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The Significance of Routine Duodenal Biopsies in Pediatric Patients Undergoing Upper Intestinal Endoscopy

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Abstract

Goals: To determine the significance of performing routine duodenal biopsies during upper intestinal endoscopy in a pediatric population and to evaluate their contribution to the overall diagnosis. **Background:** Performing duodenal biopsy during every upper endoscopy regardless of the indication for endoscopy and the macroscopic findings, is a controversial topic. Advocates of performing routine biopsies argue that unexpected pathology such as villous atrophy, may have significant clinical implications. Opponents argue that the yield of performing a biopsy on an apparently normal mucosa is low. **Study:** Duodenal biopsies, routinely taken from 201 pediatric patients during upper endoscopy over a 26-month period were retrospectively reviewed. Duodenal biopsies taken during this period for suspected mucosal lesions were not included in the analysis. Indications for endoscopy included suspected peptic disease, gastroesophageal reflux, unexplained vomiting, abdominal pain, iron deficiency anemia and Crohn disease. **Results:** Of the 201 sets of biopsies reviewed, 159 (79.1%) were normal, 7 had insufficient material for evaluation and 35 (17.4%) carried abnormalities that included: 10 *Giardia lamblia* (4.9%), 13 mild chronic inflammation (6.5%), and 8 increased intraepithelial lymphocytes (3.9%). Two biopsies showed mixed acute and chronic inflammation, 1 showed lymphatic dilatation and 1 had a mild mucosal lesion. The risk for microscopic pathology in the duodenum was higher when Helicobacter pylori was present in the gastric biopsy (25.98% vs. 12.16% $P < 0.02$). The negative predictive value of a normal appearing duodenal mucosa was 81.5%, implying that a normal appearing mucosa does not rule out pathology. No complications were encountered in our series. **Conclusion:** We suggest that the inclusion of routine duodenal biopsies as part of upper endoscopy in pediatric patients should be considered favorably. This practice may yield additional pathologic findings that otherwise could have been missed. It should be done regardless of the indication for endoscopy or the gross appearance of the mucosa. This practice does not increase the risk of the procedure.

Key Words: duodenal biopsies, giardia lamblia, intraepithelial lymphocytes

There is controversy whether each upper endoscopy should also include a duodenal biopsy, regardless of the indication for endoscopy and the macroscopic findings. Gastroenterologists who advocate performing routine biopsies argue that unexpected pathology such as villous atrophy, may have significant clinical implications.[1] Opponents argue that the yield of performing a biopsy on an apparently normal mucosa is low. Performing a duodenal biopsy increases the procedure's duration, the risk of anesthesia and procedural complications such as rare intramural duodenal hematoma.[2] Biopsy evaluation increases cost.

The purpose of this study is to retrospectively review the findings of duodenal biopsies taken routinely during upper endoscopy in our pediatric population and to evaluate their contribution to the overall diagnosis.

METHODS

All duodenal biopsies taken consecutively during upper endoscopy at the pediatric gastroenterology unit at Kaplan Hospital between December 1999 and January 2001 were retrospectively reviewed. Two hundred and twenty eight patients underwent endoscopy with duodenal biopsy. Twenty-seven sets of duodenal biopsies taken during this period for suspected mucosal lesions (celiac disease or other malabsorption syndromes) were not included in the analysis since pathologic findings were expected for all these biopsies. The remaining 201 sets of duodenal biopsies that were taken routinely during endoscopy were studied. Indications for endoscopy included suspected peptic disease, gastroesophageal reflux, unexplained recurrent or persistent vomiting, abdominal pain, iron deficiency anemia, and Crohn disease.

The patients undergoing endoscopy were between 2 and 23 years of age, mean age 14.8 ± 3.4 years. There were 123 female patients and 78 male patients.

All endoscopies were preformed by the same pediatric gastroenterologist (K.M.) using an Olympus endoscope. Endoscopy was performed under sedation or general anesthesia after receiving informed consent from the parents for the procedure including upper intestinal biopsy sampling. Two duodenal biopsies were taken from the second part of the duodenum in each patient and put into formalin 10% solution. (On rare occasions only 1 biopsy was taken due to technical difficulties.)

