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Correlation of Endoscopy and Histology in the Gastroesophageal Mucosa in Children

Are Routine Biopsies Justified?

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Abstract
Guidelines for obtaining biopsies during endoscopy in children are needed. The endoscopic evaluation may be considered deficient on many occasions if not accompanied by a histopathologic evaluation. A retrospective review of our endoscopic records and biopsies was undertaken to determine the correlation of the visualized endoscopic appearance and the histopathologic findings in the upper gastrointestinal (GI) tract in children. Over a 1-year period, 204 patients, all of whom had esophageal biopsies and 59 of whom had gastric biopsies as well, were evaluated by an upper GI endoscopy. Endoscopic findings included erythema, granularity, abnormal vascular pattern, friability, erosions, plaques, ulceration, and strictures. Histologic evaluation of biopsies was undertaken by one pathologist according to the presence of and type of cellular infiltrate and cellular morphologic abnormalities in the mucosa and submucosa where available. In this study, the correlation of endoscopic appearance with histology was rather limited in both the esophagus and the gastric mucosa. Low specificity and sensitivity of endoscopy in both locations (41% and 81% for the esophagus; and 43% and 86% for the gastric mucosa, respectively) illustrated the discrepancy. The overall accuracy of endoscopic evaluation in matching the histologic diagnosis was not more than two out of three (63.8%). No single endoscopic finding had a reliable correlation with histologic diagnosis but some had higher predictive value than others. Of the multiple indications for endoscopy in children, recurrent abdominal pain had the least diagnostic yield. Endoscopic appearance correlates poorly with histologic diagnosis in the gastroesophageal mucosa in children. Regardless of the appearance of the mucosa, routine biopsy during upper GI endoscopy in children should be encouraged.
Key Words: Endoscopy—Histology—Gastroesophageal mucosa—Children.

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With the increasing performance of pediatric endoscopy over the past two decades, there is a growing need to determine the justification for obtaining screening biopsies from normal appearing mucosa. The endoscopist is frequently criticized for performing biopsies in situations where the gross mucosal appearance is described as normal. This may have implications for third party reimbursement for health care costs as well as for hospital quality assurance programs and tissue audit committees that routinely review the justification for obtaining biopsies. Therefore, the need to evaluate the correlation is crucial. Many gastroenterologists do not routinely obtain biopsies under such circumstances despite evidence of significant discrepancy between endoscopic and histologic findings. This discrepancy has been reported in all of the regions evaluated during an upper endoscopy.[1–10] These findings have been reported in children[1,2] as well as adults.[3–10] However, data in the pediatric population is rather limited and available studies were done almost two decades ago using fiberoptic endoscopes that did not appreciate significant correlation between endoscopic appearance and histologic findings. Endoscopic technology has evolved significantly in the past 20 years with the widespread availability of videoscopes—as well as pathologic techniques and histologic classification criteria—which have improved the quality of endoscopic visualization. The question arises whether the improved visual appearance with video scopes technology will offer better correlation. There seems to be a need to reevaluate the previously noted discrepancy. So, we reviewed our recent experience of endoscopic and histologic findings in 204 children to determine the degree of that discrepancy. We performed a retrospective review comparing our own series of esophagogastroduodenoscopy (EGD) findings over a 1-year period to the final pathologic diagnosis at our institution and examined the correlation between the gross endoscopic and histologic findings.

MATERIALS AND METHODS

Medical records of patients who have undergone an EGD with biopsy between January 1, 1994 to December 31, 1994 at

