Envoi SPECIALIST PATHOLOGISTS *inside insights*

Update No.8 – 2016 *Dr Ian Brown*

Histological mimics of coeliac disease

As discussed in the previous update, a range of histological features can be seen in biopsy specimens of coeliac disease. Given that these changes reflect mucosal damage secondary to an immunological response, it is to be expected that there are other conditions that can mimic these histological changes.

Intraepithelial lymphocytosis (Marsh stage 1) (Fig. 1)

Identical changes to the Marsh stage 1 lesion are commonly encountered in routine reporting. Only 10% of biopsies with this change represent true coeliac disease. The major conditions to be considered in the differential diagnosis are:

- Coeliac disease
- Infection/bacterial overgrowth
  - Viral enteritis, Helicobacter pylori, Giardia, Cryptosporidium, tropical sprue
- Drugs
  - NSAIDs, angiotensin 2 receptor antagonists ("Sartans")
- Autoimmune disease
  - Rheumatoid arthritis, SLE, Hashimoto thyroiditis, Graves disease, psoriasis, ankylosing spondylitis, type 1 diabetes, scleroderma

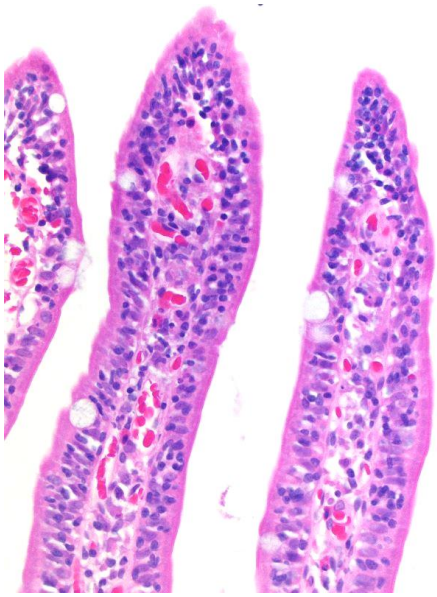

Fig.1. Intraepithelial lymphocytosis

Intraepithelial lymphocytosis with villous atrophy (Marsh stage 3)

These features are so characteristic of coeliac disease that, despite the development of sensitive and specific serological markers, histopathology remains critical in the evaluation of patients with suspected coeliac disease. The histological pattern is however, not specific and a growing list of coeliac disease mimics is emerging. These include:

- Non gluten food protein hypersensitivity
  - Cow's milk, soy products, fish, rice and chicken
- Infection/bacterial overgrowth
  - Viral enteritis, Cryptosporidium, tropical sprue
- Autoimmune enteropathy
- Immunodeficiency disorders
  - IgA deficiency, CVID, HIV enteropathy
- Drugs
  - Angiotensin 2 receptor antagonists ("Sartans")
- Collagenous sprue

In our experience, the most commonly encountered histologic mimics are recent **viral enteritis**, medications (in particular **olmesartan**), **tropical sprue** (see Fig. 2.) and **bacterial overgrowth**.

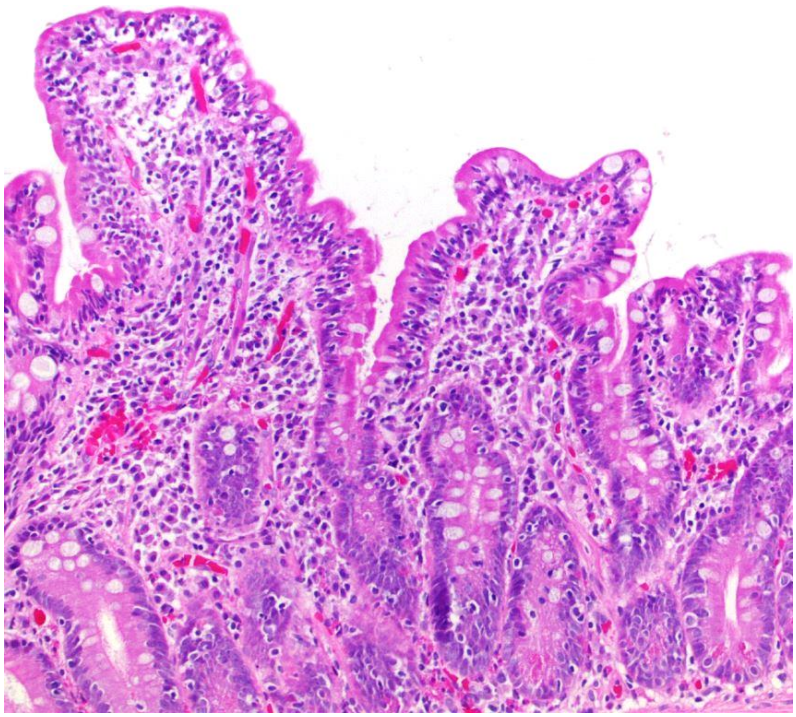

Fig. 2. Villous blunting and intraepithelial lymphocytosis in the duodenum of a patient with tropical sprue – mimicking coeliac disease

Sometimes there are histological clues that might suggest a non-coeliac aetiology. In tropical sprue the terminal ileum can also show similar changes. In cases of recent viral infection, immunodeficiency disorders and autoimmune enteropathy, apoptotic bodies may be conspicuous and in collagenous sprue there is prominent subepithelial collagen deposition. Also, most mimics of coeliac disease do not produce an entirely flat duodenal mucosa.

Although gastrointestinal pathologists are usually capable of making the distinction between coeliac disease and these mimics, the diagnosis of "coeliac mimic" enteropathy should be considered in the following circumstances:

1. atypical clinical history
2. no elevation of tissue transglutaminase
3. HLADQ2 or 8 negative
4. no response to a gluten free diet.

Further reading:

Brown IS, Bettington A, Bettington M, Rosty C. Tropical Sprue – revisiting an under recognised condition. A series of 12 cases. Am J Surg Pathol. 2014; 38(5):666-72.
Brown IS, Bettington A, Bettington M, Rosty C. Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another coeliac disease mimic. Histopathology. 2016; 68(2):254-61
De Gaetani M et al. Villous atrophy and negative coeliac serology. Am J Gastroenterol. 2013; 108: 647-653.