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REVIEW ARTICLE

Microscopic enteritis and pathomechanism of malabsorption

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Abstract Microscopic enteritis (ME) is the stage of microscopic and sub-microscopic changes (microenteropathy) associated with the symptoms of gluten sensitive enteropathy leading to micronutrient deficiencies. It is characterized by subtle mucosal abnormalities without prominent inflammation, villous effacement, erosions or ulcerations on conventional light microscopy. The intraepithelial lymphocytes are usually in normal range <25/100 enterocytes (microenteropathy) or increased (lymphocytic enteritis). ME is the entity behind atypical forms of CD previously known as potential and latent CD. Systemic inflammation predominantly is found to be engaged in pathophysiology of micro-nutrient deficiency even in absence of macroscopic mucosal changes.

Keywords Microscopic enteritis · Coeliac disease · Gluten sensitivity · Physiopathology · Malabsorption · Cytokine

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Malabsorption in Microenteropathy

Microscopic enteritis (ME) or coeliac disease (CD) with milder enteropathy (Marsh 0–II) is the most common feature of atypical gluten sensitivity [1] and CD with macroscopic enteritis (Marsh IIa–c) is less prevalent. In contrast to the previous belief, symptomatology in CD does not seems to be related to the degrees or length of affected bowel [2, 3]. The microenteropathy may eventually progress to overt villous atrophy, but interestingly severe mucosal degradation does not necessarily aggravate the symptoms. Nutritional deficiency can be detected in patients presenting with even submicroscopic enteropathy [4]. This calls into question the role of severe mucosal changes such as villous atrophy as the sole explanation for malabsorption. The reality seems to be in favour of systemic inflammation as the cause of nutritional deficiency. Proinflammatory cytokines such as TNF seem to act at the level of the enterocyte inhibiting the uptake of the micronutrients such as iron [5] and phosphate [6] (Fig. 1).

It seems that malabsorption in CD is secondary to inflammation and cytokine stimulation. This theory could perhaps explain why in some patients milder enteropathy characterized as atypical [7] behaves like full-blown CD. In fact inflammation caused by gluten-sensitized lymphocytes and cytokine stimulation seems to be behind the micronutrient deficiencies in CD patients with or without villous atrophy. This is supported by the findings of several studies demonstrating that malabsorption syndrome is not worse in patients with villous atrophy than in those with ME (Marsh 0–II) [2, 4]. The existence of nonsymptomatic silent CD with villous atrophy and persistence of mucosal lesions for years after successful treatment in many of patients with CD strongly supports this theory.

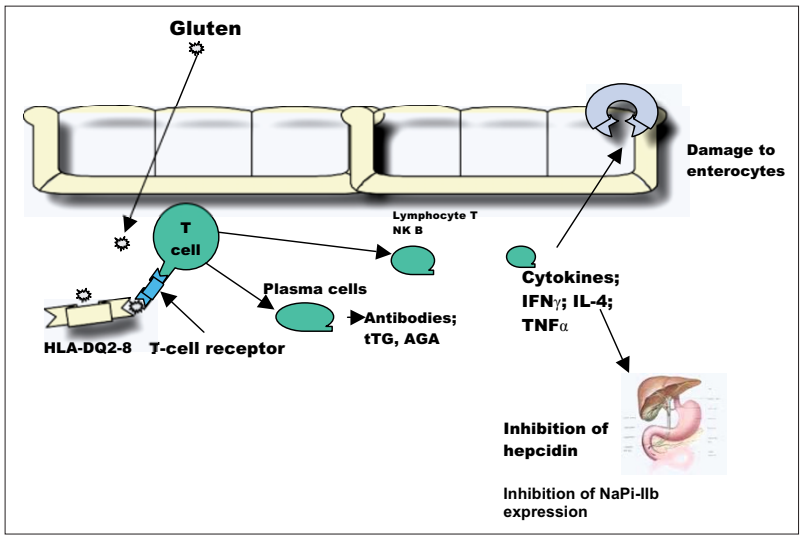

Fig. 1 Systemic inflammation, which may or may not be triggered by gluten, stimulates T cells and cytokines leading to inhibition of hepcidin, Na-Pi-IIb and other peptides that result in iron, phosphate and other micronutrient deficiencies

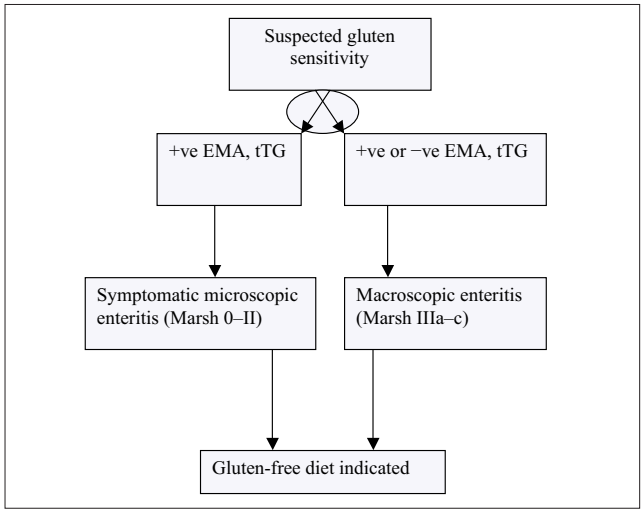

Fig. 2 Treatment pathway for symptomatic patients (*EMA* endomysial antibodies, *tTG* tissue transglutaminase antibodies)

Atypical presentation with microenteropathy resulting in micronutrient deficiencies as the sole manifestation of gluten sensitivity has been commonly identified over the last few years. Recent data presented by Kurppa et al. [8] and Ludvigsson et al. [9] have important implications for the life quality of patients with CD with milder enteropathy. We strongly agree that patients with milder enteropathy and positive serology may benefit from a gluten-free diet. Autoantibodies might have a more reliable positive predictive value than histology especially in early enteropathy [4, 10].

In practice the diagnosis of CD in the early stages can be very challenging. However, a strong body of evidence is facilitating the building of a pathway toward understanding the complex and true meaning of gluten sensitivity with microenteropathy (Fig. 2). In contrast to the older guidelines, and in the light of recent evidence, in patients with microenteropathy, symptoms of micronutrient deficiency and positive serology [11] a gluten-free diet should be considered.

Conflict of interest statement The authors declare that they have no conflict of interest related to the publication of this article.

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