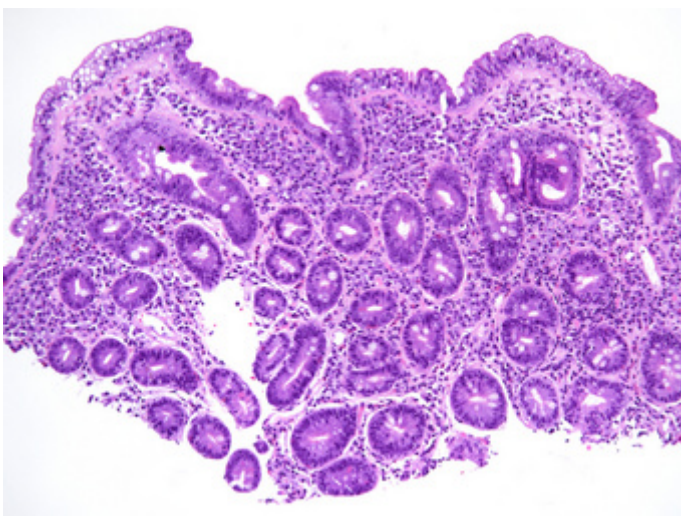
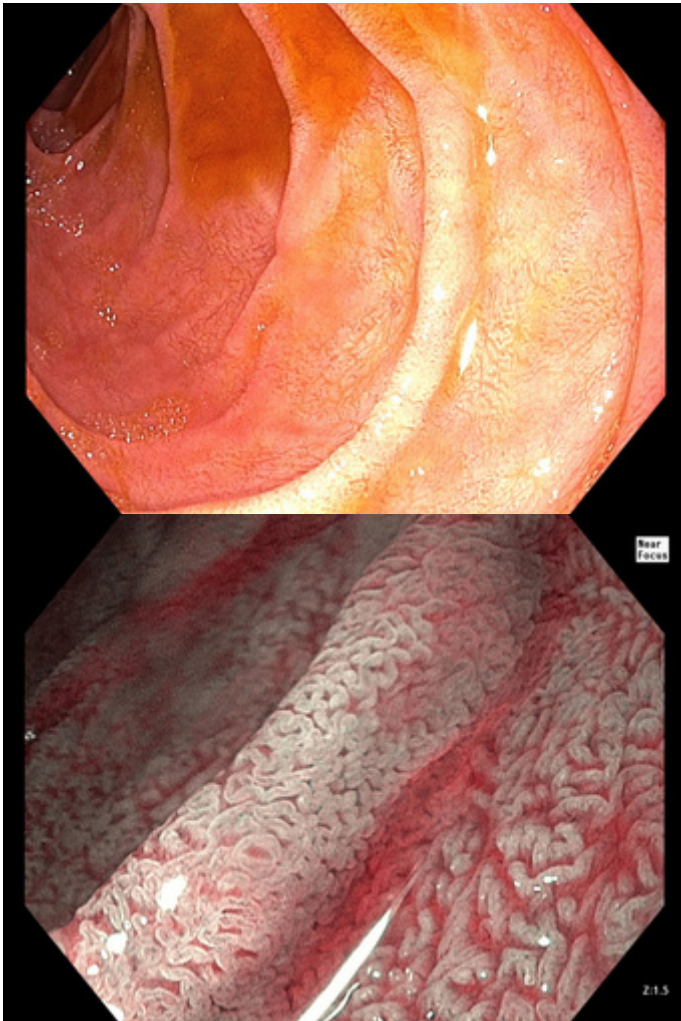
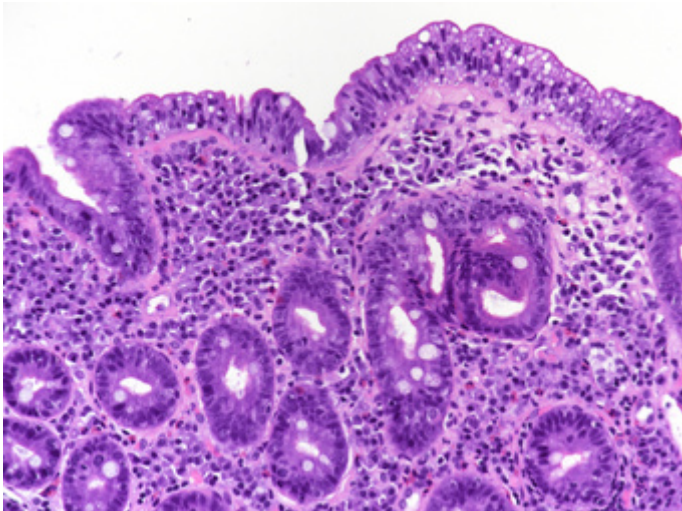
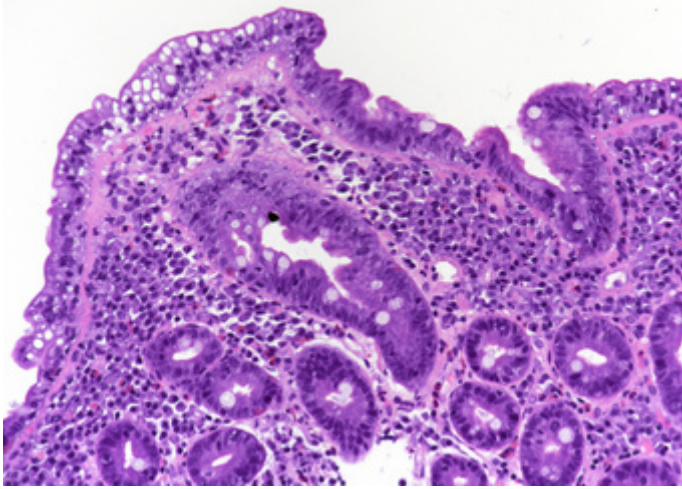
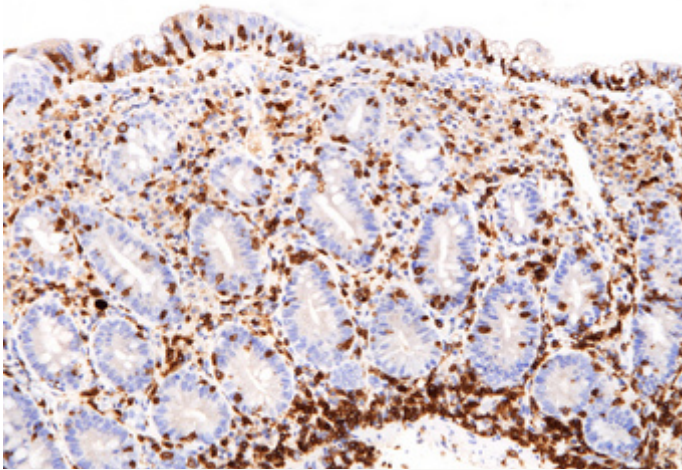
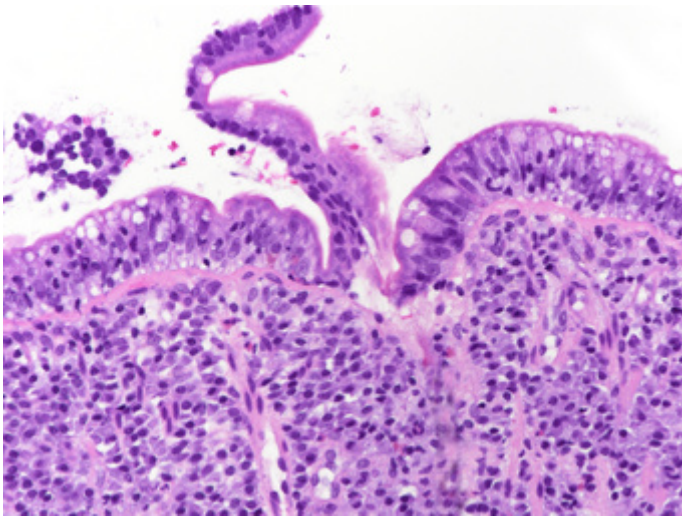


