General Pointers on GI biopsies

• Pattern based approach is the most reliable way to diagnose inflammatory conditions of the GIT
  • You are usually diagnosing a pattern of injury to the mucosa
  • Many conditions can manifest the same way in the GIT

• Use special stains and IHC sparingly
  • They are not necessary for routine reporting

• You only learn more be seeing more cases – slide meetings

• Talk your referrers and read the endoscopy report
Case 1  Female 73 – Abdominal pain; sheets of white mucosa in oesophagus
Case 1 – Histologic features

• Squamous epithelium with two-toned appearance
• “Split” in the epithelium above the granular layer
• Parakeratosis
• Some inflammation at level of split
Case 1 – Oesophagitis dissecans superficialis

Courtesy Dr N Tutticci, QEII Hospital
Oesophagitis dissecans

- Older women
- Presentation varies from asymptomatic to dysphagia or coughing up casts
- Unknown mechanism
- Disease associations
  - Physical injury – recent endoscopy, nasogastric tube
  - Thermal injury – hot beverages
  - Chemical injury – caustic agents, alcohol, medications (bisphosphonates, NASIDS, potassium chloride, SSRI)
- Benign follow up
Case 2  Male 75 – 4cm segment of Barrett’s oesophagus
P53 Immunohistochemistry
– not supplied
Case 2 – Histologic features

• Squamous and glandular mucosa in oesophagus with intestinal metaplasia - Barrett’s oesophagus
• Area with complex architecture, closely packed glands
• Cytologic atypia – rounded nuclei, nucleoli, high N:C, mitoses
• Changes extend to the surface – loss of maturation
Case 2 – Barrett’s oesophagus; high grade dysplasia
Dysplasia in Barrett’s oesophagus

- Grading dysplasia in BO
  - Negative for dysplasia
  - Indefinite for dysplasia
  - Low grade dysplasia
  - High grade dysplasia
  - Intramucosal/invasive carcinoma

- Non-intestinal type dysplasia

- Reproducibility of grading in BO
BO – negative for dysplasia

In Australia, Barret’s oesophagus MUST include intestinal metaplasia.

The more biopsy fragments, the more likely IM is present.

IM has a gradient from proximal to distal.
BO – indefinite for dysplasia

Biopsy shows atypia with some but not all the features of dysplasia

Reasons for Indefinite diagnosis:
- Technical issues
- Inflammation
- Basal dysplasia

In Australian guidelines there is a category of “indefinite for high grade dysplasia” – based on no evidence
BO - LGD

Mild to moderate atypia

No complex architecture

Looks like a usual TA from the colon
BO - HGD

Marked architectural and cytological atypia

Features extend to the surface epithelium

Typically a lesion is visible
BO – intramucosal carcinoma

Features suggestive of invasion on biopsy of HGD

Solid growth
Ulceration
Debris in glands
Single cells
Desmoplasia
Non-conventional dysplasia

• Most common morphology is intestinal type dysplasia

• Other subtypes
  • Foveolar (gastric) - rare
  • Serrated (an intestinal subtype) – very rare

• Grading and natural history are not well understood in these subtypes

• They are often mixed with more conventional intestinal type dysplasia
Variation in the diagnosis of dysplasia

• In variability studies, agreement is usually only poor to moderate
• The more you see, the better the agreement (studies with gastrointestinal pathologists)
  • LGD is probably overcalled by general anatomical pathologists

• The more people who agree on the diagnosis, the more likely it is to be accurate
• We show ALL our BO dysplasia cases to someone else
What happens after your diagnosis

Developed in 2014

In brief

Negative – surveillance every 2-5 years

Indefinite – acid suppression; close surveillance

LGD – Intensified surveillance/possibly ablation therapy

HGD/IMCa – endoscopic mucosal resection/ablation therapy
Case 3  Female 55 – EMR of oesophageal nodule
Case 3 – Histologic features

• EMR of submucosal lesion underlying normal squamous mucosa
• Well circumscribed
• Plump cells with eosinophilic, granular cytoplasm, indistinct border
• Small, round, regular nuclei
• No mitoses, no atypia, no necrosis
Case 3 – Granular cell tumour
Granular cell tumour

