Australasian Division of the International Academy of Pathology Limited
ABN 73 008 593 815
PO Box 74, Cherrybrook, NSW 2126
Tel: +61 2 9894 6811 www.iap-aus.org.au

Slide Seminar:

A cornucopia of GI busting conditions

Chairs of the Sessions

Caroline Cooper
Pathology Queensland, Princess Alexandria Hospital, Brisbane, QLD, Australia

Andrew Ruszkiewicz
SA Pathology, Lyell McEwin Hospital, Adelaide, SA, Australia

Keynote Speaker

Gregory Y. Lauwers, MD
Moffitt Cancer Centre & the University of South Florida, USA.

Case 1

View link: LAUWERS1

Clinical History:
A 55-year female patient was diagnosed with a polypoid gastric lesion detected in an otherwise unremarkable fundic mucosa.

Clinical Findings / Additional information:
The endoscopist reported a solitary small polyp characterized by a bright-red, finely granular surface.

Diagnosis:
Foveolar-type (gastric-type) dysplasia/adenoma arising in H. pylori naïve patient and presenting as Raspberry like polyp.

Discussion:
Recent Japanese studies have described examples of sporadic foveolar polypoid lesions ('foveolar-type adenomas') in individuals without prior *H. pylori* infection (H. Pylori naïve patients). Some cases present a characteristic endoscopic appearance [*raspberry* like polyps] Cases of *flat* subtype foveolar dysplasia have also been described in H. Pylori naïve patients. Different alterations have been observed in flat and raspberry-like variants of sporadic foveolar-type dysplasia developing in *H. pylori* naïve stomach. The flat-type adenomas present with variants in *APC* and *KRAS*. On the other hand, raspberry-like foveolar-type adenomas have been associated with variant in the KLF4 gene; a gene involved in various biological processes, such as homeostasis and apoptosis. The rate of neoplastic progression is reported to be extremely rare in such cases

Case 2

View link: LAUWERS2

Clinical History:
Anaemic A 28-year-old woman presenting for follow-up of gastric polyps.

Clinical Findings/Additional information:
The endoscopic noted several polyps and excised the largest one.
On microscopic examination, the lesion was immunoreactive MUC6 and MUC5AC.

Diagnosis:
Pyloric gland adenoma

Discussion:
Pyloric Gland Adenomas (PGAs) typically develop in the gastric body or fundus. Sporadic PGAs constitute approximately 3% of gastric epithelial polyps (excluding fundic gland polyps) and predominantly affect elderly female patients with autoimmune gastritis. In contrast, syndromic PGAs occur in various polyposis syndromes, including Familial Adenomatous Polyposis (FAP) and *Gastric Adenocarcinoma and Proximal Polyposis of the Stomach*, as well as McCune–Albright syndrome, juvenile polyposis, and Lynch syndrome.

Both sporadic and FAP-associated PGAs consistently demonstrate mutations in *GNAS*, *KRAS*, and *APC* genes. However, the mucosal background differs significantly between these types. Sporadic PGAs typically arise in the setting of pyloric gland metaplasia within oxyntic mucosa with chronic atrophic gastritis, while syndromic PGAs develop without associated inflammatory or metaplastic changes.

The risk of progression to high-grade dysplasia or adenocarcinoma is elevated in elderly patients with autoimmune gastritis. This neoplastic risk increases with larger lesion size, tubule-villous architecture, and a mixed immunophenotype.

Case 3

View link: LAUWERS3

Clinical History:
This gastric polypoid lesion was resected from a 60 years male during follow up for previous diagnosis of Barrett oesophagus.

Diagnosis:
Oxyntic gland adenoma (OGA)

Discussion:
This rare neoplasm (0.01%–0.07% of upper GI biopsies) belongs to the oxyntic gland neoplasm spectrum. Oxyntic Gland Adenomas (OGAs) typically present as small nodules (<10mm) with tightly packed glands showing possible anastomosis, branching, dilation, or cribriforming. Mild cytologic atypia and the mixed cellular composition are characteristic of OGAs that contain chief cells, parietal cells, or both, with possible mucous neck cells. The chief cell predominant pattern is most common.

Cytonuclear atypia is minimal with rare mitoses and low Ki67 index (<5%). The tumor typically resides in deeper mucosa beneath normal foveolar epithelium.

Immunohistochemically, OGAs are MUC6-positive, with pepsinogen I marking chief cells and H+/K+ ATPase marking parietal cells. Though some patterns mimic neuroendocrine tumors and may express synaptophysin, chromogranin A is negative.

OGAs are H. pylori-independent with recurring GNAS mutations. These slow-growing lesions may show a pushing interface with the surrounding mucosa and prolapse-type misplacement that shall not be misinterpreted as evidence of gastric adenocarcinoma of fundic gland type.

Case 4

View link: LAUWERS4

Clinical History:
A 74-year-old man presented with epigastric discomfort and dyspepsia.

Clinical Findings / Additional information:
The endoscopy revealed only an ill-defined mucosal irregularity.

Diagnosis:
Very well-differentiated gastric adenocarcinoma

Discussion:
Very well-differentiated gastric adenocarcinoma represents a rare, diagnostically challenging variant characterized by deceptively benign morphology with minimal structural and nuclear atypia. Its distinctive architectural features include anastomosing pit and glandular structures, spiky glands, distended glands, abortive glands, and glandular outgrowth, with both intestinal and gastric phenotypes documented. Diagnostic difficulties are substantial; studies report that

50% of preoperative biopsies were initially categorized as negative or indeterminate for malignancy, with poor diagnostic concordance among pathologists (approximately 35%) and a low rate of definitive malignancy diagnosis (15%). Despite its well-differentiated appearance, clinical implications are serious, with 57% of patients presenting advanced gastric cancer and 43% showing lymph node metastasis following gastrectomy. Recent molecular studies have linked the development of poorly cohesive carcinoma, particularly in intestinal-type tumors, to mutations in the RHOA gene, which encodes proteins regulating actin cytoskeleton organization and cellular shape, adhesion, and motility.

