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Research Article

Non-classic Histology in Coeliac Disease and Implications for Clinical Management

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Abstract

To evaluate the prevalence of classic histopathologic findings in serologic antibody-positive coeliac disease patients, we reviewed histology from duodenal biopsies in 20 tissue transglutaminase antibody-positive (IgA Anti-tTG) cases. Classic triad of increased intraepithelial lymphocytes, blunted villi and crypt hyperplasia were seen in only approximately one third of cases. Increased intraepithelial lymphocytes and villous blunting were more prevalent, and one fifth of cases had only increased intraepithelial lymphocytes. Villous blunting alone and histologically normal biopsies were much less common. Many patients with positive coeliac antibody serology do not show the classic triad of histologic findings. Any one of the three should allow for coeliac serologic antibody testing, if this has not already been done. Classic histology may be limited to proximal duodenum. Endoscopic biopsies should include multiple duodenal biopsies including bulb, and first (D1), second (D2) and third parts of duodenum (D3) to increase diagnostic sensitivity.

Keywords: Coeliac Disease; Increased Intraepithelial Lymphocytes; Villous Blunting; Duodenal Biopsy

Introduction

While recent studies suggest making the diagnosis of coeliac disease without tissue biopsy [1], histology has long been considered the gold standard in coeliac disease diagnosis. Classic findings on duodenal biopsy include the triad of increased intraepithelial lymphocytes, blunted villi and crypt hyperplasia [2]. Anti-tissue transglutaminase IgA antibodies are the most specific and help confirm the diagnosis. Duodenal coeliac histology can be proximal in duodenal bulb or first part of duodenum [3]. Diagnostic confirmation is important due to the increased risk of enteropathy-associated T cell lymphoma in untreated patients [4]. Following Co Path electronic archive search using keywords 'coeliac disease,' 40 small bowel histology reports of endoscopic biopsies performed to investigate the possibility of coeliac disease were reviewed. Twenty serologic antibody-positive (IgA Anti-tTG) cases were identified from 2021 through 2023. Clinical data was recorded and histologic findings were reviewed by consultant histopathologists. Patients were not on gluten-free diet. Duodenal biopsies were all from the second part of duodenum (D2) and reviewed. Patients were 15 females and five males ranging in age from 17 to 90 years (m = 55). Bloating, diarrhoea and weight loss were common symptoms. Gross endoscopic findings were not indicated. All patients had positive anti- tissue transglutaminase antibody (IgA Anti-tTG) serology. Classic triad of increased intraepithelial lymphocytes, blunted villi and crypt hyperplasia were seen in only six cases. Seven cases had increased intraepithelial lymphocytes and villous blunting, four had only increased intraepithelial lymphocytes, two had only villous blunting and one case had none of the classic findings.

Methods

Following Co Path electronic archive search using keywords 'coeliac disease,' anonymized histology final diagnosis summary reports from 40 small bowel endoscopic biopsies to investigate the possibility of coeliac disease were reviewed for histologic criteria audit. Twenty serologic antibody-positive cases were identified from 2021 through 2023. Clinical data and histologic findings were anonymously recorded from previously signed histopathology reports of serologic antibody-positive cases in Microsoft Excel. Patients were not on gluten-free diet. Duodenal biopsies were from the second part of duodenum (D2) and reviewed by consultant histopathologists.

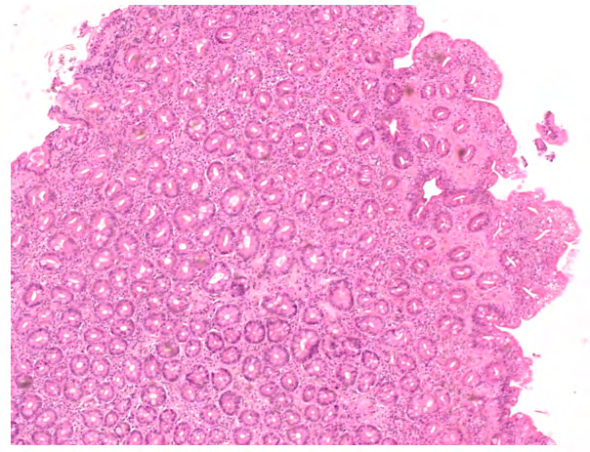

Figure 1: Classic triad of increased intraepithelial lymphocytes, villous blunting and crypt hyperplasia.

