CXCL10/CXCL11 SERUM MEASUREMENT AS POTENTIAL PREDICTOR OF SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc), amongst autoimmune rheumatic disorders, shows a heterogeneous and unpredictable course from stable/mild involvement to progressive/late stage, when irreversible multiorgan fibrosis occurs. Early SSc diagnosis remains a clinical challenge; a delay in diagnosis leads, in turn, to therapy delay and more severe patient disability. Earliest vascular immune-mediated alterations are critical in SSc, which, indeed, has been referred to as a 'vascular' disease. Recognition of biomarker(s) involved in earliest vascular derangements might represent a clinical tool potentially useful for therapeutic approach. Blood level of chemokines IFN-γ-inducible protein 10 (IP-10/CXCL10) and IFN-inducible T cell alpha chemoattractant (I-TAC/CXCL11), both involved in endothelial dysfunction, has been shown to associate with worse SSc prognosis.

Objectives: To investigate possible modifications of circulating CXCL10/CXCL11 in the shift from very early diagnosis of SSc (VEDOSS), when vasculopathy and fibrosis are still at very low degree, to definite SSc. Associations between chemokines and capillaroscopic pattern, autoantibody positivity were evaluated.

Methods: Multiplatform luminex technology was used to analyse CXCL10/CXCL11 in total 62 sera, 34 from VEDOSS and 28 from SSc patients, fulfilling the new ACR/EULAR 2013 classification criteria; none of the subjects were treated for SSc. Within VEDOSS group, we selected 29 sera of subjects with follow up (40.67±5.46 months) and, for each patient of this subcohort, chemokine levels were assessed at follow up (T1) and compared with basal level (T0). Appropriate tests were used for sample distribution and statistical analysis.

Results: Serum CXCL10/CXCL11 were significantly lower in all VEDOSS (CXCL10: 236.00±40.90 pg/ml; CXCL11: 38.00±6.97 pg/ml) vs all SSc sera (CXCL10: 633.90±97.60 pg/ml; CXCL11: 267.70±76.10 pg/ml; p<0.001 and p<0.01, respectively). Moreover, in VEDOSS subcohort, basal chemokine values (T0) were significantly higher (p<0.01) in sera of subjects who subsequently shifted to SSc (CXCL10: 237.34±27.34 pg/ml; CXCL11: 45.12±7.18 pg/ml) vs subjects not developing SSc (CXCL10: 140.06±16.17 pg/ml; CXCL11: 20.17±4.06 pg/ml). Sera analysed at follow up (T1) showed a significant increase of both chemokines vs T0 values only in patients who developed SSc (CXCL10: 536.18±54.98 pg/ml; CXCL11: 250.21±86.53 pg/ml; p<0.001; CXCL10/CXCL11 retained significant predictive values for SSc development with 165 pg/ml and 29.67 pg/ml cut-off values, respectively, as shown by receiver operating characteristic (ROC) analysis. Significant correlation of CXCL10/CXCL11 with nailfold capillaroscopic pattern was observed.

Conclusions: CXCL10/CXCL11 blood level measurement in VEDOSS patients potentially represents a noninvasive biomarker associated with vascular modifications – as shown by capillaroscopic pattern – predictive of SSc.

REFERENCES:

DECREASED DICKKOPF-1 EXPRESSION IN CLINICALLY UNINVOLVED SKIN FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Evidence suggests that the Wnt pathway is a critical mediator of the fibrotic process. The activity of the pathway is tightly regulated by several soluble inhibitors such as Dickkopf-1 (Dkk-1). We, among others, have previously shown that Dkk-1 is absent from scleroderma skin in sharp contrast to skin from healthy subjects where it is clearly expressed. Observations: Up until now, Dkk-1 skin expression has only been assessed in established fibrosis, in biopsies obtained from clinically involved areas. We aimed to assess whether the striking lack of Dkk-1 skin expression is also evident in a