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Celiac disease is not yet mainstream in endoscopy

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Since the early 1990s clinicians have been realizing more and more that the so-called "typical" picture of celiac disease, i. e., as a diarrheal illness with frequent, foul-smelling bulky stools and weight loss, is in fact the exception [1].

Celiac disease is the most frequent enteropathy in white people all over the world. It is characterized by intolerance to gluten, which causes damage to the small bowel mucosa. Such damage ranges from mild, with only an increase in intraepithelial lymphocytes and crypt hyperplasia, to severe, which involves various degrees of endoscopically relevant lesions such as villous atrophy. Although macroscopic villous atrophy requires histological confirmation, it is an important finding that ideally should be recognized during endoscopy. Other causes of villous atrophy, such as giardiasis, autoimmune enteropathy, HIV infection, and tropical sprue, should be excluded.

The role of conventional endoscopy in the diagnosis of celiac disease has been limited. Although traditional endoscopic signs have been described, these are not sensitive or specific enough for diagnostic purposes [2,3]. Indeed, so far endoscopic markers are not adequate to enable targeting of biopsy sampling to sites of villous atrophy in the duodenum.

Immersion techniques might also be considered as a follow-up in celiac disease, without taking biopsies [4]. Since 2001, video capsule endoscopy (VCE) has offered an alternative to duodenal biopsies in patients unable or unwilling to undergo conventional gastrointestinal endoscopy. In addition, VCE can be used to further evaluate patients with symptoms suggesting celiac disease who have positive serology (especially endomysial antibodies) but negative histology [5].

Celiac disease should be included in the differential diagnosis of patients with peptic ulcer disease in the stomach and duodenum that is not related to Helicobacter pylori. It has recently been suggested that routine celiac disease serological tests and small-bowel biopsy should be performed in patients with peptic ulcer disease in which neither H. pylori nor nonsteroidal anti-inflammatory drugs are involved [6].

In the past few years, newly developed procedures and technologies have improved endoscopic recognition of the duodenum. These technologies include water immersion techniques, chromoendoscopy, high resolution magnification endoscopy, narrow band imaging, and optimal band imaging [7].

Diagnosis of celiac disease

The diagnosis of celiac disease is based upon criteria defined by working groups such as those of the United European Gastroenterology Week in Amsterdam in 2001 or the Indian Task Force for Celiac Disease in 2008 [8].

In this issue of Endoscopy, Günther et al. present a prospective evaluation of endoscope-based confocal laser microscopy (CLM; Pentax) in 30 celiac patients and 30 controls. They found that CLM finding correlated well with conventional histology for villous atrophy and increased number of intraepithelial lymphocytes yet crypt hyperplasia was more difficult to assess. The results of this study are promising and teach us that endoscopists can recognize celiac disease using sophisticated endoscopic techniques. The authors suggest that this technique might help to reduce sampling error by targeting the biopsy subgroup of patients [9].

Refractory celiac disease with an increased risk of enteropathy-associated T-cell lymphoma is extremely rare and in respect of this CLM is only time-consuming and probably of no help at all [9]. The role of CLM should be evaluated in larger cohorts of patients with celiac disease versus normal controls before implications for daily practice are decided.

Immunohistochemistry and if necessary flow cytometry are indicated in all patients with celiac disease who are diagnosed above 50 years of age [10]. Compared to these techniques, the diagnostic scope of CLM is probably moderate. CLM may find its place in endoscopy, probably for detection of malignant and premalignant lesions in Barrett's esophagus, gastric dysplasia, and longstanding inflammatory bowel disease (IBD). Celiac disease has not yet achieved this level of priority in clinical gastroenterology. Endoscopists should consider the possibility of celiac disease in their daily practice, and should obtain duodenal biopsies in patients with dyspepsia, autoimmune diseases, H. pylori-negative ulcers, and iron/folic deficiency anemia in order to detect this underdiagnosed disease.

This issue of Endoscopy also publishes the report of an endocytoscopy study from Nantes in France [11]. The use of this technique has been described in the endoscopic imaging of Barrett's esophagus, gastric dysplasia, and IBD. A prototype endocytoscope (Olympus) was used and endoscopic evaluation was performed for at least 10 minutes with the patient under general anesthesia. This study gave better information on Marsh IIIa – c cases and showed that partial villous atrophy was more difficult to diagnose with endocytoscopy than total villous atrophy. Unfortunately only one patient with Marsh I disease was included and we cannot therefore assess the performance of endocytoscopy in patients with less severe celiac disease.

Not surprisingly, endocytoscopy did detect severe abnormalities. As in the CLM study from Berlin, this technique also underdiagnosed minor mucosal abnormalities, which are of interest in follow-up of patients at risk of complications, especially those patients who are over 50 years of age at diagnosis of celiac disease. A minor drawback in relation to general anesthesia is the prolongation by 10 minutes of the duration of endoscopy. In those centers where endoscopy is performed with either mild sedation or no sedation at all, this could be a significant drawback. A "less invasive diagnostic method", as the authors call it, is no alternative to biopsies, especially in complicated celiac disease and patients at high risk of enteropathy-associated T-cell lymphoma. Unfortunately, in these subgroups histological and immunohistochemical analysis are still mandatory in order to allow accurate diagnosis of type I versus type II refractory celiac disease [10].

In conclusion, the diagnosis and follow-up of celiac disease should still be based on biopsies [1, 8]. CLM and endocytoscopy will be part of mainstream endoscopic surveillance for premalignancy (esophagus, stomach, and colon). Awareness of celiac disease should be encouraged among endoscopists, who need to realize that celiac disease is as common as IBD and Barrett's esophagus in their daily practice: if their experience does not accord with this, they should do better and biopsy. We feel that higher awareness and a lower threshold for obtaining duodenal biopsies are more important to improving the diagnosis of celiac disease than the currently available sophisticated endoscopic techniques described in this very interesting issue of Endoscopy.

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