• Tumour of Schwann cell origin

• 5-10% occur in the GIT and most of these are in the oesophagus

• GCT of the GIT are almost always benign
  • Features of malignancy – necrosis, spindling, increased mitotic activity, large nucleoli, high N:C, nuclear pleomorphism

• Complete excision is usually curative
Case 4 Female 55 – Anaemia for investigation; normal stomach biopsied
Gastrin and hp

GASTRIN IHC
Case 4 – Histologic features

• Fragments of gastric mucosa

• Most show antral type mucosa with minimal changes or mild chemical gastritis features

• One fragment is inflamed
  • Chronic inflammation is both superficial and deep
  • Lymphocytes, plasma cells and eosinophils
  • Pseudopyloric metaplasia of the epithelium
  • No intestinal metaplasia

• No Helicobacter identified on H&E or IHC
Case 4 – Autoimmune atrophic gastritis
Autoimmune atrophic gastritis

• Classical clinical and pathological features of AIG

• Features of early AIG

• Risk of neoplasia in AIG
Clinical presentation

• Rarely symptomatic until a critical mass of oxyntic tissue affected

• Autoimmune destruction of gastric oxyntic cells

• Loss of parietal cells
  • Loss of acid – hypochlorhydria
    • This can lead to iron deficiency anaemia
  • Loss of Intrinsic factor – pernicious anaemia

• Chief cell loss
  • Decreased pepsin and pepsinogen
Classical histological features

- Changes only affecting the body mucosa
  - Antrum is usually normal or has chemical gastropathy type changes
- Deep inflammation – lymphocytes, plasma cells, eosinophils
  - Typically no neutrophils are present
- Loss of normal body type mucosa
- Metaplastic epithelium – intestinal, pancreatic and pseudopyloric
Early AIG

• The changes are not usually fully developed and not every change is present

• Deep/full thickness chronic inflammation
• Oxyntic gland destruction
• Prominent eosinophils
• Some metaplasia (pancreatic, pseudopyloric, intestinal)
• ECL cell hyperplasia
Neoplastic risk

- Conventional dysplasia
  - Dysplasia
  - Adenocarcinoma
- Gastric type dysplasia
  - Foveolar dysplasia
  - Pyloric gland adenoma – see upcoming case
- Neuroendocrine tumour
  - Neuroendocrine cell hyperplasia
  - Neuroendocrine tumour – type 1
Carcinoma arising in AIG
Case 5  Male 44 – Dysphagia and epigastric pain; raised erosions in stomach
Case 5 – Histologic features

- Gastric mucosa
- Diffuse inflammation in the biopsies
- Conspicuous intraepithelial lymphocytosis (>25/100 epithelial cells)
- Some active inflammation present
Case 5 – lymphocytic gastritis
Presentation

• Clinical features
  • Depends on cause

• Endoscopic appearance
  • Normal
  • Mild non-specific changes
  • Nodular erosive gastritis = varioloform gastritis = octopus sucker gastritis

• Histological features required for the diagnosis
  • >25 T lymphocytes / 100 gastric epithelial cells
  • Associated findings
    • Lamina propria inflammation
    • Neutrophils
    • Erosions
  • Inflammatory changes can occur in the body and/or antrum
Lymphocytic gastritis

• Causes
  • 1/3 Helicobacter related
  • 1/3 Coeliac disease related
  • 1/3 other
    • Crohn’s disease
    • Medication reactions
    • Infectious gastritis
    • HIV infection
    • Lymphoma
    • “Idiopathic” – may respond to antibiotic therapy against HP

• Some histological features can help distinguish these causes
Case 6  Female 86 – Haematemesis; gastric polyp
MUC stains

MUC6

MUC5aC
Case 6 – Histologic features

- Polypoid lesion in stomach
- No background tissue for analysis
- Tubular structures
- Cuboidal to columnar cells with abundant cytoplasm
- Round nuclei – occasional small nucleoli
- No mucin caps and no areas of intestinal differentiation
  - No goblet cells, no Paneth cells
- Minimal atypia
- MUC6 and MUC5AC positive
Case 6 – pyloric gland adenoma

