CIRCULATING COLLAGEN TURNOVER MARKERS ARE SPECIFICALLY CHANGED IN VERY EARLY SYSTEMIC SCLEROSIS

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Background: Timely diagnosis of patients with very early systemic sclerosis (veSSc) is essential for their personalized and optimal management. We hypothesise that changes in serum-based extracellular matrix (ECM) turnover biomarkers are already detectable in patients with veSSc, even before occurrence of specific clinical signs.

Objectives: To investigate circulating ECM turnover markers as potential biomarkers for veSSc.

Methods: Patients with veSSc, n=42, defined as presence of Raynaud’s syndrome and at least one of puffy fingers, positive antinuclear antibodies or pathological nailfold capillaroscopy, who did not meet any classification criteria for SSC, were compared to healthy controls (HC, n=29). Longitudinal assessment, data and sera collection were conducted by EUSTAR standards. ECM-degradation (BGM, C3M, C4M, C6M) and ECM-formation biomarkers (PRO-C3, PRO-C4, PRO-C5) were measured in serum using ELISA assays. The statistical analyses included Mann-Whitney U, Spearman correlation and ROC analysis. Using Kaplan-Meier plots and univariable Cox regression, we explored if biomarkers can predict progression towards definite SSC (fulfillment of ACR/EULAR criteria or minimum two points increase in the criteria score) during the longitudinal follow-up.

Results: Compared to HC, veSSc patients showed a deregulated turnover of type III and IV collagen, with higher degradation (higher C3M, C4M, both p<0.0001 and PRO-C3, PRO-C4, PRO-C5, both p<0.0001). The biglycan degradation biomarker BGM was also higher in veSSc (p=0.006), whereas the degradation biomarker for type VI collagen, C6M, was lower than in HC (p=0.002). In the ROC analysis, biomarkers of type III and IV collagen distinguished between veSSc and HC: C3M, AUC=0.95, p<0.0001; C4M, AUC=0.97, p<0.0001; turnover ratios PRO-C3/ C3M, AUC=0.80, p<0.0001; PRO-C4/C4M, AUC=0.97; p<0.0001 (Figure 1b).

Median follow up was 4.5 years (range 0.5-7.9 years), mean age was 50±2.2 years. 14/42 veSSc patients fulfilled the ACR/EULAR classification criteria at follow-up. ECM turnover is already altered in veSSc patients compared to HC. Biomarkers of type III and IV collagen distinguished between veSSc patients and HC, which may indicate them as potential biomarkers for the detection of veSSc in addition to the established immunological and capillaroscopic criteria.

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AUTOANTIBODY STATUS IN DERMATOMYOSITIS AND POLYMYOSITIS PATIENTS DEFINES BOTH CANCER RISK AND SURVIVAL WITH ANA NEGATIVITY IN CASES WITH CONCOMITANT CANCER HAVING A WORSE SURVIVAL

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Background: We previously reported that ANA-negative cases with systemic sclerosis (SSc) and concomitant cancer had a worse survival than ANA-positive cases with associated cancer possibly suggesting that humoral mediated autoimmunity conferred a survival advantage (1). Dermatomyositis (DM) and polymyositis (PM) are two immune-mediated myopathies associated with numerous autoantibodies.

Objectives: The present large-scale, population-based study tested the hypothesis that humoral autoimmunity associated with cancer in solid/haematological malignancies impacted on DM/PM patient survival.

Methods: Over 2000 cases with either DM or PM were recruited from the Clalit Health Service (CHS) chronic diseases registry, one of the largest healthcare maintenance Israeli organization, serving approximately half of the entire country’s population. Over 10000 matched controls were recruited. The data collected range from 2000 to 2018.

Results: Altogether 12,278 subjects were recruited (2,085 cases, and 10,193 controls, 5,042 males, 41.1%, and 7,236 females, 58.9%). Among cases, 1,475 individuals (70.7%) were diagnosed with DM, whereas 610 (29.3%) with PM. Mean age was 47.81±22.51 years. 1,379 cases of cancers (11.2%) were diagnosed. At the univariate analysis and as expected, the rate of malignancies was