

GIPS JOURNAL WATCH, NOV DEC 2013

Gastroenterology, Dec 2013

Molecular diagnosis of eosinophilic esophagitis by gene expression profiling.

Wen T, et al. *Gastroenterology*. 2013; 145(6):1289-99.

A diagnostic panel comprising a 96-gene quantitative polymerase chain reaction is described to diagnose EE, which works in both fresh and formalin-fixed paraffin-embedded tissue. In an analysis of 194 pediatric and adult cases, sensitivity was 96% and specificity was 98% specificity. The assay distinguished EE in remission from controls, EE from reflux esophagitis and identified EE patients likely to relapse after therapy.

<http://www.ncbi.nlm.nih.gov/pubmed/23978633>

Gastroenterology, Nov 2013

Risk of Lymphoma in Patients With Ulcerative Colitis Treated With Thiopurines: A Nationwide Retrospective Cohort Study

Khan N, et al. *Gastroenterology*. 2013; 145(5):1007-1015.e3.

In a large retrospective study, it was shown that patients with UC treated with thiopurine have a 4-fold increase in risk of lymphoma, which increases with each year of therapy.

<http://www.ncbi.nlm.nih.gov/pubmed/23891975>

Hum Pathol, Dec 2013

Helicobacter gastritis induces changes in the oxyntic mucosa indistinguishable from the effects of proton pump inhibitors.

Kumar KR, et al. *Hum Pathol*. 2013; 44(12):2706-10.

It is thought that proton pump inhibitor (PPI) leads to dilatation of fundic glands with protrusion of parietal cells. In 104 H. pylori-positive patients, glandular dilatations and parietal cell protrusions were equally prevalent with or without PPI use. The authors conclude that glandular dilatation and parietal cell protrusion is associated with PPI use in H. pylori-negative patients, while H. pylori infection itself may also lead to these changes in the oxyntic mucosa. Hence implication of PPI for these changes should be avoided in the presence of H. pylori gastritis.

<http://www.ncbi.nlm.nih.gov/pubmed/24071014>

Peritoneal elastic lamina invasion: limitations in its use as a prognostic marker in stage II colorectal cancer.

Grin A, et al. *Hum Pathol*. 2013; 44(12):2696-705.

The use of elastic stain has been advocated for detecting peritoneal elastic lamina invasion (ELI) with the premise that this will be useful in the identification of pT4 disease. In this study, 217 stage II CRC (186, pT3; 31, pT4) cases were studied with elastic stain. There was no difference in survival in tumors categorized as pT3 patients with and without elastic lamina invasion, while the survival of pT4 tumors was significantly lower than that of pT3 ELI-positive tumors. It was also difficult to identify elastic lamina in right-sided tumors. The study concludes that peritoneal elastic lamina invasion is not a significant prognostic factor, and the difficulty in identification of elastic lamina on the right sided limits the routine use of elastic stain.

<http://www.ncbi.nlm.nih.gov/pubmed/24074534>

Clinicopathologic features and prognosis of duodenal adenocarcinoma and comparison with ampullary and pancreatic ductal adenocarcinoma.

Zenali M, et al. *Hum Pathol.* 2013; 44(12):2792-8.

This study, we examined the clinicopathologic features comprises 68 duodenal adenocarcinomas (DAC), 92 ampullary adenocarcinomas, and 126 pancreatic ductal adenocarcinoma (PDA). The lymph node metastases were lower in DAC and AA, compared to PDA. The survival in DAC was better than both AA and PDA; there was no difference in survival between AA and PDA.

<http://www.ncbi.nlm.nih.gov/pubmed/24139211>

Segmental muscular defects of the intestine: a possible cause of spontaneous perforation of the bowel in adults.

Tamai M, et al. *Hum Pathol.* 2013; 44(12):2643-50.

This study identified full thickness muscular defects in adults with 'idiopathic' intestinal perforation. There was no significant inflammation in association with the defects. The etiology of these defects is not known, but may represent a focal congenital anomaly that can lead to spontaneous perforation.

<http://www.ncbi.nlm.nih.gov/pubmed/24071018>

Hum Pathol, Nov 2013

Immunohistochemical analysis of chromogranin A and p53 expressions in ulcerative colitis-associated neoplasia: neuroendocrine differentiation as an early event in the colitis-neoplasia sequence.

Shigaki K, et al. *Hum Pathol.* 2013; 44(11):2393-9.