Tissue was stained with Hematoxiline and Eosine. All biopsies were reviewed by a single pathologist (G.V.). Bi-

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opsies were evaluated with regard to the following histologic features: architectural changes, surface epithelial damage, inflammatory infiltrate in the lamina propria, subepithelial glycogen deposition, and intraepithelial lymphocytes[3]. There was no significant variation between paired samples.

Intraepithelial lymphocytes were counted for 300 surface epithelial cells, and the results expressed as a mean with a range per 100 surface epithelial cells. Anti CD3 antibodies were used and the number of labeled IEL were counted.

Statistical analysis was performed by comparison of proportions using the Fisher Exact Test.

RESULTS

Of the 201 sets of biopsies reviewed, 159 (79.1%) were normal, 7 had insufficient material for evaluation, and 35 biopsies (17.4%) had abnormalities. *Giardia lamblia* was found in 10 biopsies (4.9%). Mild chronic inflammation in the lamina propria, with increased number of plasma cells, was found in 13 biopsies (6.5%). All of these patients had Helicobacter pylori infection in their gastric biopsy. Increased number of intraepithelial lymphocytes (range 20%–25%) was found in 8 biopsies (3.9%). All these patients were later tested for antiendomisial antibodies and were negative. There were 2 biopsies with focal acute and chronic inflammation of the lamina propria, 1 in a patient with Crohn disease and 1 in a patient with lymphocytic gastritis. One biopsy showed lymphatic dilatation. One biopsy showed a mild mucosal lesion with blunting of villi and acute and chronic inflammation in the lamina propria. This patient was later tested for antiendomisial antibodies and was negative.

Table 1 presents the results of the microscopic findings correlated to the indication for endoscopy. The probability of finding duodenal pathology was 50% when the indication for endoscopy was iron deficiency anemia.

Helicobacter pylori infection was present in 127 patients and negative in 74. The risk for microscopic pathology in the duodenum was increased when Helicobacter pylori was present in the gastric biopsy (25.98% vs. 12.16% $P < 0.02$).

The macroscopic appearance of the duodenum was normal in 178 patients, duodenal ulcer was seen in 6 patients (all were Helicobacter pylori positive), duodenitis in 6 patients and other irregularities of the duodenal mucosa (a nodular mucosa) in 6 patients. The negative predictive value of a normal appearing duodenal mucosa was 81.5% (145/178), implying that a normal appearing mucosa does not rule out pathology.

No complications were encountered in our series.

DISCUSSION

Routine duodenal biopsies yielded additional pathologic findings that might otherwise have been missed in 17.4% of our population, however some of the pathologic findings observed in our patients, such as chronic inflammation without epithelial damage represents non-specific changes that might have been caused by concomitant Helicobacter infection or may be regarded as a normal variation.[4] Focal acute and chronic inflammation in the absence of Helicobacter pylori and a normal adjacent mucosa represents a pattern of involvement of the duodenum in Crohn disease.[5] Increased number of intraepithelial lymphocytes in the duodenum may also be caused by concomitant Helicobacter pylori infection, however alternatively, this may be the first marker of celiac disease,[4] as well as the mild mucosal lesion found in one other biopsy. It has been suggested that the presence of 18% or more intraepithelial lymphocytes in the surface epithelium is suggestive of celiac disease.[6] None of the patients in our study had serologic markers of celiac disease.

The most significant pathologic finding in our study population was the finding of *Giardia lamblia* in 4.9% of

TABLE 1. *Indication for endoscopy and duodenal pathology*

	Normal	Giardia lamblia	Chronic inflammation	Increased IEL	Other	Non diagnostic	Total
Peptic symptoms	130	6	10	6	1	5	158
	82.3%	3.8%	6.3%	3.8%	0.6%	3.2%	
Abdominal pain	14	3	0	0	1	1	19
	73.7%	15.7%	0	0	5.3%	5.3%	
Anemia	4	0	0	2	1	1	8
	50%	0	0	25%	12.5%	12.5%	
Vomiting	3	1	1	0	0	0	5
	60%	20%	20%	0	0	0	
Crohn's	4	0	1	0	1	0	6
	66.7%	0	16.7%	0	16.7%	0	
Other	4	0	1	0	0	0	5
	75%	0	25%	0	0	0	
Total	159	10	13	8	4	7	201