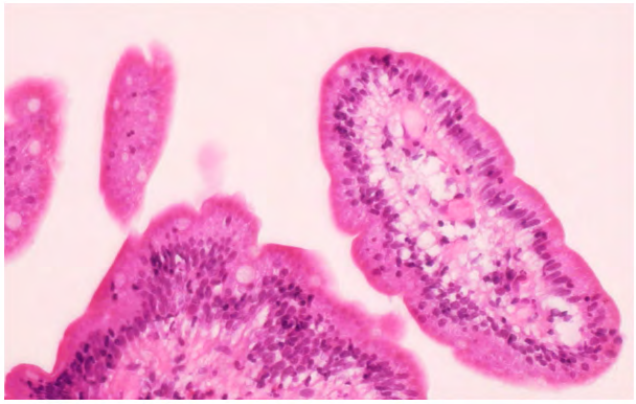

Figure 2: Increased intraepithelial lymphocytes only.

Classic triad of increased intraepithelial lymphocytes, blunted villi and crypt hyperplasia	n = 6
increased intraepithelial lymphocytes and villous blunting	n = 7
only increased intraepithelial lymphocytes	n = 4
only villous blunting	n = 2
normal	n = 1
TOTAL	n = 20

Table 1: Histopathologic findings from D2 biopsies in serology antibody-positive (Anti-Ttg) coeliac patients.

Results and Discussion

Patients were 15 females and five males ranging in age from 17 to 90 years (m = 55). Bloating, diarrhoea and weight loss were common symptoms. Gross endoscopic findings were not indicated. All patients had positive coeliac antibody serology (IgA Anti-tTG). Classic triad of increased intraepithelial lymphocytes, blunted villi and crypt hyperplasia were seen in six cases. Seven cases had increased intraepithelial lymphocytes and villous blunting, four had only increased intraepithelial lymphocytes, two had only villous blunting and one case was histologically within normal limits.

Coeliac disease is a T-cell mediated chronic inflammatory autoimmune disease [2]. People with coeliac disease develop a proximal small bowel anti-gluten T-cell response. Coeliac disease is common with an incidence of approximately 1.4% of the population, and can be asymptomatic or present with non-specific symptoms difficult to clinically diagnose. Symptoms of active or classic coeliac disease typically include diarrhea and often malabsorption of folic acid, iron, fat-soluble vitamins and calcium [3]. Improvements in histological tests and clinical symptoms are realized when patients adapt a gluten-free diet. In the absence of this, patients are at a 30-40 fold increased risk for enteropathy associated T-cell lymphoma (EATL).

The diagnosis of coeliac disease is usually defined by symptoms, the presence of HLA-DQ2/DQ8, celiac antibodies in serum, and duodenal histology [5]. Michael Marsh, a pathologist, introduced a classification system in 1922 to describe the stages of damage to the small intestine when viewed under a microscope.

His classification system ranges from 0-4, with Marsh 1 being minimal deviation coeliac disease and Marsh 4 being very severe stage of coeliac disease. In Marsh 1 findings there is an increased number of lymphocytes within surface epithelial lining, typically leading to long-standing chronic inflammation and intestinal bloating. An increased number of intraepithelial lymphocytes is the earliest pathological change following gluten challenge and a high intraepithelial lymphocyte count may be the only sign of gluten sensitivity [6]. Therefore, the finding of a raised intraepithelial lymphocytes with normal villous architecture is of sufficient clinical importance to be reported in routine small bowel biopsies [7]. Marsh 2-4 show increasing findings of increased intraepithelial lymphocytes, crypt hyperplasia and villous blunting or atrophy. Histopathologic changes of coeliac disease may be limited to the proximal duodenum, including duodenal bulb, necessitating multiple biopsies of duodenum to include D1, D2 and D3 and at least one from duodenal bulb [1,8]. for high diagnostic sensitivity. It is conceivable that restricting biopsies to D2 may miss a considerable portion of patients with proximal histopathologic changes, particularly those with 'minimal deviation' histologic findings.

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