the Children's Hospital of Michigan were reviewed. Patients who had therapeutic endoscopy for indications including esophageal dilatation, foreign body removal, variceal band ligation, sclerotherapy, or percutaneous gastrostomy tube placement were excluded. Three staff pediatric gastroenterologists with considerable experience performed the endoscopic examinations during this period. Olympus (Olympus America Inc., Melville, NY, U.S.A.) videoscopes were exclusively used in our endoscopy suite during that period. The indications for the endoscopic procedure, the patients' demographic data, and the mucosal findings were retrieved from the original endoscopic description. These findings in the esophagus included erythema, abnormal vascular pattern, edema with thickened mucosal folds, erosions, friability, plaques, granularity, strictures, ulcers, and salmon pink appearance suggestive of Barrett's esophagus. Each of these criteria was graded as absent, mild, moderate, or severe. The gastric endoscopic findings included erythema, edema, friability, erosions, nodularity or granularity, ulceration (including size), or other gross abnormalities, including polyps or vascular malformations, and were also graded as absent, mild, moderate, or severe. The presence of one or more of these findings was considered as an abnormality. An experienced pediatric pathologist (R.R.) who was unaware of the clinical or endoscopic findings, evaluated all of the biopsies. The esophageal biopsies were evaluated for the presence of basal cell hyperplasia, increased heights of the papillae, and the presence and type of cellular infiltrate. The submucosa, where available, was also assessed for the presence of inflammatory cells. The presence of columnar epithelium with or without intestinal metaplasia (consistent with Barrett's) was recorded. Each of the above criteria was scored as absent, mild, moderate, or severe. The gastric biopsies were evaluated for the presence of excess chronic inflammatory cells, eosinophils, neutrophils, glandular destruction, and lymphoid follicles and for the presence of *Helicobacter pylori* organisms. Each of these criteria was scored as absent, mild, moderate, or severe. After full evaluation of all criteria, a biopsy was designated either as normal, if no pathologic finding was present, or as abnormal. A specific pathologic diagnosis was made when appropriate findings were present, as applicable.

Statistical analysis of the data for determination of correlation was done with the χ^2 test and cross-tabulation analysis. Statistical analysis of the correlation between endoscopic and histologic findings was done using SPSS program (SPSS Inc., Chicago, IL, U.S.A.) and an IBM computer. The frequency distribution and cross-tabulation for these findings were calculated.

True-negative EGD studies of the esophagus or the stomach were defined as normal findings described by both the endoscopist and the pathologist and false-negatives were described as normal by the endoscopist but were diagnosed to have abnormalities by the pathologist. True-positives were defined as cases with abnormalities described by both the endoscopist and the pathologist whereas false-positives were defined as cases with abnormalities described by the endoscopist but that were diagnosed as normal histologically.

RESULTS

A total of 204 qualifying consecutive EGD studies with 204 esophageal and 59 gastric biopsies were done. There were 103 men and 101 women. The mean age was 8.4 years (range, 2.8–18.3 years). Of the 204 patients, 127 (62%) had more than one indication for the EGD. Table 1 summarizes the indications for the EGD. Of the 204 cases evaluated, 73 were described as having endoscopically normal appearing esophagus, 114 as having moderate endoscopic esophageal abnormalities, 12 as having severe endoscopic esophageal abnormalities, and 5 as endoscopic Barrett's esophagus. Of the 59 patients who had gastric biopsies, the endoscopist described 19 as normal, 34 as having mild to moderate endoscopic gastric abnormalities, 2 as severe endoscopic gastric abnormalities, and 4 as having gastric ulcers. Histologic diagnosis for the 204 esophageal biopsies was normal in 99 cases, reflux esophagitis in 98 cases and columnar mucosa was seen in another 7 cases with no evidence of intestinal metaplasia. Of the gastric biopsies studied, 37 were normal and 22 had gastritis, including 8 cases with *H. pylori* described on histology.

TABLE 1. *Indications for EGD in children*

Indication for EGD	% Patients*
Abdominal pain	50
Intractable asthma	14.2
Recurrent vomiting	53.9
Failure to thrive	15.2
Chronic diarrhea	7.8
Recurrent stridor	17.6
Upper GI bleeding	19.1
Other indications	14
Overall	100

*62% of patients had more than one indication for EGD.

Although it is acknowledged that in this study the evaluation of the duodenum was not included and that this may decrease the overall yield of the identified pathologies, some general trends were observed. The yield for abnormal histology in either the esophageal or the gastric mucosa among the indications for doing the endoscopy was 107 of 204 in the esophagus and 22 of 59 in the gastric biopsies. The yield was highest for patients whose indications included intractable asthma and upper gastrointestinal (GI) bleeding, where reflux esophagitis was the most common pathology identified and where the lowest for those whose indications included recurrent abdominal pain.