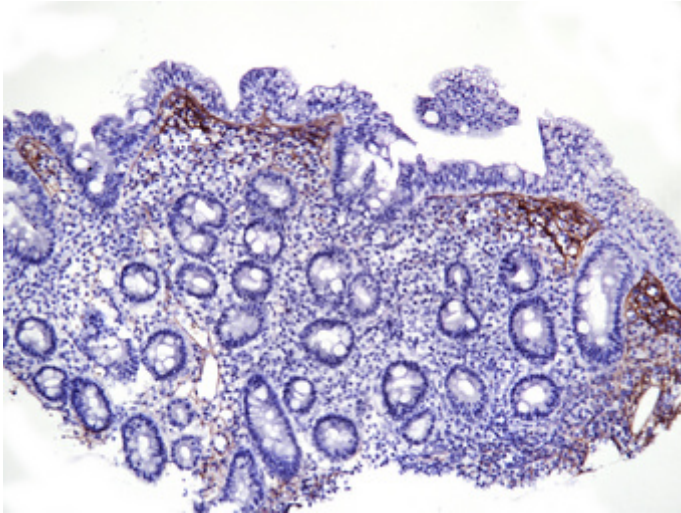
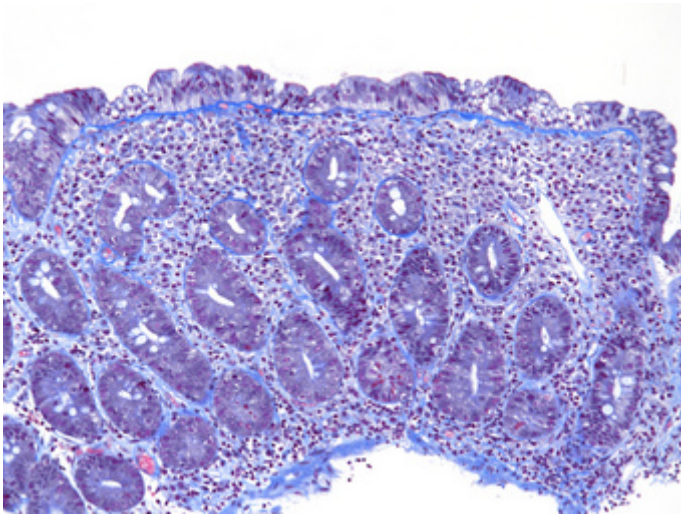
# August 2021

