Incongruence between Histologic and Endoscopic Diagnoses of Barrett’s Esophagus Using Transnasal Esophagoscopy

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OBJECTIVES: The symptoms, patterns of reflux, and clinical manifestations of laryngopharyngeal reflux (LPR) differ from those of gastroesophageal reflux disease (GERD) in many ways. The purposes of this study were to determine the prevalence of Barrett’s esophagus in patients with LPR using transnasal esophagoscopy (TNE) and to determine if there is agreement between TNE clinical findings and pathology results when using TNE for Barrett’s screening. Study Design: This study involved a retrospective review of the records of 200 consecutive patients with LPR undergoing esophageal screening. Methods: The prevalence of patients with findings clinically suspicious for Barrett’s and the biopsy results for those patients were reviewed. Results: Of the 200 patients with LPR who were screened with TNE, 10% (20 of 200) had findings suspicious for Barrett’s esophagus, and, of those, only 30% (six of 20) had biopsy-proven Barrett’s metaplasia. Conclusion: Although TNE may be a useful screening tool for Barrett’s, there is incongruence between TNE findings and biopsy results, which likely reflects suboptimal biopsy methods with TNE. New biopsy techniques such as the CDx brush biopsy may enhance the sensitivity of TNE biopsies, and future studies are needed in this area. Key Words: Barrett’s esophagus, transnasal esophagoscopy, gastroesophageal reflux, laryngopharyngeal reflux. Laryngoscope, 116:303–306, 2006

INTRODUCTION

Over recent years, transnasal esophagoscopy (TNE) has been identified as a useful tool for office-based diagnosis of various esophageal pathology, including esophageal strictures, esophagitis, and Barrett’s esophagus.1–3 Unlike traditional flexible esophagoscopy, TNE requires no sedation and is performed using only topical nasal anesthesia with the patient in a seated position.

The prevalence of Barrett’s esophagus among patients with gastroesophageal reflux disease (GERD) is estimated to range from 5% to 20%.4,5 Little is known about the prevalence of Barrett’s esophagus in patients with laryngopharyngeal reflux (LPR). One study with limited sample size (n = 58) found Barrett’s metaplasia in 7% of patients with LPR,1 but no further studies are available to corroborate this data. The goal of this study was to determine the rate of Barrett’s metaplasia among a large series of consecutive patients with LPR who had undergone TNE surveillance, with a special emphasis on the relationship between endoscopic findings and histopathologic results.

METHODS

TNE findings from the last 200 consecutive patients presenting to the Center for Voice and Swallowing Disorders of Wake Forest University with clinical laryngopharyngeal reflux were reviewed. These patients were suspected to have LPR based on symptoms and laryngeal findings using a validated reflux symptom index (RSI) and reflux finding score (RFS) developed at our center.6,7 Our TNE technique has been well described previously.2,3 It is performed with the patient in a seated position with topical nasal anesthesia and no sedation. In this study, all TNE examinations were performed using an endoscope with a distal chip camera (Vc-1530; Pentax Precision Instrument Corp., Orangeburg, NY). The examinations were performed by two attending laryngologists and a laryngology fellow. All examinations were videotaped. Endoscopic findings of the fellow were confirmed by review with at least one of the attending laryngologists; the attending laryngologists did not review one another’s evaluations. Endoscopic Barrett’s was defined by the visualization of finger-like projection(s) of salmon pink mucosa beyond the squamocolumnar junction of the GE junction (Fig. 1) with short-segment Barrett’s involving less than a 3-cm projection and long segment involving a projection of 3 cm or more. All patients with TNE findings suggestive of Barrett’s esophagus underwent directed biopsies with a 1.8-mm cup biopsy forceps. Specimens were reviewed in the pathology department where histologic diagnosis of Barrett’s was made based on the presence of specialized intesti-
tinal metaplasia with goblet cells with or without dysplastic changes.

