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Editorial

The search for new biomarkers in systemic sclerosis

A busca por novos biomarcadores na esclerose sistêmica

Systemic sclerosis (SSc) is a chronic autoimmune rheumatic disease with a heterogeneous course, whose follow-up and treatment remain challenging. In this context, the identification of biomarkers for assessing the disease activity, the risk of involvement of internal organs, and of their prognosis is extremely important.

In recent years, there have been many advances in the identification of serum biomarkers and of certain phenotypes associated with an increased risk of developing certain manifestation such as interstitial lung disease, pulmonary arterial hypertension, and renal scleroderma crisis.[1] Thus, the presence of anti-Scl70 antibodies is associated with the diffuse cutaneous clinical form and with a worse prognosis. Serum KL-6, surfactant D protein, lysyl oxidase (LOX), tenascin-C, CXCL4, and CCL18 seem to be promising biomarkers for assessing the severity of fibrosis in interstitial lung diseases associated with SSc.[2,3] On the other hand, the levels of natriuretic peptides BNP and NT-proBNP have been used as pulmonary arterial hypertension biomarkers.[1] A recent study showed significantly higher serum levels of placental growth factor and soluble receptor 1 of VEGF in patients with pulmonary hypertension compared to SSc patients without pulmonary hypertension, indicating their potential as biomarkers for pulmonary hypertension.[4] Despite these advances, further studies are required in order to identify and validate biomarkers for patients with SSc.

In this issue, four studies evaluating different clinical and laboratory characteristics of patients with SSc were published.

Olewicz-Gawlik et al. evaluated the serum levels of Clara cell protein (CC16) in patients with SSc.[5] CC16 is a protein expressed in the respiratory tract, secreted by cells located in the bronchial epithelium, which has anti-inflammatory and anti-oxidant properties. Although no difference was found in serum levels of CC16 between SSc patients and controls, an association between CC16 levels and a more severe pulmonary involvement was observed. The results corroborate the findings of a previous study, which found an association between levels of CC16 and lung activity in scleroderma patients,[6] and suggest that CC16 may be a potential serum biomarker in the evaluation of interstitial lung disease.

On the other hand, Sampaio-Barros et al. found a significant correlation between serum levels of 25-hydroxyvitamin D (25OHD) and quality of life in patients with diffuse SSc.[7] These authors also found a negative correlation between a higher degree of devascularization in nail fold capillaroscopy and levels of vitamin D, as well as reduced levels of vitamin D in patients with anti-Scl70 antibody positivity. These results suggest that serum levels of vitamin D can be used as biomarkers for worse quality of life. However, one cannot conclude that the reduction in vitamin D levels would be directly related to a poorer quality of life of these patients, or if such correlation is related to a more severe disease since the authors assessed only patients with diffuse disease. On the other hand, the findings are consistent with many studies describing a high frequency of 25OHD deficiency in patients with SSc. Additionally, *in vitro* studies suggest that multiple endogenous forms of vitamin D3 have antifibrotic properties and may be a future therapeutic target in SSc.[8]

Finally, two studies of the same group evaluated two aspects that demonstrate the clinical heterogeneity of SSc.[9,10] In the first study, a high frequency of polyautoimmunity and of familial autoimmunity in a group of 60 patients with SSc was observed.[9] The second study aimed to analyze the characteristics of patients with and without arthritis or with overlap syndrome with rheumatoid arthritis.[10] The frequency for arthritis was 26%, and that for overlap with rheumatoid arthritis was 6.6% – findings similar to previous studies. Interestingly, patients with arthritis and overlap syndrome showed a tendency to a poorer quality of life compared to

patients without arthritis. There was also a high frequency of radiographic changes characterized by joint space narrowing and/or subchondral bone erosion, suggesting that, in these patients, arthritis can develop more aggressively.

In summary, the studies published reveal the multiple facets of SSc and reinforce the need to find reproducible, easily applicable in clinical practice, biomarkers in order to identify patients at risk of developing more serious manifestations and, finally, for an early treatment.

Conflicts of interest

The author declares no conflicts of interest.

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