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ORIGINAL ARTICLE

Utility of liquid-based cytologic examination of distal esophageal brushings in the management of Barrett esophagus: a prospective study of 45 cases

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Introduction The goal of Barrett esophagus surveillance is to identify high-grade dysplasia (HGD) for eradication. Surveillance programs currently rely on limited histologic sampling; however, the role of cytology in this setting is not well studied.

Materials and methods From December 1, 2011 to March 30, 2014, 45 patients underwent 4 circumferential brushings of the distal tubular esophagus followed by standard 4-quadrant biopsies. One ThinPrep slide and 1 Cellient cellblock (Hologic, Boxborough, Mass) were prepared. Six cytopathologists evaluated each for adequacy, intestinal metaplasia (IM) and dysplasia. Findings were classified using the traditional 5-tier system used for biopsies. A prospectively modified 3-tier cytologic classification was also tested: negative for HGD, indeterminate for HGD, and HGD. Sensitivity, specificity, and kappa values (interobserver agreement) for cytology were calculated.

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Results Ten of 45 patients had nondiagnostic cytologies; none of whom had dysplasia on biopsy. Cytology had good sensitivity (82%) and specificity (88%) for identifying IM compared with biopsy with moderate interobserver agreement (pairwise average of Fleiss and Krippendorf kappa value = 0.589, 79% agreement). One case had IM on cytology not detected on histology. Six of 45 patients had dysplasia on biopsy including 1 intramucosal adenocarcinoma, 1 indeterminate for dysplasia, 2 high-grade dysplasias, and 2 low-grade dysplasias. A non-negative adequate cytology sample had a sensitivity of 100% and a specificity of 88% and 94% for the 5-tier and the 3-tier classification, respectively.

Conclusions Cytology appears to have good sensitivity and specificity for diagnosis of HGD, and cytology may be poised to synergize with advances in other techniques for management of patients with Barrett esophagus. Improvements in brushing devices may help to decrease the nondiagnostic rate.

Introduction

Barrett esophagus (BE) is defined in the United States as endoscopically confirmed salmon-colored mucosa (columnar metaplasia) in the distal tubular esophagus (DTE), showing intestinal metaplasia (IM) on histology.[1] The diagnosis of BE is crucial due to the associated risk of developing esophageal adenocarcinoma. A diagnosis of BE is estimated to confer a 20-fold increased risk of developing esophageal adenocarcinoma and up to 0.1% to 0.5% of patients with BE in the United States progress to invasive adenocarcinoma annually.[2,3] Currently, the American Gastroenterological Association (AGA) recommends the histologic presence of IM as a requirement for a diagnosis of BE.[1] However in a shifting paradigm, there is recent evidence suggesting that even nonintestinalized columnar mucosa in the DTE is associated with a significant risk of developing malignancy and also harbors molecular rearrangements similar to those seen in intestinalized columnar mucosa.[4,5]

For patients with established BE, periodic endoscopic surveillance is the recommended follow-up. To enable the early detection of treatable precancerous lesions (mucosal dysplasia), systematic but laborious 4-quadrant biopsies are performed at every 1 to 2 cm of columnar mucosa in the DTE.[6] Suspicious nodules, masses, or ulcers are also biopsied. Dysplasia in the setting of BE is currently classified according to modifications of the original Vienna classification system,[7] a 5-tier system. Though each category has specific treatment guidelines,[1] the ultimate goal of surveillance is to be able to detect high-grade dysplasia (HGD) efficiently to allow its eradication. It is well-known that this classification system, especially the equivocal category of indeterminate for dysplasia, suffers from poor interobserver agreement (IA) among pathologists.[8]

Ultimately, the early detection of HGD relies on good sampling. Recently there has been an increasing interest to perform fewer, more directed biopsies.[1] Innovations in endoscopic imaging techniques coupled with the emergence of more advanced and safer endoscopic mucosal resection techniques offer the potential to radically change the management of BE.[9,10] In spite of these advances, the pathophysiology of BE and its progression to cancer is still not clearly understood, and the potential advantages offered by new endoscopic techniques are still essentially reliant on the ability to detect alterations in cell and tissue morphology to help improve sampling. In this setting it may be useful to investigate alternative, safer, more cost-effective methods of obtaining a broad sample that could potentially be easily used for molecular studies in the setting of BE. Our study begins to define the limitations and potential advantages of cytologic examination of DTE brushings in the management of patients with BE. We also briefly review the cytomorphologic features of DTE esophageal brushings in this setting.

Materials and methods

Forty-five patients seen in the high-risk esophageal cancer clinic in our institution from December 2011 to March 2014 were consented for involvement in the study. During routine endoscopic surveillance (in accordance with AGA guidelines), patients with DTE mucosal changes consistent with columnar metaplasia that had no visible masses, nodules, or ulcers were included in the study. To ensure adequate sampling, an arbitrarily agreed on 4 circumferential brushings of the DTE using a 3.0-mm diameter brush with a 1.8-mm catheter (Telemed Systems, Hudson, Mass) were performed, followed by routine 4-quadrant biopsy. To enable multiple brushings from a single brush, the brush was rinsed into sterile 2-ml aliquots of Hanks saline. After the fourth brush, the saline was added to 45 ml of CytoRich Red (Beckton, Dickinson, and Company, Franklin Lakes, NJ). The samples were then centrifuged at 800 g and the pellets resuspended in PreservCyt fixative vials (Hologic, Marlborough, Mass). One liquid-based ThinPrep slide (Hologic) was made, and if >5 cc or >5 visible particles remained, 1 Cellient automated cellblock (Hologic) was made for each specimen. These were stained with Papanicolaou (ThinPrep) and hematoxylin and eosin (cellblock) and examined by routine light microscopy. Evaluation of the cytologic brushings and cellblocks (when applicable) was done by 6 cytopathologists consisting of 1 cytopathology fellow and 5 board-certified cytopathologists with post-fellowship experience varying from 1 to 20+ years, including 1 cytopathologist with additional gastrointestinal