the duodenal biopsies. None of these biopsies had mucosal architectural changes. One may argue that finding *Giardia* in the duodenal biopsy may have no significance, *Giardia* being an innocent bystander, or that *Giardia* could have been diagnosed by testing stools for parasites. Zafar[7] determined the frequency of giardiasis in adult patients undergoing endoscopy for dyspepsia or other gastrointestinal disorders in Pakistan and found *Giardia* in 9% of duodenal aspirates and 1.8% of biopsies, concluding that giardiasis is a cause for dyspepsia. A multicenter questionnaire based case control study conducted in Germany, compared symptoms of adult patients with *Giardia* in the duodenal biopsies to symptoms of patients without *Giardia*. The study concluded that no symptoms could reliably allow the recognition of giardiasis in patients undergoing endoscopy.[8] Of the 10 patients in our study who were positive for *Giardia*; 6 had peptic symptoms, 3 abdominal pain, and 1 recurrent vomiting. All were treated with metronidazole. Our study does not address whether these patients' symptoms improved after treatment, although most did. Some patients had concomitant Helicobacter pylori infection and it would be difficult to determine if the improvement was related to the treatment of Helicobacter pylori or *Giardia*.

Leopold et al[9] examined the utility of routine duodenal biopsies in an American pediatric population during upper endoscopy and found only 5% of the biopsies to be abnormal. All biopsies with pathologic findings had an abnormal appearing mucosa. In their study the negative predictive value of a normal appearing mucosa was 100% leading them to conclude that routine biopsies are not clinically important, and lead only to increased costs and risks. Studies advocating the performance of routine duodenal biopsies in pediatric populations are lacking and there is diversity in practice among pediatric gastroenterologists. Some advocators of performing routine biopsies of the duodenum emphasize the increased diagnosis of celiac disease with this approach. Dickey & Hughes[1] performed 150 biopsies in adult patients with gastrointestinal symptoms or iron deficiency anemia. They found a high incidence of endoscopic markers for villous atrophy (4.6%), with villous atrophy on biopsy in 5.3%. This study emphasizes the importance of inspecting the duodenal mucosa during upper endoscopy and biopsying any pathologic appearing mucosa as well as normal appearing mucosa. In our population, no cases of unexpected celiac were diagnosed.

CONCLUSIONS

We suggest the inclusion of routine duodenal biopsies as part of upper endoscopy in pediatric patients to be considered favorably. This practice may yield additional pathologic findings that might otherwise have been missed and may have clinical significance. It should be performed regardless of the indication for endoscopy or the gross appearance of the mucosa. This practice does not increase the risks of the procedure.

REFERENCES

1. Dickey W, Hughes D. Prevalence of celiac disease and its endoscopic markers among patients having routine upper gastrointestinal endoscopy. *Am J Gastroen.* 1999;94:2182–2186.
2. Szajewska H, Albrecht P, Ziolkowski J, et al. Intramural duodenal hematoma: an unusual complication of duodenal biopsy sampling. *J Pediatr Gastroenterol Nutr*. 1993;16:331–333.
3. Perera DR, Weinstein WM, Rubin CE. Symposium on pathology of the gastrointestinal tract—part II. Small intestinal biopsy. *Human Pathology.* 1975;6:157–217.
4. Marsh MN. Gluten, major histocompatibility complex, and the small intestine. A molecular and a immunologic approach to the spectrum of gluten sensitivity. *Gastroenterology*. 1992;102:330–354.
5. Wright CL, Riddel RH. Histology of the stomach and duodenum in Crohn's disease. *Am J Surg. Path.* 1998;22:383–390.
6. Leonard N, Feighery CF, Hourihane DO. Peptic duodenitis- does it exist in the second part of the duodenum? *J Clin Path*. 1997;50:54–58.
7. Zafar MN, Baqui R, Lodi TZ, et al. Giardia lamblia in patients undergoing upper G.I. endoscopy. *J Pak Med Assoc.* 1991;41:74–75.
8. Oberhuber G, Stolte M. Symptoms in patients with giardiasis undergoing upper gastrointestinal endoscopy. *Endoscopy*. 1997;29:716–720.
9. Leopold ER, Bornstein JA, Wensett D, et al. Utility of routine duodenal biopsies during esophagogastroduodenoscopy, abstract. In 1st world conference of pediatric gastroenterology and nutrition. August 2000. Boston, USA.