DOI: 10.1111/apt.17501

INVITED EDITORIAL

AP&T Alimentary Pharmacology & Therapeutics WILEY

Editorial: type 1 diabetes, microscopic colitis and the need to explore the complex mechanisms of this association

Microscopic colitis (MC) is a cause of watery diarrhoea, whose aetiology and pathogenesis is not yet completely understood. Several hypotheses have been raised including immune dysregulation, i.e., innate and adaptive immune responses to luminal antigens, genetic risk, and autoimmunity.[1] Several population-based studies have demonstrated that up to one out of three patients suffer from concomitant autoimmune diseases, including celiac disease, thyroid disorders, rheumatic and connective tissue diseases, and diabetes.[2–4] Kang et al[5] sought to address the relationship between MC and type 1 diabetes (T1D) in a matched case–control study using a large nationwide Swedish cohort, by adjusting for multiple confounding variables, including demographics, familiarity, drug use and concomitant immune-mediated conditions. The authors found T1D diagnosis was almost 80% more prevalent in MC patients compared to general population,[5] providing additional insights to the results of a recent Danish case–control study.[2] This association was stronger for collagenous compared to lymphocytic colitis, comparable in patients of both sexes, but attenuated by the exposure to statins among females.

MC and T1D have apparently opposite epidemiological characteristics: While MC is primarily diagnosed in the middle-aged and elderly women, former or current smokers with several concomitant diseases,[6] the onset of T1D usually occurs before the fourth decade in life and a higher incidence is reported among men compared with women.[7] Therefore, the diagnosis of T1D would precede that of MC by decades and, over time, contribute by itself or through the development of complications to MC onset. In contrast, type 2 diabetes (T2D) is distributed more similarly to MC.

Variants at the HLA gene level have been involved in the immune pathogenic origin of MC and T1D. Kang et al also suggest closer relationships between both diseases in terms of common pathophysiological alterations in mucosal immunity, gut permeability and their interplay with intestinal microbiota.

Up to 75% of diabetic patients may experience gastrointestinal symptoms, due to gastrointestinal dysfunction usually in the setting of autonomic neuropathy.[8] The effects of diabetes on the entire GI tract including the colon lead to neuropathic changes involving the vagus nerve as well as autonomic nerves, likely caused by increased glycation end-products which also promote the production of collagen.[9] Changes in microbiota caused by altered motility modify gut permeability to luminal antigens, including microbial products and drugs. The study by Kang et al found a higher consumption of drugs associated with the risk of presenting MC among patients with T1D, which suggests that the presence of disease complications contributes significantly to the risk of MC. It is unknown if adequate glycaemic control would reduce the risk of developing MC among T1D patients, but the inverse association between treatment with oral antidiabetic drugs in T2D and risk of MC represents reason for hope.[10] Meanwhile, it would be essential to investigate the intimate mechanisms underlying the strong association between T1D and MC, as well as its modulation by genetic, immunological and sex-related factors. A first approach to prevent MC by optimising T1D treatment could be then considered.

AUTHOR CONTRIBUTIONS

Alfredo J Lucendo: Conceptualization (equal); writing – original draft (equal).

ACKNOWLEDGEMENTS

None.

LINKED CONTENT

This article is linked to Kang et al. papers. To view these articles, visit https://doi.org/10.1111/apt.17473 and https://doi.org/10.1111/apt.17518

Alfredo J. Lucendo[1,2,3,4]

[1]*Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Spain*
[2]*Instituto de Investigación Sanitaria Princesa, Madrid, Spain*
[3]*Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain*
[4]*Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Toledo, Spain*

Correspondence
Alfredo J. Lucendo, Department of Gastroenterology. Hospital General de Tomelloso, Vereda de Socuéllamos, s/n, 13700 Tomelloso, Ciudad Real, Spain.
Email: ajlucendo@hotmail.com

AP&T correspondence columns are restricted to invited editorials and letters discussing papers that have been published in the journal. An invited editorial or letter must have a maximum of 500 words, may contain one table or figure, and should have no more than 10 references. It should be submitted electronically to the Editors via http://mc.manuscriptcentral.com/apt.

ORCID

Alfredo J. Lucendo https://orcid.org/0000-0003-1183-1072

REFERENCES

1. Zabana Y, Tontini G, Hultgren-Hörnquist E, Skonieczna-Żydecka K, Latella G, Østvik AE, et al. Pathogenesis of microscopic colitis: a systematic review. J Crohns Colitis. 2022;16:143–61.
2. Wildt S, Munck LK, Winther-Jensen M, Jess T, Nyboe Andersen N. Autoimmune diseases in microscopic colitis: a Danish nationwide case–control study. Aliment Pharmacol Ther. 2021;54:1454–62.
3. Vigren L, Tysk C, Ström M, Kilander AF, Hjortswang H, Bohr J, et al. Celiac disease and other autoimmune diseases in patients with collagenous colitis. Scand J Gastroenterol. 2013;48:944–50.
4. Roth B, Manjer J, Ohlsson B. Microscopic colitis is associated with several concomitant diseases. Drug Target Insights. 2013;7:19–25.
5. Kang X, Liu S, Roelstraete B, Khalili H, Ludvigsson JF. Type 1 diabetes and microscopic colitis: a nationwide matched case-control study in Sweden. Aliment Pharmacol Ther. 2023;57:1423–31.
6. Guagnozzi D, Lucendo AJ, Angueira-Lapeña T, González-Castillo S, Tenias Burillo JM. Prevalence and incidence of microscopic colitis in patients with diarrhoea of unknown aetiology in a region in Central Spain. Dig Liver Dis. 2012;44:384–8.
7. Harding JL, Wander PL, Zhang X, Li X, Karuranga S, Chen H, et al. The incidence of adult-onset type 1 diabetes: a systematic review from 32 countries and regions. Diabetes Care. 2022;45:994–1006.
8. Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes Care. 2017;40:136–54.
9. Piper MS, Saad RJ. Diabetes mellitus and the colon. Curr Treat Options Gastroenterol. 2017;15:460–74.
10. Fernández-Bañares F, de Sousa MR, Salas A, Beltrán B, Piqueras M, Iglesias E, et al. Epidemiological risk factors in microscopic colitis: a prospective case-control study. Inflamm Bowel Dis. 2013;19:411–7.