Immunohistochemistry for chromogranin and p53 was performed in 26 low-grade dysplasia (LGD), 32 high-grade dysplasia (HGD) and 27 invasive cancers (INV). Chromogranin A was more often positive in HGDs (58%) and INVs (47%) than LGDs (32.0%)(5% staining was considered positive). p53 was more often positive in HGD (60%) and INV (60%) than LGD (31%). The results with co-expression of chromogranin and p53 were similar: HGD 31%, INV 27% and LGD 12%. The use of both markers increased the sensitivity (67%) and specificity (80%) for HGD as compared to p53 alone (sensitivity 58%; specificity 68%). The authors conclude that neuroendocrine differentiation is common in early UC-related neoplasia and can be useful for grading dysplasia.

<http://www.ncbi.nlm.nih.gov/pubmed/24029705>

Lynch syndrome-associated colorectal carcinoma: frequent involvement of the left colon and rectum and late-onset presentation supports a universal screening approach.

Hartman DJ, et al. *Hum Pathol.* 2013; 44(11):2518-28.

This study reiterates some of the findings previously reported in literature: left-sided cancers were not uncommon in Lynch syndrome, 32% of Lynch-associated colorectal cancers occurred >60 years and histologic findings were no reliable in identifying every case. The authors advocate universal screening approach for identification of Lynch syndrome.

<http://www.ncbi.nlm.nih.gov/pubmed/24034859>

Comparison of 2 monoclonal antibodies for immunohistochemical detection of BRAF V600E mutation in malignant melanoma, pulmonary carcinoma, gastrointestinal carcinoma, thyroid carcinoma, and gliomas.

Routhier CA, et al. *Hum Pathol.* 2013; 44(11):2563-70.

This study compares the sensitivity and specificity of two commercially available BRAF V600E antibodies for the detection of the BRAF V600E mutation in 152 tumors: 31 melanomas, 25 lung carcinomas, 32 gastrointestinal carcinomas, 23 thyroid carcinomas, 35 gliomas, and 6 others. The concordance between immunohistochemistry and mutational analyses was 97% for VE1 and 88% for anti-B-Raf. Discordance between IHC and mutational analysis was seen in 4 cases with VE1 and 18 cases in anti-B-Raf. The authors conclude that monoclonal VE1 is better performance compared with anti-B-Raf.

<http://www.ncbi.nlm.nih.gov/pubmed/24071017>

Gut, Dec 2013

Aberrant p53 protein expression is associated with an increased risk of neoplastic progression in patients with Barrett's oesophagus

Kastelein F et al. *Gut* 2013;62:1676-1683.

<http://gut.bmj.com/content/62/12/1676.full.pdf+html>

Utility of p53 is evaluated in assessing dysplasia in patient's with Barrett esophagus. Authors studied 720 patients prospectively in a case-control study. Those who developed high-grade dysplasia or adenocarcinoma (HGD or AC) were counted as cases; patients without neoplastic progression were counted as controls. More than 12000 biopsies from 635 patients were analyzed for p53 immunohistochemistry. 49 patients (8%) developed HGD or AC, and p53 overexpression was associated with an increased risk of neoplastic progression. Risk was even higher with loss of p53 expression. PPV for neoplastic progression increased from 15% with a diagnosis of LGD to 33% with LGD and concurrent aberrant p53 expression.

AJSP, Nov 2013

[*Appropriate Use of Special Stains for Identifying Helicobacter pylori: Recommendations From the Rodger C. Haggitt Gastrointestinal Pathology Society*](#)

Batts KP et al. *Am J Surg Pathol.* 37(11):e12-e22, Nov 2013.

The GIPS group publishes its recommendations on use of special stains and immunostains for identifying *H. pylori* – routine “up front” use of such stains is generally not useful, but it is recommended that special stains be used in cases of chronic or chronic active gastritis without detectable organisms on H&E stain.

[*Clinicopathologic Features of Synchronous Colorectal Carcinoma: A Distinct Subset Arising From Multiple Sessile Serrated Adenomas and Associated With High Levels of Microsatellite...*](#)

Hu H et al. *Am J Surg Pathol.* 37(11):1660-1670, Nov 2013.

58 patients with two invasive primary colorectal adenocarcinomas were identified over a ten-year period of cases. In comparison to controls, these patients were older, with tumors mostly involving right colon, more often MSI-high, and more frequently associated with precursor

sessile serrated adenomas (all to statistical significance). Five-year overall survival also was improved in patients with synchronous tumors (92% versus 56%, P=0.02). No patient with SSA-associated synchronous colorectal carcinomas died of disease or developed recurrence at last follow-up. The improved prognosis for these patients is addressed.