Case 5

View link: LAUWERS5

Clinical History:
This gastric polypoid lesion was excised from a 63 years female complaining of vague abdominal discomfort. She eventually underwent a gastrectomy. The case was received in consultation.

Diagnosis:
Mixed adenocarcinoma-neuroendocrine neoplasm (MINEN)

Discussion:
Gastric Mixed Neuroendocrine-Non-neuroendocrine Neoplasm (MiNEN) is characterized by distinct morphological features of both neuroendocrine and non-neuroendocrine components. Typically, MiNENs consist of adenocarcinoma associated with high-grade neuroendocrine carcinoma (NEC) or, less frequently, with a well-differentiated neuroendocrine tumor (NET).

This case presents a particularly unusual combination, featuring a very well-differentiated adenocarcinoma alongside a neuroendocrine tumor component. The neuroendocrine component was confirmed through positive immunohistochemical expression of specific neuroendocrine markers.

Case 6

View link: LAUWERS6

Clinical History:
The patient, an 80-year-old male presented with a large necrotic gastric ulcer. Biopsies were taken.

Additional information:
The neoplastic cells were positive for AE1-AE3 as well as vimentin. Negative ancillary studies included EBV-ISH, CD45, SALL4, OCT4, SOX10 and Melan A.

Diagnosis:
Gastric undifferentiated carcinoma

Discussion:
Gastric undifferentiated carcinoma typically presents as a large, ulcerated, extensively

necrotic tumor mass, frequently accompanied by synchronous regional metastases. Most patients with initially localized disease rapidly develop distant metastases following diagnosis, with mortality occurring within one year in the majority of cases.

Histologically, this carcinoma consists of anaplastic, large polygonal cells arranged in solid or discohesive sheets. Characteristic features include pleomorphic tumor giant cells and cells with rhabdoid phenotype. Spindled cells and osteoclast-like giant cells may also be observed. Abundant necrosis is common. Extensive tissue sampling is essential to identify diagnostic areas of adenocarcinoma.

Molecular studies indicate that in some cases, the undifferentiated phenotype is driven by alterations in components of the SWI/SNF chromatin-remodeling complex. Loss of SMARCB1 (INI1), SMARCA2, and SMARCA4 (BRG1) can be detected by immunohistochemistry, providing valuable diagnostic insights.

Case 7

View link: LAUWERS7

Clinical History: A 75-year male presented to his internist with diarrhea, peripheral edema and weight loss.

Clinical Findings/Additional information:
The endoscopist described the presence of diffuse gastric mucosal edema and thickening.

Diagnosis: Cronkhite Canada polyp

Discussion:
Cronkhite-Canada syndrome (CCS) is a rare non-hereditary condition characterized by diffuse gastrointestinal polyposis and distinctive ectodermal abnormalities. Pathologically, small polyps resembling sporadic hyperplastic polyps typically overlay enlarged, diffuse, and irregular rugae in the gastric fundus and antrum. These polypoid changes frequently extend throughout the small bowel and colon. Unlike typical hyperplastic polyps, the polyps generally lack prominent inflammation or muscularis mucosae hyperplasia. Dense eosinophilic infiltration serves as an important diagnostic clue. IgG4-positive plasma cell infiltration has been documented, suggesting a possible autoimmune etiology, though the exact pathogenesis remains undefined.

Clinically, gastrointestinal symptoms typically precede extraintestinal manifestations. Characteristic ectodermal changes include alopecia, onychodystrophy (nail dystrophy), and cutaneous hyperpigmentation. The condition carries a poor prognosis with approximately 55% mortality rate at 5 years. Major causes of death include gastrointestinal hemorrhage, sepsis, and congestive heart failure. The association with increased malignancy risk remains controversial.

Case 8

View link: LAUWERS8

Clinical History: The patient is a 62-year woman with an history of malignant melanoma.

Clinical Findings/Additional Information: Mucosal oedema was reported by the gastroenterologist. No other alteration was reported. She had been treated 10 months before by nivolumab.

Diagnosis:
Drug Induced Mucosal Injury / Immune check point inhibitor (ICI) gastritis

Discussion:
ICIs have become crucial in cancer therapy, and associated immune-related adverse events (irAEs) have garnered significant attention, particularly colitis. Reports of associated immune related gastritis is an uncommon diagnosis, representing only approximately 5% of all GI luminal immune-related adverse events. Studies have reported the overall incidence of ICI-related gastritis to be 0.35–1.46%. Notably, 70% of patients had concurrent ICI enteritis/colitis, while only 30% of patients presented with isolated gastritis.
There is an increased risk of ICI gastritis associated with pre-existing gastroesophageal disorders. Risk of irAEs in general is associated with chronic use of proton pump inhibitors, diuretics, and anti-inflammatory drugs.
The median time from ICI initiation to onset of gastritis is variable. One study found the timeline to be 3.4 months, while another the median time to onset was 6.7 months. One case has been reported up to 9 months after initiation.
It is difficult to diagnose ICI-related gastritis based on symptoms alone, and endoscopy with pathologic diagnosis is necessary. Common endoscopic findings include erythema, edema, and friability. Erosion and hemorrhagic gastritis are also reported. Common microscopic patterns include chronic active gastritis, reactive gastropathy, and focally enhanced gastritis. Discontinuing immune checkpoint inhibitors and symptomatic management with PPIs may be insufficient, and corticosteroid therapy combined with high-dose proton pump inhibitor therapy is often required.