

GIPS JOURNAL WATCH, MAR APR 2013

Gastroenterology, Mar 2013

Long-term Outcomes After Resection for Submucosal Invasive Colorectal Cancers
Ikematsu H, et al. *Gastroenterology* 2013; 144:151–159.

This study examines the outcome of colorectal cancers with submucosal invasion after endoscopic or surgical resection. In patients with high risk histologic factors (poor differentiation, vascular invasion and/or depth of invasion >1000µm), the risk fo recurrence after endoscopic resection of rectal cancers was significantly higher compared to colonic cases. The authors recommend that all rectal cancers with high risk histologic feature(s) should undergo surgical resection.

<http://www.ncbi.nlm.nih.gov/pubmed/23232297>

Am J Gastroenterology, Mar 2013

Should patients with suspected eosinophilic esophagitis undergo a therapeutic trial of proton pump inhibition?

Hirano I. *Editorial: Am J Gastroenterol.* 2013;108:373-5.

Some cases with increase in intraepithelial eosinophils, but without clear evidence of gastroesophageal reflux disease (GERD) respond to PPI therapy. It is not clear whether these cases represent eosinophlic esophagitis (EoE), GERD, or PPI-responsive esophageal eosinophilia that is unrelated to EoE and GERD. At present, a trial of PPI is considered a pre-requisite for the diagnosis of EoE. The response to PPI may be related to anti-inflammatory properties of the drug rather than acid suppression.

<http://www.ncbi.nlm.nih.gov/pubmed/23459046>

Am J Gastroenterology, Apr 2013

Risk of cancer in patients with autoimmune pancreatitis.

Shiokawa M, et al. *Am J Gastroenterol.* 2013;108(4):610-7.

Autoimmune pancreatitis (AIP) and pancreatic adenocarcinoma have been reported in the same case. This study examined 108 cases of AIP and found that 15 (13.9%) developed pancreatic adenocarcinoma over a median follow-up period of 3.3 years. Most cancers were detected in the first year of the diagnosis. The study emphasizes the risk of adenocaricnoma in the setting of AIP, and the authors suggest that AIP may be a paraneoplastic phenomenon in some cases.

<http://www.ncbi.nlm.nih.gov/pubmed/23318486>

Human Pathology, Apr 2013

Prolapse-related changes are a confounding factor in misdiagnosis of sessile serrated adenomas in the rectum.

Huang CC, et al. *Hum Pathol.* 2013;44:480-6.

This study reviewed all rectal polyps that had been diagnosed as sessile serrated adenoma (SSA). One-fourth of the cases were reclassified as hyperplastic polyp with prolapsed. The results advise caution in the diagnosis of SSA in the presence of prolapsed-related changes even when basal crypt flattening and dilatation is seen.

<http://www.ncbi.nlm.nih.gov/pubmed/23069257>

Glypican-3 expression in gastrointestinal and pancreatic epithelial neoplasms.

Mounajjed T, et al. *Hum Pathol.* 2013;44:542-50.

The study highlights glypican-3 (GPC-3) expression in gastrointestinal and pancreatic tumors that can lead to diagnostic errors if GPC-3 is used to determine primary vs. metastatic origin of liver tumors. GPC-3 expression was observed in 7/12 (58.5%) acinar cell carcinomas, 8/29 (27.5%) of squamous cell carcinomas, 20% (6/30) of ADCA (2 each esophageal, gastric, small intestinal and 1 colonic), and 1/39 (2.5%) of neuroendocrine carcinomas of the GI tract. All pancreatic adenocarcinomas, pancreatic neuroendocrine neoplasms and cholangiocarcinomas were GPC-3 negative.

American Journal of Clinical Pathology, March 2013

Increased IgG4+ Cells in Duodenal Biopsies Are Not Specific for Autoimmune Pancreatitis

Katherine M. Cebe, et al. *AJCP* 2013 139:323-329 MARCH

The purpose of this study was to investigate the specificity of increased IgG4+ plasma cells in ampullary mucosa for a diagnosis of autoimmune pancreatitis (AIP). In clinical practice ampullary biopsies would be easier and safer than pancreatic biopsies to make this diagnosis and recent reports show that increased IgG4+ plasma cells in duodenal mucosa is associated with AIP. The authors of this study evaluated a selection of normal and pathological specimens by immunohistochemistry for IgG4 and found that, while increased IgG4+ plasma cells (defined as greater than 10/high power field) were seen in patients with AIP and not in normal biopsies, the finding was also present in a significant portion of mucosal samples from patients with celiac disease, duodenitis, and pancreatic cancer. The conclusion drawn from the evidence was that increased IgG4+ plasma cells (at least with the defined cutoff value) is not specific for AIP.