This study involved review of both the prevalence of suspected Barrett’s on TNE and the prevalence of pathologically confirmed Barrett’s metaplasia. Finally, manometry and pH probe data on patients with Barrett’s esophagus was recorded. Criteria for abnormal pharyngeal reflux includes one or more pharyngeal reflux episode with pH $< 4$. Our laboratory criteria for abnormal esophageal reflux are similar to those from other laboratories and include greater than 8% of upright time with a pH $< 4$, greater than 2.8% of supine time with pH $< 4$, greater than 5.4% of total study time with a pH $< 4$, or greater than 50 total number of esophageal reflux episodes.

RESULTS

Of the 200 TNE studies performed on consecutive patients with LPR, 20 (10%) demonstrated findings suggestive of Barrett’s esophagus (Figs. 1 and 2). This included 12 males and eight females with a mean age of 51 years. All 20 of the patients demonstrated findings of short-segment (<3 cm) Barrett’s. Biopsy results demonstrated normal gastric fundic mucosa ($n = 4$), normal squamous mucosa ($n = 3$), squamous mucosa with chronic reflux esophagitis ($n = 7$), and intestinal metaplasia consistent with Barrett’s ($n = 6$). None of the Barrett’s metaplasia biopsies demonstrated evidence of dysplasia. Barrett’s metaplasia endoscopic and histologic congruence was not significantly different for the first 100 examinations (three of nine) when compared with the second hundred examinations (three of 11).

Manometry had been performed in all patients with histologically confirmed Barrett’s esophagus. It was found to be normal in five patients, with decreased motility but normal lower esophageal sphincter pressure in one patient. pH probe testing had been performed on five of the patients with Barrett’s. Two patients demonstrated normal pharyngeal and esophageal probe findings and three patients demonstrating globally abnormal studies (as previously defined) with both abnormal pharyngeal and esophageal acid exposure.

DISCUSSION

Barrett’s esophagus is defined as the replacement of the squamous epithelium of the distal esophagus with columnar-appearing epithelium extending beyond the GE junction. Barrett’s esophagus predisposes to the development of esophageal adenocarcinoma, which is the fastest rising malignancy in the United States over recent decades. Histologically, Barrett’s is confirmed by the presence of specialized intestinal metaplasia with goblet cells. Endoscopically, Barrett’s appears as salmon pink mucosa, often with finger-like projections, extending beyond the squamocolumnar junction of the GE junction (Fig. 1). Short-segment Barrett’s esophagus extends a distance of less than 3 cm beyond the GE junction, whereas long-segment Barrett’s (extending 3 cm or more) is less common but associated with an increased risk of developing high-grade dysplasia and adenocarcinoma. Although it has been suggested that LPR patients have a higher rate of long-segment Barrett’s, long-segment Barrett’s was not found in any cases in the present study. These findings may reflect the study sample size (short-segment Barrett’s being more common overall), and long-segment Barrett’s would likely be detected with a larger LPR study population.

