Barretts Esophagus
Part 1: Pretest

Hines Case Archives
Barretts Esophagus

• The following 25 images are taken from patients with Barretts Esophagus.

• These cases are from the Hines VA Medical Center and Loyola University Medical Center in Maywood, Illinois USA

• Each case has follow up including subsequent biopsy material, resection, and/or other therapeutic outcome

• Each case has been reviewed by Drs Stephen Stontag and Greg Chejfec as well as several other pathologists
Barretts Esophagus

• Each image is taken from a tissue sample taken from a patient with Barretts esophagus as defined by the presence of intestinal (goblet cell) metaplasia

• Each of the following 25 images should be placed in one of the following 5 categories:
  – Negative for dysplasia
  – Indefinite for dysplasia
  – Low grade dysplasia
  – High grade dysplasia
  – Invasive Carcinoma
Barretts Esophagus
Pathology of Dysplasia

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Barretts Esophagus
Part 2:
Learning Exercise

Hines Case Archives
Barretts Esophagus

- Barretts Esophagus is defined as columnar epithelium replacing the squamous epithelium of the esophagus.
- Only intestinal (goblet cell) metaplasia has been shown to carry risk of developing carcinoma in the setting of Barretts Esophagus.
- Molecular and histochemical abnormalities found in Barretts Esophagus include expression of sulfomucins with high iron diamine, aberrant Lewis antigen, overexpression of p53 protein, 17p deletion, aneuploidy and cellular dysplasia.
Dysplasia in Barrett's Esophagus

• Dysplasia is defined as preneoplastic changes in epithelium that are intermediate between metaplasia and carcinoma

• Dysplasia in Barrett's Esophagus is divided into Low and High Grade Dysplasia
Histology of High Grade Dysplasia

- Loss of mucin production (mucin depletion)
- Marked nuclear enlargement, hyperchromasia, irregular contour and variation in size
- Loss of nuclear polarity
- Increased mitotic activity with abnormal mitotic figures
- Lack of inflammation
Histology of Low Grade Dysplasia

- The same histologic abnormalities found in High Grade Dysplasia but to a lesser degree
- Cells tend to retain more nuclear polarity, have more cytoplasmic maturation than High Grade Dysplasia
- Considerable interobserver variation in diagnosis of Low Grade Dysplasia
Indefinite for Dysplasia

• Histologic abnormalities that meet criteria for dysplasia but are occurring in the setting of inflammation

• Histologic abnormalities resembling dysplasia but may be “reactive”, a result of inflammation and which would disappear once inflammation resolves
Negative for Dysplasia

• Columnar epithelium with or without intestinal metaplasia

• The surface columnar cells are well spaced, regular, mature and have oval to round, basally located nuclei, 1-2 times the size of a mature lymphocyte

• The following 3 images are examples of Barretts mucosa and are negative for dysplasia
Image 9: Negative for Dysplasia

- This is an example of columnar epithelium that shows foveolar type mucin in the apices of the surface cells.
- The nuclei are basally located, small and ovoid.
- There is a sparse round cell population in the lamina propria.

- One area shows mild hyperplastic features with pseudostratified nuclei that retain their orientation.
This is another example of columnar epithelium that is negative for dysplasia.
The surface epithelium is regular with apically oriented cytoplasm and basally oriented nuclei.
The lamina propria contains a sparse lymphocytes and plasma cells.
A close up of part of the surface shows goblet cells.
Image 18
Negative for Dysplasia

This image of Barretts shows surface epithelium that is oriented with nuclei at the base. There is a minimally increased inflammatory cell population in the lamina propria, including eosinophils.

A few of the surface nuclei are enlarged, but they do not exceed 2 times nuclear diameter of lymphocytes.
Histology of Dysplasia

• A diagnosis of high grade dysplasia in Barretts esophagus indicates an elevated risk of cancer development

• High grade dysplasia is the easier of the two levels of dysplasia to distinguish from Barretts mucosa that is negative for dysplasia
Histology of High Grade Dysplasia

- Changes in morphology found in High Grade Dysplasia
  - Loss of mucin production (mucin depletion)
  - Marked nuclear enlargement, hyperchromasias, irregular contour and variation in size
  - Loss of nuclear polarity
  - Increased mitotic activity with abnormal mitotic figures
  - Lack of inflammation
Image 10: High Grade Dysplasia

This image shows:
- The nuclei of the surface epithelium has lost basal polarity
- The cytoplasm is scant and does not contain apical mucin
- The nuclei are enlarged greater than 2 times the size of a lymphocyte
- The nuclei are hyperchromatic
High Grade Dysplasia

- Loss of nuclear polarity in the surface epithelium
- Surface nuclei are enlarged and hyperchromatic
- Increased nuclear to cytoplasmic ratio: immature cytoplasm occupies smaller volume
- Loss of goblet cells at surface (present in gland at bottom left)
Image 19: HG Dysplasia

