transcription (RT-PCR) of TGF-β_Smad2/3 dependent pathway, TGF-β1, Fn14 and TIMP-1 (pro-fibrotic pathways), augmented synthesis of MMPs and IL-1β.

Conclusions: HRUS and LoScat score proved to be the most accurate monitoring tolls in these subset of patients. Medium-dose UVA-1 are likely to elicit local anti-fibrotic inflammatory reaction that stimulates collagen digestion and ECM remodeling.