Dear Editor,

I read with great interest the paper recently published by Sebastian et al., in which the authors summarized the previously used and current classification criteria for secondary Sjögren’s syndrome (sSS), and underlined “the need for labial salivary gland biopsy in all cases in which we suspect sSS to confirm the diagnosis” [1].

As is well known, labial salivary gland (LSG) biopsy is anything but easy and straightforward. Vivino et al. [2] reported that a second expert evaluation of 58 LSGs re-analyzed by a single center led to revision of the initial diagnosis in 53% of the patients. More recently, Costa et al. [3] reported a multicenter cohort study in which LSG biopsies were analyzed with a standard blinded assessment by two different pathologists at a 2-month interval. The analysis included the measurement of focus score (FS) and detection of germinal center (GC)-like structures. The inter-observer variability comparison revealed poor agreement for the detection and calculation of FS and detection of focal lymphocytic sialadenitis (FLS), lack of concordance for the presence of duct dilation and (less for) fibrosis. In more than 12% of the cases, the second evaluation by trained pathologists led to a diagnosis change [3].

In older patients, the presence of age-related findings may generate further confusion. For example, some investigators found that acinar atrophy and fibrosis are common in healthy individuals aged over 65 years, FS may be higher in older age groups, and the increased area of fat tissue may be a selective feature of aging [4–6].

More recently, the Sjögren’s histopathology workshop performed by the EULAR Sjögren’s Syndrome Experimental and Translational Investigative Alliance (ESSENTIAL) study group provided a consensus guidance for the use of LSG histopathology in clinical trials. The diagnostic importance of foci that are adjacent to normal parenchyma was emphasized and several recommendations were proposed. In particular, recommendation number 6 suggested that the extent of the atrophic features should be graded as mild, moderate, and severe, in addition to the presence or absence of FLS. Instead, recommendation number 10 underlined the necessity that all foci should be included in the FS and in foci calculations, even when adjacent to abnormal acini or ducts. However, the level of these recommendations was low [7].

As for today, there is still a strong need to achieve a consensus among experts on how to differentiate in LSG biopsy the Sjogren’s typical findings from the age-related ones [8]. The use of a grading score taking the destruction of acinar tissue and fibrosis into account could help (Table I).

Furthermore, as recently highlighted by Mavragani and Moutsopoulos [10], immunohistochemical studies comparing the composition of lymphocytic infiltrates in LSG biopsy revealed differences almost exclusively in rheumatoid arthritis associated with sicca-related manifestations, and not in other systemic autoimmune rheumatic diseases associated with Sjögren’s syndrome.

Therefore, is LSG biopsy crucial to confirm the diagnosis of sSS? Not always. It often becomes itself an element of discussion or confusion.

The author declares no conflict of interest.
References