Only one of the five patients suspected to have Barrett's mucosa at endoscopy had histology compatible with Barrett's; three had severe esophagitis and one had normal histology. Six other patients had histologic findings of columnar mucosa without intestinal metaplasia. All of them had abnormal endoscopic evaluation; and, in three, the abnormalities were described as severe. The specificity, sensitivity, and positive and negative predictive values, as well as the overall accuracy of endoscopic findings for the esophagus and for the gastric mucosa as related to histology, are shown in Table 2.

Although the overall correlation was limited, some endoscopic criteria seemed to have better predictive

TABLE 2. *Summary of the correlation of endoscopy and histology of upper GI tract in children*

	Esophagus	Stomach*
Sensitivity	81.6%	86.3%
Specificity	41.6%	43.2%
PPV	66.6%	47.5%
NPV	61.4%	84.2%
Accuracy	65%	59%

*Only 29% of the patients included had gastric biopsies obtained.

PPV, positive predictive value; NPV, negative predictive value.

value than others. Table 3 summarizes the concordance of multiple endoscopic findings with abnormal histology in the esophagus and in the gastric mucosa. Of the findings describing the esophageal mucosa at endoscopy, friability appeared to have the highest correlation with histologic reflux esophagitis, whereas erythema had the least correlation. The presence of gastric ulceration on endoscopy always correlated with abnormal histology, whereas nodular gastric mucosa correlated with gastritis in less than one-third of the cases.

DISCUSSION

EGD is a well-established diagnostic and therapeutic procedure in the pediatric patient. This study shows that the limited correlation of endoscopic and histologic findings in the esophagus and gastric mucosa despite the advances made with endoscopic and histologic techniques. It also demonstrates the need for screening biopsies as an integral part of such a procedure because the rates of both false-negative and false-positive endoscopy findings appear to be unacceptably high. In 1980, Benjamin et al.[9] suggested that an abnormal mucosal histology in view of normal endoscopy findings and barium swallow may be considered to be a false-positive. However, this cannot be substantiated, particularly because there is no available data on mucosal histology of a large number of normal asymptomatic children to serve as true controls. In 1983, Biller et al.[2] reported a similarly poor correlation of endoscopy and histology for the esophageal mucosa in children in a retrospective review with only 45% true-positive and as high as 30% false-negative cases. The correlation of gastric mucosa endoscopy and histology was also reported to be quite limited by Sauerbruch et al.[6] in a prospective study of the three anatomic regions of the stomach with the positive predictive value of all the endoscopic findings rarely exceeding 50%. The limited correlation seen in our study might have been exaggerated by multiple factors, including the relatively small sample size, the inclusion of some endoscopic criteria that tend to be frequently observed, such as erythema, and the technique of biopsy from a representative mucosal lesion. This may be particularly relevant in the case of ulcerating lesions where the endoscopist typically avoids biopsying the center of the ulcer or the active part of the lesion to minimize the risk of bleeding. Interobserver variability is another potential factor in this retrospective review to consider when evaluating the endoscopic findings. However, no significant statistical differences were found when comparing the sensitivity and specificity of endoscopic findings among the three endoscopists. Work by Biller et al.[2] showed no improvement of the endoscopic and histologic correlation when the presence of erythema as an endoscopic abnormality was excluded. Other factors may include the fact that the inflammatory changes of the mucosa are frequently patchy and focal with the potential of sampling error adding to the lack of correlation. Black et al.[1] similarly demonstrated that the correlation between endoscopy and histology in gastroduodenal mucosa in children was poor; and, he recommended that the endoscopist should limit the diagnosis to a descriptive one, such as erythema or erosions, and not attempt to make a histologic diagnosis, such as gastritis. In our study, this also appears to be relevant for the esophageal mucosa.

TABLE 3. *Endoscopic abnormalities and percentages of their abnormal histologic yields*

Endoscopic finding	Abnormal histology esophagus	Abnormal histology stomach
Erythema	63%	43%
Friability	71%	30%
Erosions	68.5%	50%
Edema	65%	43%
Ulcer	NA	100%
Granularity	NA	30%

NA, not applicable.

