Case Presentation: High-grade esophageal dysplasia suspicious for invasive adenocarcinoma within the context of long-segment Barrett's esophagus.

Abstract: High grade dysplasia with suspicion of invasive adenocarcinoma was found in multiple esophageal biopsy specimens from a relatively young male with history of long-segment Barrett's esophagus. Barrett's esophagus is a known precursor lesion to dysplasia and adenocarcinoma, and the risk increases with long-segment involvement. There is a high inter-observer variability between diagnosing metaplasia, regenerative changes and low grade dysplasia. Additionally, the distinction between high grade dysplasia and intramucosal adenocarcinoma can be difficult to diagnose accurately on biopsy specimens that lack adequate preservation of the muscularis mucosa.

Introduction: A 47 year old male with history of Barrett's esophagus presented for routine follow up with an upper gastrointestinal endoscopy. Results of the procedure showed mucosal changes consistent with long-segment Barrett's esophagus spanning 10 cm in length. Four quadrant biopsies were performed every 1-2 cm of the esophagus.

Gross: The esophagus and gastroesophageal junction were examined with white light and narrow band imaging (NBI) from a forward view and retroflexed position. There were esophageal mucosal changes consistent with long-segment Barrett's esophagus. These changes involved the mucosa at the upper extent of the gastric folds (39 cm from the incisors) extending to the Z-line (29 cm from the incisors). Salmon-colored mucosa was present. The maximum longitudinal extent of these esophageal mucosal changes was 10 cm in length. Mucosa was biopsied in 4 quadrants at intervals of 1 cm in the lower third of the esophagus. The stomach and duodenum were normal.

Microscopic: Tissue levels of the biopsy material showed fragments of gastric-type columnar mucosa with extensive low-grade dysplasia with scattered acute inflammation. Multiple areas throughout the esophageal biopsies showed features that were suggestive of high-grade dysplasia, however the presence of acute inflammation somewhat hindered the interpretation. The case was sent for expert consultation to The University of Michigan Pathology and Clinical Laboratories and the report stated some parts of the biopsy were consistent with Barrett's mucosa in the appropriate endoscopic setting. In addition, there were cytologic changes with enlarged, hyperchromatic and pleomorphic nuclei and loss of nuclear polarity extending to the surface, consistent with high-grade dysplasia. Furthermore, multiple foci of complex architecture and intraluminal necrotic debris were seen, suspicious for adenocarcinoma invading lamina propria. (Figure 1 and Figure 2).

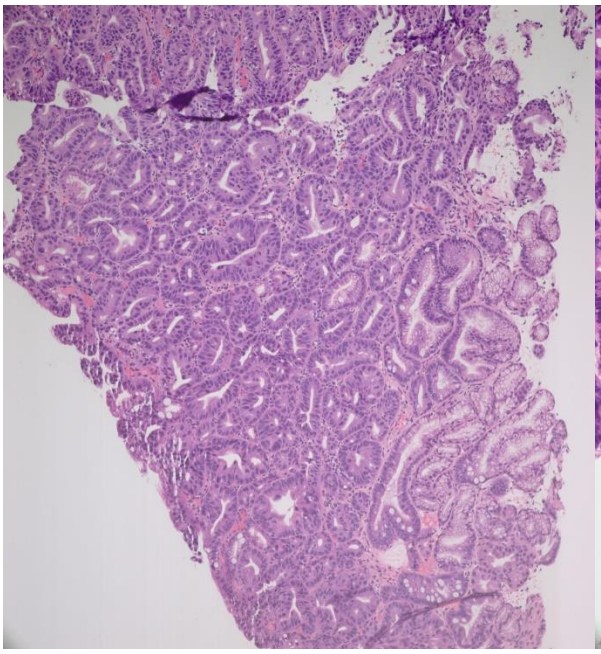

Figure 1

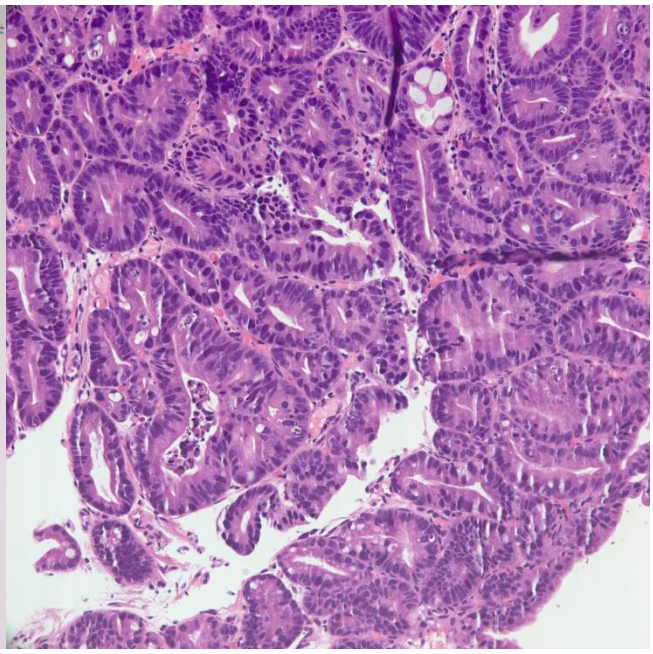

Figure 2

Discussion:

Barrett's esophagus is known as a precursor to the development of carcinoma as it typically progresses sequentially from inflammation, metaplasia, dysplasia, and ultimately carcinoma due to the accumulation of multiple genetic and epigenetic alterations. However, it is still unknown how rapidly or how often high-grade dysplasia will progress to cancer. One study has discovered that the risk of progression to carcinoma can be approximately 0.12-0.43% per year and if combined with high grade dysplasia and carcinoma, the risk ranges between 0.26-0.63% per year.

High inter-observer variability between pathologists exists in distinguishing metaplasia and regenerative changes from low grade dysplasia. Additionally, the difference between high-grade dysplasia and intramucosal adenocarcinoma (neoplastic cells extending beyond the basement membrane into the lamina propria or muscularis mucosa) is difficult, particularly when seen in a biopsy specimen where the depth of the specimen can be inadequate and muscularis mucosa is often not well preserved. The inter-observer variability improves significantly when dysplasia is seen on endoscopic mucosal resection specimens due to the ability to see the submucosa which is critical for an accurate diagnosis and staging purposes.

References:

WHO Classification of Tumors Editorial Board. Digestive System Tumors. Lyon (France): International Agency for Research on Cancer;2019. Tumors of the Oesophagus, p 32-35; WHO classification of tumors series, 5th ed., vol1.

Sachin, W, et. Al. “Greater Interobserver Agreement by Endoscopic Mucosal Resection Than Biopsy Sample in Barrett’s Dysplasia.” Clinical Gastroenterology and Hepatology, 2010-09-01, Volume 8, Issue 9, Pages 783-788.e2.

Yerian, L. “Histology of Metaplasia and Dysplasia in Barrett’s Esophagus.” Surgical Oncology Clinics of North America, 2009-07-01, Volume 18, Issue 3, Pages 411-422.

Falk, G. “Barrett’s Oesophagus: Frequency and prediction of dysplasia and cancer.” Best Practice & Research: Clinical Gastroenterology, 2015-02-01, Volume 29, Issue 1, Pages 125-138.