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Association of oral lichen planus with thyroid disease in a Finnish population: A retrospective case-control study: "A different finding from a Mediterranean area"

To the Editor:

Siponen et al.[1] report an association of oral lichen planus/oral lichenoid lesions (OLP/OLL) with thyroid disease in the Finnish population. As they point out, OLP has been associated with a number of systemic disorders, generally of autoimmune origin (myasthenia gravis, Sjögren's syndrome, ulcerative colitis, psoriasis, celiac disease, some liver diseases, thymoma, and lupus erythematosus); however, only in a few conditions has this link been confirmed.[2-6] For example, the correlation between chronic hepatitis C virus (HCV) infection and OLP would be one of these, even if many contrasting results have been published,[7-14] and the partial dependency on geographic factors as well as genetic differences has been focused.[15,16] Furthermore, autoimmune conditions, such as systemic lupus erythematosus, rheumatoid arthritis, and celiac disease have also been simply found to be associated with autoimmune thyroid diseases,[17] but without great and definitive evidence.

Hence, the association between OLP/OLL and thyroid diseases/thyroid medication, in particular hypothyroidism, have been reported in some studies[18-20] up to the recent study by Siponen et al.,[1] who analyzed retrospectively 222 OLP/OLL patients and 222 controls, with a marginal significant association (95% confidence interval [CI] = 1.03 to 4.90) between OLP/OLL and hypothyroidism (10% versus 5% in controls). Finally, the authors suggested that the association of OLP and hypothyroidism could be linked to a similar, but still unknown, immune-mediated mechanism, warranting further studies in a different population.

With this regard, we would like to share our findings from a cross-sectional study performed in Sicily (West Mediterranean area). We consecutively recruited 125 resident patients, of these 74 had Hashimoto's thyroiditis or Graves disease (70 female and 4 male; mean age: 47 ± 15.2 years; range: 14 to 79 years; of which 58 patients had Hashimoto's thyroiditis and 16 had Graves disease) as the test group; these 2 autoimmune pathologies share with OLP a common immune-mediated pathogenesis, causing hypothyroidism and hyperthyroidism, respectively. Controls were 51 patients (42 female; 9 male; mean age: 54.6 ± 11.5 years; range: 24 to 73 years) suffering from goiter, an endemic disease in Sicily without autoimmune pathogenesis,[21] and were found to be matched for age and gender with the test group ($P > .2$ by Student t).

In all samples, thyroid diseases were diagnosed both serologically and histologically; all patients underwent total thyroidectomy and subsequent replacement with thyroxin medication. All patients underwent oral examination, independently, by 2 of the authors (C.D. and C. P.), both experts in oral medicine. In our study, all patients who were HCV-positive or with OLL potentially associated with drugs,[22] amalgam fillings, or topical allergens were excluded, different from Siponen et al.,[1] to reduce biases on the final results.

One patient with Hashimoto's thyroiditis showed oral lesions with a reticular aspect bilaterally on the buccal mucosa and atrophic/erosive features on the masticatory mucosa, compatible with the diagnosis of OLP. The patient underwent incisional oral biopsy and the subsequent histologic examination confirmed the diagnosis of OLP. None of the controls showed clinical signs of OLP/OLL.

Different from Siponen et al.,[1] we did not find any significant association between autoimmune thyroid

diseases and OLP or between thyroxin drug use and OLL, presumptively high because of the endemic status of thyroid diseases in our population and the consequent use of thyroxine-based drugs.

In conclusion, with regard to the findings by Siponen et al.,[1] we do not think that the data to date show definitively an association between OLP/OLL and, at least, hypothyroidism, especially with the potential for biases from sample size calculation and consequently from type I error.

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In reply:

We thank Dr Compilato et al. for their interest in our study and for sharing their own findings. We also fully agree with their statement ". . . we do not think the data to date show definitively an association between OLP/OLL and, at least, hypothyroidism" up to this point. Nothing in our article indicates a different conclusion; yet, we are unable to follow their argument to the end. For example, the meaning of "bias from sample size calculation" remains obscure to us, such a bias not being described in any well-known textbook on epidemiologic methods. Therefore, we would like to elaborate some methodological issues that we consider essential when evaluating observational evidence provided either by any single study, including theirs and ours, or jointly by several independent studies on the same question.

A major problem encountered in any epidemiologic study addressing the existence, direction, and strength of a conceivable association between thyroid diseases