Duodenal biopsies in a 50-year-old female.

What is your diagnosis?







## Diagnosis:

Celiac disease with thickening of the subepithelial collagen band (suspicious of collagenous sprue).

## Comment:

The biopsies are from a patient with previously established diagnosis of celiac disease. Despite gluten-free diet, the patient is symptomatic and suffers from severe osteoporosis. A systematic endoscopic and histological re-evaluation is performed.

Endoscopy shows a slightly abnormal mucosal pattern without definitive evidence of villous blunting (Panels A-B). Upon histology, we see crypt hyperplasia and villous blunting, qualifying for Marsh-Oberhuber category 3C (Panel C). Intraepithelial lymphocytes are significantly increased (Panels D-E) and show a normal immunophenotype (equally positive for CD3 and CD8), suggesting refractory disease type I. The surface enterocytes demonstrate intracytoplasmic lipid accumulation ("lipid hang-over").

Interestingly, the subepithelial collagen band is thickened, sometimes measuring less, sometimes measuring more than 10 $\mu$  (Panel F-G). Trichrome staining is helpful in detecting the thickening of the collagen band (Panel H). Positivity for tenascin is found in the subepithelial region (Panel I).

Celiac disease features duodenal intraepithelial lymphocytosis with or without villous atrophy. Our case illustrates the problems of persistent symptoms despite gluten-free diet. The histology is clearly abnormal, the immunophenotype of the intraepithelial T-cells however inconspicuous (refractory celiac disease type I). On a previous occasion, we had additionally checked biopsy material from the patient for T-cell monoclonality (with

negative result). The thickening of the collagen band is a new finding in our patient, who had several endoscopic investigations in the last years. The thickening may be related to the persistence of clinical symptoms.

Is this bonafide “collagenous sprue”? The reported cut-off value of 10 $\mu$  is reached here and there (and the tenascin positivity favours this diagnosis). Still, most cases with collagenous sprue show more severe histological changes. The significance of minor subepithelial collagen band thickening (which is in fact not so rare and seems to occur more often in refractory disease) is largely unclear.

### For further reading:

- › Vakiani E, Arguelles-Grande C, Mansukhani MM, Lewis SK, Rotterdam H, Green PH, Bhagat G. Collagenous sprue is not always associated with dismal outcomes: a clinicopathological study of 19 patients. *Mod Pathol*. 2010; 23: 12-26.
- › Freeman HJ. Update on collagenous sprue. *World J Gastroenterol*. 2010; 16: 296-8.
- › Zhao X, Johnson RL. Collagenous sprue: a rare, severe small-bowel malabsorptive disorder. *Arch Pathol Lab Med*. 2011; 135: 803-9. Freeman HJ. Collagenous sprue. *Can J Gastroenterol*. 2011; 25: 189-92.
- › O'Brien BH, McClymont K, Brown I. Collagenous ileitis: a study of 13 cases. *Am J Surg Pathol*. 2011; 35: 1151-7.
- › Brown IS, Smith J, Rosty C. Gastrointestinal pathology in celiac disease: a case series of 150 consecutive newly diagnosed patients. *Am J Clin Pathol*. 2012; 138: 42-9.
- › Lan N, Shen B, Yuan L, Liu X. Comparison of clinical features, treatment, and outcomes of collagenous sprue, celiac disease, and collagenous colitis. *J Gastroenterol Hepatol*. 2017; 32: 120-7.
- › Smyrk TC. Practical Approach to the Flattened Duodenal Biopsy. *Surg Pathol Clin*. 2017; 10: 823-39.
- › Kung VL, Liu TC, Ma C. Collagenous Enteritis is Unlikely a Form of Aggressive Celiac Disease Despite Sharing HLA-DQ2/DQ8 Genotypes. *Am J Surg Pathol*. 2018; 42: 545-52.
- › Brown I, Bettington M, Rosty C. The role of histopathology in the diagnosis and management of coeliac disease and other malabsorptive conditions. *Histopathology*. 2021; 78: 88-105.

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