The incidence of esophageal adenocarcinoma in patients with Barrett’s esophagus is estimated to be 0.5% per year. It is thought to occur through a progression from Barrett’s metaplasia to dysplasia to adenocarcinoma. Low-grade dysplasia has been shown to progress to cancer with an incidence of 12% over a 5-year period, whereas high-grade dysplasia progresses in up to 25% over the same period. Based on this, the American College of Gastroenterology screening recommendations differ based on biopsy results with surveillance for nondysplastic Barrett’s recommended every 3 years, low-grade dysplasia every year, and high-grade dysplasia every 3 months (or esophagectomy).
Among patients with GERD, it is estimated that 5% to 20% of patients undergoing endoscopy will demonstrate endoscopic findings that are pathologically confirmed as Barrett’s esophagus.4,5 The current study suggest the rate of TNE endoscopically detected Barrett’s esophagus in patients with LPR may be similar (10%), but histologically proven Barrett’s was detected in only 3%. This correlation between endoscopic findings and histology results is much lower than that described in the gastroenterology literature, which shows histologic agreement with endoscopic Barrett’s findings in nearly 90% of cases.5 Thus, although detection of dysplasia within a Barrett’s segment is a challenge for gastroenterologists, there is generally not disagreement between endoscopic findings of Barrett’s and the final histological diagnosis as was seen in this study. This discrepancy could have several possible explanations. First, recommended biopsy technique in the gastroenterology literature involves four-quadrant biopsies every 1 to 2 cm of endoscopically recognized areas of Barrett’s.13 In cases with large areas of Barrett’s, this can result in an extensive number of biopsies with prolonged procedure time. This would not be well tolerated or technically feasible with TNE, so biopsies are generally limited to two or three regardless of the surface area of the Barrett’s. Second, the gastroenterology literature also recommends biopsy with endoscopic “jumbo forceps,” which measure just under 3.6 mm in diameter.5 Although this is easily done with the large, traditional flexible esophagoscope, the TNE measures only 5.1 mm in diameter (for atraumatic nasal passage) with a 2-mm working channel. Thus, the biopsy cups and resultant specimen size are limited when working with TNE. The ability to accurately biopsy the target is also difficult using the small biopsy cups in an awake patient, and this difficulty may explain the three samples of normal squamous mucosa that were found in patients with suspected Barrett’s (if the salmon pink mucosa were biopsied, it may represent Barrett’s, gastric mucosa, or severely inflamed squamous epithelium, but would not be consistent with normal squamous epithelium, which is lighter in color). Third, rather than being reviewed by a gastroenterology pathologist, each specimen was evaluated in the pathology department by a general pathologist, which may have negatively influenced the histologic interpretation. Finally, examiner interpretation of TNE findings can have much interobserver variability based on experience and the quality of the TNE examination. Although the use of a distal chip camera endoscope results in high-quality examinations relative to a traditional fiberoptic scope, examiner skills such as insufflation, suctioning, and irrigation may also affect examination quality and sampling. However, if examiner experience was the main reason for the findings in this study, congruence between the endoscopic and histologic findings would be expected to improve throughout the series, and this did not occur. Our institution recently reported our experiences with over 700 TNE examinations, which to our knowledge is the largest experience in the United States3 with the largest series of TNE examinations to date being 1,100 consecutive patients in France.14 Despite this, we acknowledge that our interpretation skills continue to improve as our experience with TNE broadens.

In contrast to the results of this study, one previous gastroenterology study involving 32 patients with known Barrett’s metaplasia found that biopsy results from transnasal upper endoscopy were positive for Barrett’s metaplasia in 31 of the patients, and dysplasia was detected at a similar rate to those biopsies obtained on the same patients with conventional upper endoscopy.15 Because the study was prospective and involved patients known to have Barrett’s metaplasia, its design was much different from the present study. Furthermore, the technique included quadratic mucosal biopsies at 2-cm intervals, which we have been unable to consistently perform on awake patients.

Unexpectedly, two of the six patients with pathology-confirmed Barrett’s had globally negative pH probe studies, but clinical history and examination were consistent with LPR. Although it is unclear why the pH probe evaluations were negative, it may imply that patients should be screened for Barrett’s based on LPR symptomatology and laryngeal examination findings rather than pH probe-documented reflux. LPR symptoms have recently been shown to be better than gastroesophageal symptoms for the prediction of esophageal adenocarcinoma.16

Future, prospective studies comparing TNE biopsy results with gastroenterology esophagoscopy obtained biopsy results in the same patients would be helpful in establishing the sensitivity of the TNE biopsy technique. Use of new tools like the CDx brush (CDx Laboratories, Inc., Suffern, NY) may also be important. We are currently investigating the use of the CDx brush with TNE. When used correctly, the CDx brush permits full-thickness sampling of epithelium down to the basement membrane. The sampled cells then undergo specialized computer analysis, which detects the abnormal cells in the sample and displays them for pathologist interpretation. Currently at our institution, patients with endoscopic Barrett’s with or without biopsy confirmation are either followed closely with TNE surveillance every 6 to 12 months or are referred to gastroenterology. After the sensitivity of TNE biopsies for Barrett’s is better established, our accepted surveillance algorithm may become analogous to that of the American College of Gastroenterology.15

CONCLUSION

In conclusion, the current study demonstrates a low rate (3%) of biopsy confirmed Barrett’s esophagus among patients with LPR with a higher rate (10%) of Barrett’s findings on endoscopy. This incongruence between endoscopic and histologic diagnoses warrants further study.

BIBLIOGRAPHY

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