

## Letter

### Questions From Patients and Doctors on Negative Minor Salivary Gland Biopsy in Sjögren Syndrome

To the Editor:

I read with interest the editorial in *The Journal of Rheumatology* entitled, "With Minor Salivary Gland Biopsy in Sjögren Syndrome, Is a Negative Result Possible?" by Drs. Monsalve and Anaya<sup>1</sup>. It is a comment on the article by Sharma, *et al*<sup>2</sup>, arguing that in the case of a negative biopsy of minor salivary glands (MSG), the presence of positive anti-Ro autoantibodies is sufficient for the diagnosis of Sjögren syndrome (SS). Drs. Monsalve and Anaya consider the anti-Ro autoantibodies as key in these patients and refer to the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for the diagnosis of the disease<sup>3</sup>. Monsalve and Anaya discuss the possibility that the intensity of mononuclear cell infiltration in the salivary glands may correlate with longer disease duration, but without showing a relationship with the volume of salivary secretion. They also comment on the protocol for the preparation of small salivary gland samples and the determination of focus score in patients with SS, as well as the poor reproducibility of H&E-stained biopsy specimens. In this sense, if the result of the biopsy is negative, the diagnosis of SS can be accepted when positive anti-Ro autoantibodies have been detected.

The ACR/EULAR classification criteria for primary SS contain 2 objective markers: pathomorphological and immunological. Studies on the sensitivity and specificity of ACR/EULAR criteria have shown that they could also be used to diagnose secondary SS<sup>4</sup>. It is known that antinuclear antibodies (ANA) may precede the clinical manifestations of autoimmune diseases by years, especially in genetically predisposed individuals. Positivity of anti-Ro52 and anti-Ro60 autoantibodies, in parallel with carrying other antinuclear autoantibodies, may point at credible clinical associations. Positivity of anti-Ro52 autoantibodies may be associated with overlap syndrome, progressive systemic sclerosis (SSc), rheumatoid arthritis, and systemic lupus erythematosus (SLE); positivity of anti-Ro60 autoantibodies, with SLE; and the presence of both Ro52 and Ro60 peptides, the overlap between progressive SSc and SS, as well as SLE<sup>5</sup>.

In this sense, testing for Ro52 and Ro60 peptides and obtaining a positive result supports the need to investigate other ANA specificities, as well as HLA analysis for alleles that are associated with certain systemic autoimmune rheumatic diseases. The evaluation of the test results of anti-Ro

autoantibodies and ANA (with titer and type of luminescence) may refer the specialists to relevant clinical associations.

Per se, autoantibodies mark an intermediate stage on the path to the evolution of the autoimmune disease and can be positive for years before clinical manifestations. The predictive value of anti-Ro60, anti-dsDNA, anti-Sm, and anti-Scl-70 may be positive from 1.2 to 9 years until the clinical manifestation of the disease<sup>6</sup>.

Extended immunological tests and the HLA allele analysis would provide sufficient evidence and enable measures for the early prevention, timely diagnosis, and adequate therapeutic actions in patients with a negative MSG biopsy but positive for anti-Ro autoantibodies in the immunological test.

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