No single endoscopic criteria had significant positive predictive value to diagnose histologic inflammation in the esophageal or gastric mucosa. However, some were more reliable than others, such as ulceration, friability, and erosions compared with erythema and granularity. Even though the overall correlation between endoscopy and histology was rather limited in this study, there was a slightly better correlation of the findings in the esophagus when compared with the gastric mucosa. This may reflect the different nature of the pathologic processes involving both locations. Alternatively, this may merely reflect a statistical error related to the small number of gastric biopsies performed in our study. As only about 29% of the patients had gastric biopsies, one cannot assume that the observations made for some of the patients could be accurately extrapolated to the others. Indeed, this does limit the ability of our study to ideally compare the two sites.

In this study, the yield for endoscopic evaluation for recurrent abdominal pain was limited compared with

other indications for the procedure. This result seems to be in keeping with work done by other investigators.[1,2] Other endoscopic visualization-enhancing techniques, such as chromoendoscopy, with the use of special fluorescence dye testing or the use of infrared emitting fluorochromes or special stains, such as Lugol, may prove more accurate for detecting early mucosal lesions in the GI tract, but they are not yet well established in pediatric endoscopy and may take some time to become widely available to the practicing pediatric gastroenterologist. Moreover, the presence of such early histologic lesions would need to be correlated to symptoms before their value could be determined, an issue that has not fully been resolved in standard light microscopy. Nevertheless, histology still provides more standard, objective, and verifiable evidence of abnormality than endoscopic description alone, as this study demonstrated.

The presence of abnormal histologic findings on endoscopically "normal" mucosa may provoke additional questions regarding the need for a repeat endoscopy in the future and how soon microscopic changes are expected to resolve or to progress to more appreciable endoscopic findings. Furthermore, the clinical relevance of some minor histologic abnormalities may be difficult to determine in many patients whose endoscopic evaluation may otherwise be normal. Our study has not addressed the question of what to do about such histologic abnormalities if they do not fit the patient's problems. Nevertheless, "insignificant" or "irrelevant" findings in the past have subsequently been shown to be clinically important, such as in the case of *H. pylori* infection of the gastric mucosa. Similarly, one may speculate whether the presence of certain types of cellular infiltrates or other, now considered nonspecific, histologic findings of the GI tract mucosa or submucosa, could soon prove to be markers of diseases now thought to represent "functional" GI disorders. Unless we routinely do endoscopic biopsies in patients with clinical symptoms, this question may never be answered.

Although we did not include the small bowel endoscopic or histologic findings in our study, some GI pathologies involving the duodenum are essentially microscopic with minimal or no gross morphologic findings, as in eosinophilic gastroenteritis, partial villous atrophy, and giardiasis. Chawla et al.[8] reported no more than 80% correlation between endoscopic and histologic duodenitis. Similarly, in the lower GI tract, microscopic colitis syndrome is another condition that has normal or near normal gross endoscopic appearance and that could not be diagnosed without a biopsy.[11] Such conditions would be easily missed if the endoscopist did not obtain biopsies from normal-appearing mucosa. Therefore, the practice of obtaining screening biopsies of the entire GI tract should be encouraged during endoscopy studies, at least during the first endoscopic evaluation of a patient, regardless of the appearance of the mucosa.

Although the limited correlation between endoscopic and histologic findings in the gastroesophageal mucosa was demonstrated in our study, our results are rather limited by the retrospective design and by not including the duodenum or obtaining gastric biopsy in every patient. The best way to examine this correlation may be a prospective study with all patients having biopsies in the esophagus, stomach (various parts), and duodenum and possibly a follow-up evaluation with pre-decided intervention plans for histologic abnormalities with and without clinical relevance to the patients indications for endoscopy.

Although in our study the pathologist had to be blinded to the clinical history and endoscopic findings, we do not recommend this for patient care outside of a research setting. This information may be important in the final pathologic interpretation, as has been expressed in the recently published "Updated Sydney System," for classifying and grading gastritis that includes morphologic histologic, endoscopic, and etiologic information.[12]

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