The Benefit of Separate Bulb Biopsy in Children Undergoing an Esophagogastroduodenoscopy

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Abstract

Background: Esophagogastroduodenoscopy (EGD) is an essential diagnostic test in children with gastrointestinal diseases. Small bowel biopsies (SBB) are usually collected from the distal duodenum. A duodenal bulb biopsy (DBB) is recommended in children with celiac disease (CD), because up to 8% can have exclusive bulb injury. This study aims to assess the benefit of separate bulb biopsy in children who underwent EGD and had DBB performed.

Methods: We reviewed the electronic medical records between 01-1998 and 05-2014. All children who underwent an EGD with separate DBB were included. Demographic, clinical, and histopathological parameters were recorded.

Results: A total of 211 children were identified. The average age was 10 years (range 1-17 years). Fifty-eight patients had CD, and 153 were non-CD. All patients with CD had positive celiac serology, whereas in non-CD, 10 had positive serology (5 TTG IgA with negative TTG IgA, 1 TTG IgA, and 4 DGP IgG with normal villous architecture). In patients with CD, DBB was diagnostic in 2 (3%) with exclusive bulb injury and confirmatory in 3 (5%) with partial villous atrophy in the bulb and only increased intraepithelial lymphocytes (IEL) distally. In the non-CD group, 7 (4.5%) patients had exclusive bulb injury (4 peptic duodenitis and 3 IEL).

Conclusions: In children with CD, DBB increased the diagnostic yield by 9%. In the non-CD group, isolated bulb injury was found in 4.5%, with unclear clinical significance suggesting that DBB may carry higher specificity to CD.

Keywords: Celiac Disease; Duodenum; Histology

Abbreviations

CD: Celiac Disease; DBB: Duodenum Bulb Biopsy; EGD: Esophagogastroduodenoscopy; EMA: Endomysial Antibodies; DGP: antideamidated Gliadin Peptide; IEL: Intraepithelial Lymphocytes; SBB: Small Bowel Biopsy; TTG IgA/IgG; Antitissue Transglutaminase Immunoglobulin A or G antibodies.

Introduction

Esophagogastroduodenoscopy (EGD) is an important diagnostic test in diagnosing and treating children with gastrointestinal disorders. The use of endoscopic approach in children has increased and become the essential method for collecting duodenal biopsies[1]. More attention has been focusing on the procedures, technique related to number and location of biopsies. In eosinophilic esophagitis, the guidelines suggest the need for multiple esophageal biopsies from multiple levels to increase the diagnostic sensitivity of the biopsies [2]. Also, in celiac disease (CD), many studies advocate obtaining multiple duodenal biopsies, including separate duodenum bulb biopsy (DBB)[3]. It is known that the endoscopic findings of CD are specific but not sensitive for the disease, so pathomorphonomic endoscopic features may be helpful; but, their absence does not eliminate CD. In general, the complications of EGD include bleeding and perforation. However, such complications are rare. Most people will probably experience nothing more than a mild sore throat after the procedure.

CD is an inherited immune-mediated enteropathy, driven by ingestion of gluten, a protein present in wheat, rye, and barley, leading to damage of the small intestinal mucosa in individuals who carry the HLA-DQ2 and HLA-DQ8 genes [4,5]. Untreated or poorly controlled CD can result in many complications [6,7]. Therefore, it is important to improve the diagnostic yield to minimize the gap between diagnosed and undiagnosed CD and improve patient outcome [8]. Despite that current celiac serologic tests are highly sensitive and specific, small bowel biopsy (SBB) is still the gold standard test to confirm CD. SBB should show the characteristic histological changes of CD including villous atrophy, crypt hyperplasia, and infiltration of the lamina propria with lymphocytes [9-12]. It is recommended that multiple (at least four) biopsies should be taken from the distal duodenum. Proximal and bulb biopsies were avoided due to the presence of Brunner glands in the bulb, which interfere with the assessment of the villous-to-crypt ratio and the perceived risk of increased rate of procedure-related complications [13,14]. It has been indicated that DBB increases the sensitivity of the procedure because between 2% and 10% of CD patients can have villous atrophy solely in the bulb [15-17]. We aimed in this article to assess the benefit of separate bulb biopsy in all children who underwent an EGD and had DBB.

Materials and Methods

A retrospective review of the electronic medical record was performed between January 1998 to May 2014 using a data abstraction form that included demographic data (age, gender) and information during the healthcare encounters (initial presenting signs and symptoms in the child). The study protocol was approved by the Mayo Clinic Institutional Review Board.

Data on serological markers: anti-tissue transglutaminase IgA (TTG IgA), endomysial antibodies (EMA) and deamidated gliadin peptide antibodies DGP, EGD, and pathology reports were also collected. Inclusion criteria included all children aged 1 to 17 years who underwent an EGD with both DBB and distal biopsy. Patients were excluded if only distal duodenal samples were obtained. The diagnosis of CD was established in children with positive celiac serology and characteristic histological changes on the SBB.