• Neoplasm showing differentiation towards gastric pyloric type glands
• Usually not a “pure” lesion
• Seen in stomach, duodenum and gallbladder but also reported in lots of other places as well
• Risk of malignancy up to 20%
• Association with colorectal cancer syndromes
• Genetics
Case 7  Male 65 – Recent distal pancreatectomy for pancreatic ductal carcinoma; erosion at duodenal papilla
Case 7 – Histologic features

- Small intestinal mucosa
- Oedema, surface erosion, some (but not much) inflammation
- Numerous mitotic figures, including abundant ring mitoses in the proliferative zone and on the surface
Case 7. – Taxol-induced erosion

• Similar features seen in colchicine toxicity – treatment for gout AND pericarditis
• Both medications cause mitotic arrest and therefore mitoses are readily apparent

• The effect can be observed soon after administration of taxol chemotherapeutic agents – in this case it was paclitaxel; changes resolve with time
• Taxanes affect the mitotic spindle protein tubulin

• Mitoses get paused at metaphase/anaphase

• This induces apoptosis
Case 8  Female 60 – Diarrhoea; normal colon
Case 8 – Histologic features

- Colonic mucosa
- Increased inflammation in lamina propria
- Mild intraepithelial lymphocytosis
- Thickened subepithelial collagen layer with entrapped vessels
  - Up to 45 µm thick
- Discohesive surface epithelium
- No chronic architectural changes
Case 8 – Collagenous colitis
Collagenous colitis

• Chronic watery diarrhoea typically occurring in older women
• It is probably caused by an immunological response to intraluminal dietary or bacterial elements
• There is increased fibro genesis (with deposition of type VI collagen) and decreased collagen degradation

• Association with coeliac disease, autoimmune diseases, drugs (PPI)
Case 9  Female 72 – Abdominal pain; red patch at splenic flexure
Case 9 – Histologic features

• Preserved crypt architecture but with degenerating crypts and areas of crypt loss
• Some surface degeneration

• Fibrous solidification of the lamina propria
• Minimal acute or chronic inflammatory cell infiltrate

• Oedema, haemorrhage, cryptitis and crypt abscess formation, pseudomembrane formation, capillary microthrombi
Case 9 – Acute ischaemic colitis pattern

• Due to hypoperfusion of the colonic mucosa
• Causes
  • Large vascular occlusion of any type – trauma, thrombosis, embolus
  • Small and medium vessel disease – vasculitis
  • Hypercoagulable states – Protein C or S defects, 
  • Colonic obstruction – carcinoma, volvulus, diverticular disease
  • Global hypoperfusion – cardiac failure, long distance running
  • Infection – E. coli (0157:H7), shigella, C. difficile, CMV
  • Numerous drugs – catecholamines, digoxin, cocaine, oestrogens, constipating agents
Presentation

- Abdominal pain, bloody diarrhoea

- Changes are classically said to affect the splenic flexure and sigmoid colon but can affect anywhere in the colon

- Typical endoscopic appearance is patchy oedema, haemorrhage and erosions of the colon

- Mass forming lesions can be seen as well
Case 10  Female 42 – Iron deficiency anaemia; 4cm flat lesion in rectum
Case 10 – Histologic features

• Colonic mucosa
• Most looks normal/mild prolapse type changes
• Some areas show small glands in a slightly cellular stroma
• Bland cytology, no atypia is present

• Cells stain with CK7, ER, CD10 – not supplied

Oestrogen Receptor IHC
Case 10 – Endometriosis

• Usually affects outer layers of bowel wall but can occasionally involve the mucosa

• This particular lesion was biopsied twice because the surgeons didn’t believe the diagnosis
Glandular mimics of colorectal adenocarcinoma

• Endometriosis
• Mucosal prolapse
• Mass forming ischaemia
• Colitis cystica profunda
• Heterotopia

• Metastatic malignancy
Mucosal prolapse
Mass forming ischaemia
Metastatic malignancy

Endometrial adenocarcinoma

Lobular breast carcinoma

Prostatic acinar carcinoma
Gastric heterotopia
Case 11  Male 81 – Anaemia for investigation; 1cm rectal polyp