Letters to the Editor

Re: Tager and Tikly. Clinical and laboratory manifestations of systemic sclerosis (scleroderma) in Black South Africans

Sr, We read with interest the article by R. E. Tager and M. Tikly entitled ‘Clinical and laboratory manifestations of systemic sclerosis (scleroderma) in Black South Africans’ [1]. The authors claimed that there had been no studies on the overall spectrum of clinical and laboratory manifestations of systemic sclerosis (SSc) in the general Black population. Unfortunately, the authors have not focused enough attention on some clinical aspects of the disease and, in particular, on the presence of autoantibodies.


Almost 20 yr have passed since the first detailed report about autoantibodies in SSc [5]. Further refinements in the methodology of autoantibody detection followed, some of them increasing the sensibility of the assays, which may, on the other hand, lessen their overall discriminatory values. Some postulates concerning the detection of autoantibodies have been accepted during the meetings of the European Workshop for Rheumatology Research—The Consensus Finding Study Group on Antibodies in Rheumatic Diseases (EWRR). They include methods which have been validated by leading European laboratories undertaking analysis of sera in the workshops. These methods have proved to be practically useful and leading to consistent inter-laboratory results [6].

Therefore, we think that several statements in the article [1] should be discussed in more detail. From the clinical point of view, the definition of myositis was weakly based, omitting electromyography, which made the authors unable to discern between inflammatory myositis and myopathy concomitant with SSc [7]. Disregarding this fact, the percentage of myositis was unusually high [1], as the frequency of myositis does not exceed 19%, even in diffuse scleroderma, according to Medsger [8].

As for the presence of specific autoantibodies inferred from the antinuclear antibody (ANA) staining pattern, it is believed that ANA patterns are only indicative. Precise determination of antibody specificities always needs confirmation by other laboratory techniques such as counterimmunoelectrophoresis (CIE), enzyme-linked immunosorbent assay (ELISA), Western blotting, RNA or protein precipitation. This holds true especially because autoimmune sera mostly contain a mixture of antibody activities at different concentrations ([9, 10] our observations on over 10000 sera tested on Hep2 cells per year).

The speckled nuclear pattern, more precisely speckled/homogeneous nuclear staining and homogeneous staining of the chromosomes in metaphase, is indeed seen in sera with anti-Scl-70 antibodies [4, 11, 12]. In cases of polyclonal sera (containing antibodies to Ro, La, U1RNP, Sm etc.), there can be some confusion due to mixed pattern staining. In SSc overlapping with myositis, one should be extremely aware of other possible antibody specificities, i.e. against Ku, PM/Scl, fibrillarin, U1RNP, and Jo-1. Except for anti-Jo-1 these antibodies contribute similar nucleolar patterns on Hep2 cells. Anti-Ku antibody is found in 50% of patients with polymyositis–scleroderma overlap syndromes and in a high number of scleroderma patients with primary pulmonary hypertension [13–15]. The antigen for antibodies against PM/Scl or nucleolin complex comprises at least 10 polypeptides, the major antigenic components having molecular weights of 75 kDa and 100 kDa. These antibodies give a similar nucleolar pattern of homogeneous nuclear staining to anti-Ku antibodies [16]. Anti-fibrillarin antibodies, highly specific for SSc associated with skeletal muscle disease and pulmonary hypertension, are more frequent in Blacks. They are directed towards the 34 kDa fibrous protein in U3 small nuclear ribonucleoprotein particles bound to DNA and involved in ribosomal RNA processing [17, 18]. Such antibodies...
yield a nucleolar clumpy pattern (brightly clustered large granules in the nucleoli of interphase cells), which tends to homogeneity. In mitotic cells, the antigens remain associated with condensed chromosomal material. The antibodies are rarely found in association with anticentromere or anti-Scl-70 antibodies.

The presence of 8% anti-Sm antibodies in SSc [1] is highly unlikely regardless of the Black population studied. We were able to find only two reports of anti-Sm antibodies in SSc without overlap syndromes. Clegg et al. [19] detected two anti-Sm-positive patients in 46 SSc cases, using an immunodiffusion technique. Barakat et al. [20] were able to find autoantibodies in 6.3% of 32 SSc patients by ELISA, using the synthetic peptide (fragment 1–20 of the Sm D autoantigen). Numerous other studies, just to mention some of them, did not find any association of anti-Sm autoantibodies with SSc: Bernstein et al. [21] using CIE, immunodiffusion and facilitated immunoprecipitation from HeLa cell extracts in 55 SSc patients, Homma et al. [22] in 24 SSc patients using immunodiffusion, 3P immunoprecipitation and radioimmunoassay, De Rooij et al. [23] using an immunoblotting technique in 33 SSc patients, Bunn et al. [4] in 374 SSc patients using CIE (our observations using CIE and immunoblotting technique).

In the EWRR consensus trials [6], the performance of ELISA for anti-Sm detection was found to be less satisfactory because of the relatively complex molecular structure of the antigen, pointing to the necessity of using at least two methods to confirm anti-Sm activity [6, 10, 24]. Commercial ELISA kits can sometimes give a very high rate of false positive results (unpublished observation of the members of EWRR, including our experience).

We believe that the presence of 42% anti-RNP (U1RNP?) was extremely high as well [1]. The majority of papers describe the presence of anti-U1RNP in SSc patients without overlap syndromes, but the prevalence was regularly not higher than about 10%: 2.5% [21], 7% [19], two of 33 SSc patients [23], one of nine patients, using CIE [25], 15 of 230 SSc patients with passive haemagglutination technique [26]. Bunn et al. [4] were part of the huge series of 374 SSc sera not able to detect any anti-U1RNP activity, using CIE. Therefore, it is very likely that some of the patients diagnosed as SSc had in fact mixed connective tissue disease.

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20. Barakat S, Briand JP, Weber JC, van Regenmortel MHV, patients, using CIE [25], 15 of 230 SSc patients with passive haemagglutination technique [26]. Bunn et al. [4] were part of the huge series of 374 SSc sera not able to detect any anti-U1RNP activity, using CIE. Therefore, it is very likely that some of the patients diagnosed as SSc had in fact mixed connective tissue disease.