Virchows Archiv (2019) 474:639–640
https://doi.org/10.1007/s00428-018-02518-0

LETTER TO THE EDITOR

# Letter to the Editor

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Received: 21 December 2018 / Accepted: 27 December 2018 / Published online: 14 January 2019


Dear Editor,

We read with great interest and attention the paper by Kirmizi et al. entitled "Discriminant value of IEL counts and distribution pattern through the spectrum of gluten sensitivity: a simple diagnostic approach" published in Virchows Arch 2018 473:551–558. Being involved in the field of non-celiac gluten sensitivity (NCGS) research, we focused our attention on the histopathological characteristics of this condition and we proposed the following considerations about the comparison with our experience on the same matter [1].

a) In the study by Kirmizi et al., the authors reported that the diagnosis of NCGS is based on the exclusion of other causes and on the response to gluten-free diet, but we suggest that these criteria should be confirmed by a single-blind or double-blind placebo-controlled challenge with gluten, as stated in the Salerno Experts' Criteria [2].
b) Moreover, the authors compared their findings in the group of patients with non-celiac IELosis with our suggested histological features in patients with NCGS. In our opinion, the two groups are not comparable because, despite the retrospective fashion of both studies, in our paper, people with NCGS was highly selected, and we strictly applied the Salerno Experts' Criteria for the diagnosis of NCGS.
c) Regarding the histological assessment, the authors stated they did not spot any foci of eosinophils in the lamina propria, or a linear disposition of lymphocytes in the deeper mucosa; they also underlined that inflammatory cells comprising plasma cells, lymphocytes, eosinophils, and macrophages normally reside in the basal lamina propria of the small intestine. We aim to specify that in our study, eosinophils were carefully recognized from other inflammatory cells and their peculiar focus (> 5 per high power field) was evaluated with accuracy. As we stated in our conclusion, we fully agree with the authors that our study need to be confirmed by further possibly prospective investigations, but we emphasize that in our experience, CD3 immunohistochemistry used for T lymphocytes revealed a normal CD3 count in NCGS (< 25/100 epithelial cells); since all biopsies were correctly oriented on acetate cellulose filters [1, 3], their evaluation disclosed the peculiar linear distribution of CD3 T lymphocytes in the deeper mucosa and the presence of small clusters of T lymphocytes 3/4 in the superficial epithelium.
d) We finally agree with the authors that the cutoff value of normal T CD3+ lymphocytes is probably under 25/100 epithelial cells, in line with our previous experience [4].

Based on these comments, we believe that assessing histopathological features of NCGS is extremely important to correctly select the study population and we strongly encourage further researches on this entity based on a strict collaboration between the clinicians and the pathologists.

## Compliance with ethical standards

The authors declare that the study has been done according to ethical standards.

**Ethical responsibilities of authors section** All the authors are qualified for the following criteria: (1) substantial contributions to the conception or design of the study; or the acquisition, analysis, or interpretation of data for the study. (2) Drafting the study or revising it critically for important intellectual content. (3) Final approval of the version to be published. (4) Agreement to be accountable for all aspects of the study in ensuring that questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

**Conflict of interest** The authors declare that they have no conflicts of interest.

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