Biopsies and Histology

Separate DBB was performed only if the endoscopist suspected mucosal abnormalities like erythema, erosions, or scalloping in the duodenal bulb. Obtaining separate DBB biopsies in children with positive celiac serology was not a routine practice in our institution. All biopsies were reviewed by an experienced gastroenterology pathologist. All the following histologic findings were reported: normal, intraepithelial lymphocytosis (IEL) greater than 25 per 100 epithelial cell, villous atrophy (partial or total), Crohn disease, Brunner gland hyperplasia, chronic peptic duodenitis and acute duodenitis.
Serology

Serology including TTG IgA, anti-tissue transglutaminase immunoglobulin G (TTG IgG), EMA IgA, DGP IgA, and DGP IgG were considered in the study. TTG IgA titer was considered positive if it was greater than four; a TTG IgG titer was considered positive if it was greater than six, and a DGP IgA/DGP IgG titer greater than 20 was considered positive. EMA was considered positive if >1:4. TTG IgA positivity was classified into; mild if TTG IgA > 4-10, moderate 10-40 and highly positive if > 40.

Statistical analysis

Exact Fischer test was performed to assess the association between positive TTG IgA and the presence of DBB villous atrophy. Also linear regression analysis was performed to assess if degree of TTG IgA positivity would correlate with the degree of histologic injury on the DBB.

Results

A total of 211 children who had DBB were identified between January 1998 and May 2014. There were 96 (45%) girls and 115 (55%) boys, with mean age (mean ± SD) of 10 ± 6 years at the time of procedure. Out of 211 patients, 58 (27%) had CD confirmed by positive serology then biopsy, and 153 (73%) were non-CD. All patients with CD had positive TTG IgA, whereas in non-CD patients, 10 (7%) had positive serology (five had positive TTG IgG with negative TTG IgA, one had positive TTG IgA and four had positive DGP IgG with negative TTG IgA; these 10 patients had normal villous architecture). In the CD group, 2 out of 58 had normal DBB and 8 had IEL on DBB. Among the CD group, biopsy was diagnostic in two children (3%) who had exclusive histological changes of CD to the duodenal bulb with normal histology distally and confirmatory in 3 (5%) with partial villous atrophy in the bulb and only IEL distally. In the CD group there were four DBB showing normal villous architecture (Two had normal histology and two IEL) with clear abnormalities confined to the distal duodenum. Out of 153 in the non CD group, 128 had normal DBB, 23 had IEL on DBB and 2 had partial atrophy on both DBB and distal duodenum with negative serology. In the non-CD group, 7 patients (4.5%) had exclusive bulb injury (4 peptic duodenitis and 3 IEL). Two of these seven patients had positive serology (one with TTG IgG and one with DGP IgG). None of the 153 patients in the non-CD group had exclusive changes of CD in the bulb. The presence of positive TTG IgA was highly associated with the presence of villous atrophy on the DBB using exact Fischer test with P < 0.001. Furthermore linear regression analysis showed that the degree of TTG IgA positivity (normal < 4, mild 4-10, moderate 10-40 and highly positive > 40) correlated with the degree of duodenal bulb finding (IEL, partial atrophy and total villous atrophy) with R value of 0.21 and P < 0.001.

There were no differences between the two group's demographics and presenting symptoms. The most common indications for SBB in all 211 patients were abdominal pain (111/211), diarrhea (40/211), weight loss (28/211), vomiting (21/211) and anemia (5/211). A complete list of indications is included in the Table 1.

<table>
<thead>
<tr>
<th>Indication for EGD (n = 211)</th>
<th>CD Group, No. (%) (n=58)</th>
<th>Non-CD Group, No. (%) (n=153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>37 (64)</td>
<td>74 (48)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10 (17)</td>
<td>30 (20)</td>
</tr>
<tr>
<td>Poor weight gain</td>
<td>8 (14)</td>
<td>20 (13)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (2)</td>
<td>20 (13)</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>2 (3)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Asymptomatic with positive celiac serology (TTG IgG/IgA)</td>
<td>0 (0)</td>
<td>6 (4)</td>
</tr>
</tbody>
</table>

Table 1: Indications for EGD in Both Groups

Discussion

The benefit of separate DBB in patients with CD showing the characteristic histological changes is evident in many studies [18-21]. A separate DBB should be taken in patients who are suspected to have CD, because mucosal injury associated with CD can be patchy and limited to the bulb or be more prominent in the bulb [22-24]. In these studies, the percentage of children with isolated bulb injury varied between 2.4% to 10.6% [25-27]. In our study, separate bulb biopsy increased the diagnostic yield in children suspected of CD by 9%. Two children had histologic changes that are characteristic of CD in the bulb only, and three children had isolated villous atrophy in the bulb only and IEL distally. The injuries associated with CD are believed to be most serious in the duodenal bulb where the gluten concentration is maximal, but in our study we identified 4 patients who had villous atrophy that was limited to the distal duodenum [28]. Hence in children with positive celiac serology and suggestive symptoms both proximal (bulb) and distal biopsies should be obtained. Even though only 58 patients were diagnosed with CD, we found that none of the non-CD group had histologic findings consistent with CD in the DBB. This may imply that DBBs may have a high specificity for CD diagnosis. Also, isolated mucosal injury was noted in seven patients without clear clinical significance. Our results are consistent with the outcome reported by Levinson-Castiel, et al [20].

This study has many limiting factors including 1) retrospective nature of the study results, 2) not all patients with CD suspicion underwent a separate DBB. The decision about performing a separate DBB was dependent on the endoscopist’s perception of mucosal abnormalities in the duodenal bulb, which can vary between endoscopists.

Conclusions

In children with positive serology and symptoms suggestive of CD, DBB should be obtained routinely in addition to distal duodenal biopsies to increase the diagnostic yield. Separate bulb biopsy might not be beneficial in children who do not have signs, symptoms, or serology pointing toward CD.

References


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