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Celiac disease: Diagnosis of celiac disease in pediatric patients

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Abstract

Children and adolescents with untreated celiac disease display disease-related, histological alterations in the duodenal bulb, according to a new study. In 16 of the 665 patients enrolled in the study, lesions were confined to the duodenal bulb.

Celiac disease is a common chronic disorder with a prevalence that approaches 1% of the general population worldwide, although many cases remain unrecognized.¹ Intestinal biopsy is currently the standard diagnostic test for celiac disease.^{1, 2} Collection and analysis of multiple biopsy specimens obtained from the distal segments of the duodenum are recommended in anyone in whom celiac disease is suspected, irrespective of the results of serological tests or the endoscopic appearance of the duodenum.^{2, 3}

Can biopsy specimens of the duodenal bulb be used for the diagnosis of celiac disease? Studies in children and adolescent patients demonstrated that the characteristic lesions of celiac disease were present in the duodenal bulb in all patients with confirmed celiac disease, and the bulb was the only site where the celiac-disease-related, pathologic change was observed in some of these patients.^{4, 5} Bonamico *et al.*⁶ recently investigated this topic further in a multicenter study that had a larger sample size than other similar studies.^{4, 5} During each endoscopy, one tissue sample was collected from the duodenal bulb, and three or four were collected from the distal duodenum. The bulb samples of all 665 children and adolescents with untreated celiac disease who were enrolled in the study displayed histological lesions of celiac disease, as evaluated in accordance with the Marsh classification (as modified by Oberhuber). More importantly, in 16 (2.4%) of the patients with celiac disease, the lesions were present only in the duodenal bulb. Conversely, none of the 348 age-matched and sex-matched controls showed any mucosal changes compatible with celiac disease in the duodenal bulb. The reason why the proximal intestine is more frequently affected by celiac disease than the distal intestine is unknown, but possible explanations are that the duodenum is the first part of the intestine to be reached by the antigenic peptides, or that a larger amount of partially digested gluten is present in the proximal intestine than in the distal intestine.^{7, 8}

Usually, biopsy specimens used to diagnose celiac disease are taken from distal segments of the duodenum or from its second part.³ Endoscopic biopsy specimens of the descending duodenum were initially shown to be as diagnostically revealing as jejunal specimens taken by capsule or suction tube.⁹ Data from the early 1960s supports the propensity of the proximal intestine to injury in patients with untreated celiac disease.^{8, 10} Furthermore, a wireless capsule endoscopy study published in 2008 demonstrated that, in patients with

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Competing interests statement

The authors declare no competing interests.

untreated celiac disease, visually detectable damage to the proximal intestine (including the duodenum) is a very common finding, whereas jejunal injury in the absence of duodenal involvement is very rare.⁷ The collection of duodenal biopsy specimens, therefore, seems to be an adequate strategy for diagnosis of celiac disease.^{1, 3} Currently, the collection of multiple biopsy specimens (between four and six) obtained from distal segments of the duodenum is recommended, because intestinal injury in celiac disease is patchy, the orientation of the biopsy specimens is variable (which increases the possibility of inconclusive histological diagnosis) and the presence of Brunner glands in the duodenal bulb could interfere in the evaluation of the villous:crypt ratio.^{2, 3}

The study by Bonamico *et al.* confirms that, in children and adolescents with celiac disease, the mucosa of the duodenal bulb always shows celiac-disease-related pathological lesions.⁶ This study also reports that the duodenal bulb was the only area of the intestine affected in 2.4% of children and adolescents with celiac disease, and that no mucosal changes compatible with celiac disease were observed in the duodenal bulb of controls. We propose the term 'short-segment celiac disease' to describe histological lesions that are restricted to the duodenal bulb.

This study has several limitations that need to be considered. No information on the number or expertise of pathologists who reviewed the biopsy specimens is provided; these data are very important, given the multicenter design of this study. How authors controlled potential interobserver and center-to-center variability, which may affect the results of the study, is not described either. An expert pathological examination is essential for the correct identification of villous atrophy in the duodenal bulb, as the villi can be shorter than normal or even absent (pseudoflattening) in healthy mucosa that overlies Brunner glands. Inexperienced pathologists are at risk of overestimation of atrophic lesions.⁴ Data on the degree of mucosal injury in the duodenal bulb and distal duodenal segment observed in biopsy specimens were not provided. The question of whether the degree of villous atrophy in the distal segments of the duodenum is different from that of the duodenal bulb cannot, therefore, be answered. More than 80% of the patients with celiac disease showed total or subtotal villous atrophy, so an important investigation would be to evaluate the diagnostic accuracy of the duodenal bulb biopsy in patients who have milder intestinal damage than that present in Bonamico *et al.*'s population.

How can clinicians incorporate Bonamico *et al.*'s interesting findings⁶ into practice? We believe that this study strongly supports a change to the commonly taught and practiced sampling of the distal segments of the duodenum alone in patients in whom celiac disease is suspected. Collection of biopsy specimens from the duodenal bulb in addition to those from distal segments of the duodenum should be recommended, as this practice may improve the rate of celiac disease detection in children and adolescents, particularly in those affected by short-segment celiac disease in whom the distal duodenum seems normal. Serology provided important evidence that supports the presence of celiac disease in patients with pathology limited to the duodenal bulb.⁶ Whether Bonamico *et al.*'s findings apply to adults, who have a higher prevalence of peptic ulcer disease and NSAID use than children or adolescents, however, remains to be proven. Finally, as the frequency of complications related to diagnostic endoscopy with biopsy of the distal duodenum is very low, prospective studies need to investigate whether the rate of complications (that is, perforation) would be adversely affected by the routine collection of biopsy samples from the duodenal bulb.

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Practice point

- In pediatric patients in whom celiac disease is suspected, the diagnostic work-up should include the collection and analysis of biopsy specimens from both the duodenal bulb and the distal segments of the duodenum
- Positive celiac serology (antibodies to tissue transglutaminase or endomysium) provides important evidence that supports the presence of celiac disease