<http://www.ncbi.nlm.nih.gov/pubmed/23429368>

American Journal of Clinical Pathology, April 2013

Objective Criteria for Crohn-like Lymphoid Reaction in Colorectal Cancer

Hideki Ueno, et al. *AJCP* 2013 139:434-441 APRIL

This study looked at the Crohn-like lymphoid (CLR) reaction in colorectal cancer with the goal of determining specific semiquantitative criteria that would be of predictive use. Criteria originally proposed by Graham and Appleman (Graham's method), which the authors of this article describe as somewhat subjective, are discussed. In this study the two primary features evaluated in Graham's method, number and size of lymphoid aggregates, were separately evaluated and correlated with outcomes. The authors found no correlation with the number of lymphoid

aggregates and outcome but did find a correlation with aggregate size, specifically a lymphoid aggregate with a diameter of 1 mm or greater corresponded to a favorable outcome. The authors propose that the "1 mm rule" might provide a simple rule for predicting a favorable outcome.

<http://www.ncbi.nlm.nih.gov/pubmed/23525613>

Gut, March 2013

Serrated polyposis: rapid and relentless development of colorectal neoplasia.

Edelstein DL et al. *Gut* 2013;62:404-408.

44 patients with serrated (hyperplastic) polyposis (SP; multiple colorectal hyperplastic polyps, often with sessile serrated adenomas/polyps or adenomas) were studied over a median follow-up of 2.0 years. Upper and lower endoscopy findings suggest that these patients have a strong tendency for continued development of colorectal neoplasia, and the authors propose consideration of annual colonoscopy for surveillance, possible colectomy in SP patients, and frequent surveillance post-surgery.

<http://gut.bmj.com/content/62/3/404.full.pdf+html>

Letter: High prevalence of hyperplastic polyposis syndrome (serrated polyposis) in the NHS bowel cancer screening programme.

Biswas S et al. *Gut* 2013;62:475.

<http://gut.bmj.com/content/62/3/475.1.full.pdf+html>

Letter: High prevalence of serrated polyposis syndrome in FIT-based colorectal cancer screening programmes.

Moreira L et al. *Gut* 2013;62:476-477.

<http://gut.bmj.com/content/62/3/476.full.pdf+html>

Two letters in the same issue address the increased frequency of serrated polyposis syndrome in fecal occult blood test-based cancer screening programs in the UK and Barcelona, Spain. WHO criteria for the syndrome are: either more than 20 hyperplastic polyps throughout the colon or five hyperplastic polyps in the proximal colon with two that are at least 10 mm in size. Surveillance strategies are addressed in each letter.

Gut, April 2013

Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system.

Hirano I et al. *Gut* 2013;62:489-495.

<http://gut.bmj.com/content/62/4/489.full.pdf+html>

A grading system is proposed for endoscopic evaluation of eosinophilic esophagitis. The authors note that endoscopy can detect the impact of esophageal remodelling in a way that biopsies cannot, given their limited tissue depth. The system has good interobserver agreement

for four of the major features of EoE (kappa=0.40-0.54, 71-81% agreement) including fixed rings, exudates, furrows, and edema as well as stricture and crepe paper esophagus.

AJSP, March 2013

[Dedifferentiation in Gastrointestinal Stromal Tumor to an Anaplastic KIT-negative Phenotype: A Diagnostic Pitfall: Morphologic and Molecular Characterization of 8 Cases Occurring Either De Novo or After Imatinib Therapy](#)

Antonescu CR et al. Am J Surg Pathol. 37(3):385-392, March 2013.

The authors describe eight cases of dedifferentiation in GIST to an anaplastic CD117-negative phenotype (five patients had no prior history of imatinib treatment, whereas chronic imatinib can lead to altered morphology and loss of CD117 reactivity as seen in the other three patients). Both the classic and dedifferentiated components had the same KIT genotype; the various mutations seen are described in detail.

[Reproducibility of the Villous Component and High-grade Dysplasia in Colorectal Adenomas <1 cm: Implications for Endoscopic Surveillance](#)

Mahajan D et al. Am J Surg Pathol. 37(3):427-433, March 2013.

High-grade dysplasia and villous component are criteria for an advanced adenoma (AA) in patients with 1 or 2 adenomas less than 1 cm in size. Current guidelines are that patients with AA get increased postpolypectomy surveillance; this study assesses interobserver variability of VC and HGD in these small polyps before and after development of consensus criteria in a group of five GI pathologists. Interobserver agreement remained poor, raising concern for the validity of clinical decision making based on assessment of adenomas with a VC, HGD, or AA.

[Multiplicity and Molecular Heterogeneity of Colorectal Carcinomas in Individuals With Serrated Polyposis](#)

Rosty C et al. Am J Surg Pathol. 37(3):434-442, March 2013.

Pathologic and molecular profiles of colorectal cancers are delineated in 38 individuals meeting WHO criteria for serrated polyposis (WHO criteria for the syndrome are: either more than 20 hyperplastic polyps throughout the colon or five hyperplastic polyps in the proximal colon with two that are at least 10 mm in size). The molecular profile of such cancers includes *BRAF* mutation (46%), *KRAS* mutation (5%), and MMR deficiency by immunohistochemistry (38%); almost half of the cancers were wild-type for *BRAF/KRAS* with MMR proficiency (84%). 13 cases showed overexpression of p53 and/or evidence of beta-catenin activation. Ten patients had synchronous or metachronous carcinomas. The authors propose that patients with serrated polyposis should undergo frequency surveillance and consideration of more extensive colectomy at the time of cancer diagnosis.

