Analysis of the evolution of UCTD to defined CTD after a long term follow-up

Sirs,

It is well known that the onset of connective tissue diseases (CTD) may be undifferentiated (1-6). The term undifferentiated connective tissue diseases (UCTD) has been widely used to identify CTDs not fulfilling classification criteria for defined connective tissue diseases (CTD) (1-4). The question as to whether these conditions represent an atypical or delayed onset of systemic autoimmune diseases or distinct clinical entities has been discussed in the literature over the past decades. In previous papers we have described the outcome of a cohort of 91 UCTD patients followed at our Unit, showing that about 30% of patients with an undifferentiated onset will develop a defined CTD, mainly SLE, while the remaining will maintain an undifferentiated profile, suggesting that stable UCTD represent distinct clinical entities (1-4).

Here we describe the outcome of our cohort of 91 UCTD patients, after an additional period of 5 years since the last analysis. Out of the original cohort, two patients died of causes not related with the CTD during follow up, six UCTD patients with a follow up of less than 5 years were excluded from the study, therefore 83 patients (F: 80, M: 3) have been included. Fifty-three patients remained undifferentiated over a mean follow up of 181 months and constitute the "stable UCTD". The most common manifestations of stable UCTD were joint involvement, Raynaud's phenomenon, leukopenia, thrombocytopenia. As previously described, antinuclear antibodies were positive in 100%, anti-Ro/SSA in 40%, anti-RNP in 19%, anti-dsDNA (19%), ACLA IgG (13%), anti-La/SSB (6%), anti-Sm in 2% of these patients. At the last observation 14 patients (26%) did not receive any therapy, of the 39 patient under treatment, 27 were treated with glucocorticoids, 25 with anti-malarial drugs, no patients were treated with immunosuppressive drugs.

During the follow up 30 patients (36%) developed a defined CTD, in detail 22 patients systemic lupus erythematosus (SLE), 3 primary Sjögren's syndrome (pSS), 3 rheumatoid arthritis (RA), 1 systemic sclerosis (SSc) and 1 mixed connective tissue disease (MTCD). Interestingly the evolution to SLE occurred earlier in the disease course (mean disease duration 62.4 months), while the development of the other CTDs occurred late (mean 165.8 months). Whether these "late-occurring CTDs" have a slowly evolving clinical picture cannot be derived from our cohort due to the small number of patients and deserves additional multicenter evaluations. A delayed identification of slowly evolving CTDs may have therapeutic and prognostic consequences and may be related with the paucity of disease specific assessment and biomarkers that could guide in the diagnosis, particularly in the presence of less defined clinical pictures (7, 8).

These results show that with a prolonged follow up, an increased number of UCTD patients will develop a defined CTD, nonetheless the majority of UCTD patients will maintain an undifferentiated profile over time. As in other CTDs, these patients are treated with low dose steroids and antimalarial drugs, while the use of immunosuppressive drugs is rare (1-4, 9). The identification of specific disease biomarkers could help the early identification of those patients who will develop defined CTDs and may impact on therapeutic approaches.

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Competing interests: none declared.

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