Background: Endothelial-to-mesenchymal transition (EndoMT), a newly recognized type of cellular transdifferentiation, seems to be involved in systemic sclerosis (SSc) pathogenesis. In this process endothelial cells lose their specific markers, and acquire a mesenchymal phenotype, thus expressing cell products such as alpha smooth muscle actin (α-SMA) (1,2). Circulating endothelial progenitors cells (EPCs) derive from bone marrow stem cells and contribute to de novo vessels formation. Several studies, although with conflicting results, have shown that EPCs in the peripheral blood of patients with SSc are impaired in their number and function (3).

Objectives: to assess the expression of α-SMA, possibly associated with a pro-mesenchymal switch (EndoMT) of the circulating Early (CD34+KDR+CD 133+) and Late (CD34+KDR+) EPCs in the peripheral blood of SSc patients and of patients with Very Early Diagnosis of Scc (VEDOSS) compared with healthy controls (HC) using flow cytometry.

Methods: we enrolled 11 patients (7 SSc and 4 VEDOSS), classified according to the classification criteria for Scc (4) and for VEDOSS not fulfilling SSc criteria (5), and 10 HC. Phenotypic characterization was performed as previously described by Vasa et al. using a FACS Calibur (BD Immunocytometry Systems). EPCs number was expressed as a percentage of cells within the lymphocyte gate.

Results: we found a significantly higher percentage of α-SMA positive Early EPCs (CD34+KDR+CD 133+α-SMA+) in all patients respect to HC (0.06% ±0.03 vs 0.03% ± 0.01; p=0.0149) particularly in VEDOSS patients (0.07%±0.01 vs 0.03±0.01 p=0.008). Moreover, in VEDOSS patients, also the percentage of Early EPCs (CD34+KDR+CD 133+), Late EPCs (CD34+KDR+) and α-SMA positive Late EPCs (CD34+KDR+α-SMA+) were significantly higher than in HC (0.05%±0.01 vs 0.03%±0.01 p=0.05; 0.07%±0.01 vs 0.04±0.002 p=0.04; 0.06%±0.01 vs 0.04%±0.02 p=0.05). Besides Early EPCs and α-SMA positive Early EPCs percentages seem to be significantly reduced in patients taking iloprost (p=0.05 and p=0.01 respectively), calcium channel blockers (CCB) (p=0.05 and p=0.03) and DMARDs (p=0.017 and p=0.013).

Conclusion: EndoMT seems to be involved in the pathogenesis of SSc and circulating EPCs seem to be impaired in number and function in SSc patients. In our study we found higher levels of EPCs, in particular α-SMA positive Early EPCs in both groups of patients (SSc and VEDOSS) respect to HC. Thus, we can hypothesis a predominant pro-mesenchymal phenotype of this kind of EPCs. This could be considered the expression of the involvement of EPCs in EndoMT process and could better explain the controversial role of EPCs in SSc pathogenesis. Very interesting is the finding of a lower percentage of Early EPCs, and in particular of α-SMA positive Early EPCs, in those patients taking iloprost, CCB and DMARDs, suggesting a potential effect of these drugs on this subgroup of EPCs.

REFERENCES:

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