AJSP, April 2013

[Frequency of HER-2 Positivity in Rectal Cancer and Prognosis](#)

Conradi L-C et al. Am J Surg Pathol. 37(4):522-531, April 2013.

Of 264 patients with protocol-based multidisciplinary treatment (German Rectal Cancer Study Group trials), patients with HER-2 positivity (12.4% of biopsies, 26.7% of resections) showed better disease-free survival and cancer-specific survival (P=0.1 and 0.03, respectively) over a 46.5-month median follow-up period. Overall survival at 5 years was 96.0% (HER-2 positive) and 80.0% (HER-2 negative).

[*Is the Presence of 6 or Fewer Crypt Apoptotic Bodies Sufficient for Diagnosis of Graft Versus Host Disease? A Decade of Experience at a Single Institution*](#)

Lin J et al. Am J Surg Pathol. 37(4):539-547, April 2013.

78 colon biopsies were reviewed from 66 patients who received either hematopoietic stem cell or cord blood cell transplantation and whose biopsies showed apoptotic bodies. Of these, 41 cases had 6 or fewer apoptotic bodies, and of these 41, 7 had coexisting GVHD in skin or liver. GI symptoms of at least 4 HSCT patients with 6 or fewer apoptotic bodies resolved in the absence of further treatment for GVHD; the authors suggest that this cutoff should be the threshold to alert treating clinicians as to the possibility of GVHD without rendering a definitive diagnosis of GVHD on pathology alone ("indeterminate for GVHD").

[*Inflammatory Fibroid Polyps of the Gastrointestinal Tract: Spectrum of Clinical, Morphologic, and Immunohistochemistry Features*](#)

Liu T-C et al. Am J Surg Pathol. 37(4):586-592, April 2013.

This is the largest series of inflammatory fibroid polyps reported to date (83 obtained over >10 years). These are rare, benign tumors, and their growth pattern, anatomic distribution, and associated histological features are described in detail (classically with perivascular onion-skinning and eosinophil predominance, but alternately with a short fascicular growth pattern, sparse number of eosinophils, and prominent hyalinization).

[*Prognosis of Minimally Invasive Carcinoma Arising in Mucinous Cystic Neoplasms of the Pancreas*](#)

Lewis GH et al. Am J Surg Pathol. 37(4):601-605, April 2013.

Noninvasive mucinous cystic neoplasms (MCNs) of the pancreas are cured surgically, but the behavior of surgically resected minimally invasive adenocarcinomas in MCNs has not been established. 16 such cases with unifocal or multifocal microscopic invasion are studied (confined to ovarian stroma of the MCN without capsular or pancreatic parenchymal invasion). Only one of these cases recurred, and it was one without extensive pathologic sampling, suggesting that in cases of thorough histologic examination, most such patients are cured.

[*Tumor Staging But Not Grading Is Associated With Adverse Clinical Outcome in Neuroendocrine Tumors of the Appendix: A Retrospective Clinical Pathologic Analysis of 138 Cases*](#)

Volante M et al. Am J Surg Pathol. 37(4):606-612, April 2013.

138 appendiceal neuroendocrine neoplasms were reviewed using 2000 and 2010 WHO classifications and European Neuroendocrine Tumor Society and American Joint Committee on Cancer staging criteria. A third of cases showed malignancy-associated pathology, but of these,

only 4 patients died of disease. Factors significantly associated with poor outcome include: extramural extension (including mesoappendix), well-differentiated carcinoma diagnosis (2000 WHO criteria), pT3-T4 stage, older age, and presence of positive resection margins. Tumor size, mitotic/proliferative rate, and 2010 WHO grading criteria are not significantly associated with poor outcome. Tumor stage and 2000 WHO classification are the most applicable to assess clinically aggressive tumor behavior.

Histopathology, April 2013

Diagnostic value of HMGA1, p53 and β -catenin in discriminating adenocarcinoma from adenoma or reactive atypia in ampulla and common bile duct biopsies (pages 778–787)

Zakharov V et al. Histopathology 2013, 62, 778-787.

48 biopsies (10 common bile duct, 38 ampullary) were included. Of these, 14 were reactive atypia, 12 adenomas, and 22 adenocarcinomas. The majority of adenocarcinomas express HMGA1 and HMGA2 and at higher intensity than adenomas or reactive atypia; their co-expression is particularly specific (86% of adenocarcinomas, no reactive atypia, 8% of adenomas). P53 and beta-catenin did not provide additional utility in classifying these lesions.

Arch Pathol Lab Med, March 2013

Dysplastic Lesions in Inflammatory Bowel Disease

Matkowskyj KA et al. Arch Pathol Lab Med. 2013;137:338-350.

[Abstract](#)

As part of the Northwestern University Special Section reports, this is a review of IBD-related dysplasia and tumor development. Surveillance recommendations of the major American gastroenterology societies also are addressed.

Raga Ramachandran, MD, PhD
University of California, San Francisco

Steven D Hart, MD
University of California, Los Angeles

Sanjay Kakar, MD
University of California, San Francisco