Features of HG Dysplasia present in this image

- Loss of nuclear polarity of surface nuclei
- Nuclear enlargement and hyperchromasia
- Loss of goblet cells and cytoplasmic immaturity

Features of HG Dysplasia present in this image

- Loss of nuclear polarity of surface nuclei
- Nuclear enlargement and hyperchromasia
- Loss of goblet cells and cytoplasmic immaturity
Low grade dysplasia

• Low grade dysplasia is more difficult to assess in Barretts

• There is less agreement between pathologists on the diagnosis of low grade dysplasia: greater interobserver variation

• There is also less consistency in the diagnosis of one pathologist reviewing the same section more than one time
Histology of Low Grade Dysplasia

• By definition, low grade dysplasia are the same histologic abnormalities found in High Grade Dysplasia but present to a lesser degree

• Cells tend to retain more nuclear polarity, have more cytoplasmic maturation than High Grade Dysplasia but are abnormal when compared to mucosa that is negative for dysplasia
Image 4 Low Grade Dysplasia

Features of Low Grade Dysplasia that are present in this image:
The changes are **patchy or focal**

- Loss of cytoplasmic maturation
- Loss of nuclear polarity
- Increase in nuclear size
Image 20: Low Grade Dysplasia

Features of Low grade dysplasia in this image:

- Focal loss of basal orientation of surface nuclei
- Focally enlarged and hyperchromatic nuclei
- Focal loss of cytoplasmic maturation
Image 24 Low Grade Dysplasia

Focal loss of basal orientation of surface nuclei

Focal loss of cytoplasmic maturation

Focally enlarged and hyperchromatic nuclei

Inversion of cytoplasm with mucin basally oriented
Indefinite for Dysplasia

• Indefinite for dysplasia is the third category of morphologic changes that carry elevated risk of cancer development

• By definition, indefinite for dysplasia are histologic abnormalities that meet criteria for dysplasia but are occurring in the setting of inflammation

• These abnormalities resemble dysplasia but may be “reactive”, a result of inflammation and would disappear once inflammation resolves
This image of Barretts shows neutrophilic infiltration of the surface epithelium. The following features of dysplasia are also present:
- Nuclear enlargement and hyperchromasia
- Focal loss of cytoplasmic maturation
- Focal loss of basal orientation of nuclei

Changes of dysplasia + inflammation = indefinite for dysplasia
Image 1 Indefinite for dysplasia

Features of dysplasia present:
- Loss of cytoplasmic maturation
- Nuclear enlargement and hyperchromasia of surface cells
- Focal loss of basal polarity of surface nuclei

Neutrophils infiltrating lamina propria and surface epithelium

Changes of dysplasia + inflammation = indefinite for dysplasia
Image 15 Indefinite for dysplasia

Neutrophils infiltrating lamina propria and surface epithelium

Features of dysplasia:

- Focal loss of cytoplasmic maturation
- Nuclear enlargement and hyperchromasia of surface cells
- Focal loss of basal polarity of surface nuclei

Changes of dysplasia + inflammation = indefinite for dysplasia
Image 2: Adenocarcinoma

Image shows surface changes of high-grade dysplasia.
- Loss of basal orientation
- Enlarged hyperchromatic nuclei
- Loss of cytoplasmic maturation

In addition, there are irregular nests of epithelium in the lamina propria representing invasion by cells of carcinoma.
Image 11: Adenocarcinoma

Nests of mucin producing cells of adenocarcinoma undermining squamous mucosa
Adenocarcinoma infiltrating as single cells (diffuse or signet ring type). Although the cells resemble plasma cells, they are larger and many have vacuoles.
Barretts Esophagus
Dysplasia

Practice Quiz
Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Answer:

A. Negative for dysplasia
Image B

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Image B

Answer:
E. Adenocarcinoma
Image C

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Image C

Answer:
D. High grade dysplasia
Image D

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Answer:
B. Indefinite for dysplasia
Image E

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Answer:

C. Low grade dysplasia
Image F

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Image F

Answer:

A. Negative for dysplasia
Image G

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Image G

Answer:
D. High grade dysplasia
Image H

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Answer:
B. Indefinite for dysplasia
Image I

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Image 1

Answer:
E. Adenocarcinoma
Image J

Answers:
Chose from below

A. Negative for dysplasia
B. Indefinite for dysplasia
C. Low grade dysplasia
D. High grade dysplasia
E. Adenocarcinoma
Answer:  
C. Low grade dysplasia
Resources

Post learning Test

Barretts Esophagus
Dysplasia
Post learning test

• Please use the second answer sheet labeled post learning examination
• As before there is a choice of one of five answers.
• When you have finished, please email your answers to both the prelearning and post learning exams to ___
• Thank you for your participation
Image 31
The End

Thank you for your participation
Any suggestions or comments
Please email ewiley@uic.edu