[Grading of Well-differentiated Pancreatic Neuroendocrine Tumors Is Improved by the Inclusion of Both Ki67 Proliferative Index and Mitotic Rate](#)

McCall CM et al. Am J Surg Pathol. 37(11):1671-1677, Nov 2013.

Current WHO criteria for pancreatic neuroendocrine tumor (PanNET) recommend assigning the higher grade as determined by Ki-67 labelling and mitotic count on H&E stain. To examine whether this approach is justified, the authors studied 297 WHO grade 1 and 2 PanNETs using Ki67. Grade-discordant mitotic grade 1 PanNETs were more likely to have lymph node metastasis and distant site involvement as well as decreased overall survival (median 12 years for discordant mitotic grade 1 tumors versus 16.7 years for concordant grade 1 tumors). Mitotic grade 1/Ki67 grade 2 tumors showed few significant differences from mitotic grade 2 and either Ki67 grade 1 or 2 tumors. The authors recommend Ki67 labelling routinely be performed for accurate grading.

AJSP, Dec 2013

[PEComa of the Gastrointestinal Tract: Clinicopathologic Study of 35 Cases With Evaluation of Prognostic Parameters](#)

Doyle LA et al. Am J Surg Pathol. 37(12):1769-1782, Dec 2013.

35 cases of gastrointestinal PEComa are analyzed in detail; tumors can be epithelioid, mixed epithelioid and spindle, or purely spindle (rarest). Marked nuclear atypia can be seen (16 cases). The majority are positive for HMB45, melan-A, MitF, SMA, desmin, and a minority for TFE3, S100, KIT, EMA, and keratin. 13 patients developed metastases and 5 died of disease.

[Focally Enhanced Gastritis in Newly Diagnosed Pediatric Inflammatory Bowel Disease](#)

Ushiku T et al. Am J Surg Pathol. 37(12):1882-1888, Dec 2013.

119 newly diagnosed IBD patients (62 CD and 57 UC) were studied to look at whether focally enhanced gastritis is more specific of CD in the pediatric setting. FEG was present in 43% of IBD patients in all (55% CD, 30% UC) and was more common in children age 10 and below. Of CD patients, those with FEG were more likely to have active ileitis and granulomas elsewhere in the GI tract. There was no correlation between FEG and other findings of UC.

Histopathology, Nov 2013

[Value of \$\alpha\$ -methylacyl-CoA racemase immunochemistry for predicting neoplastic progression in Barrett's oesophagus \(pages 630–639\)](#)

Kastelein F et al. Histopathology 2013, 63, 630-639.

720 Barrett esophagus patients were studied, with those who progressed to high-grade dysplasia or adenocarcinoma classified as cases (49 patients). Strong AMACR expression was associated with increased risk of neoplastic progression. PPV of strong AMACR expression is slightly higher than that of low-grade dysplasia (22% vs. 15%).

[Annexin A10 is an immunohistochemical marker for adenocarcinoma of the upper gastrointestinal tract and pancreatobiliary system \(pages 640–648\)](#)

Lu S-H et al. Histopathology 2013, 63, 640-648.

Annexin A10 is expressed in 83% of metastatic pancreatic and 47% of metastatic gastric adenocarcinomas but in only 2% of metastatic adenocarcinomas from other sites. Its normal expression pattern also is presented.

American Journal of Clinical Pathology, Dec 2013

Histologic findings and clinical characteristics in acutely symptomatic ulcerative colitis patients with superimposed Clostridium difficile infection.

Wang T, et al. Am J Clin Pathol. 2013 Dec;140(6):831-7.

The stated purpose of this study was to identify histologic and clinical features that might differentiate patients with symptomatic flairs of ulcerative colitis (UC) who are *C. difficile* positive vs. negative. Histology from a cohort of UC patient's with positive toxin testing (9 patients) was compared with histology from controls (28 patients with UC flairs and 8 patients *C. difficile* and no ulcerative colitis). Interestingly ischemic like damage, a feature often seen in cases of *C. difficile* colitis, was not seen in any case of ulcerative colitis, with or without positive *C. difficile* toxin. "Mushroom" or "volcano" like pseudomembranes were identified in 44% of the biopsies from *C. difficile* positive UC patient's but also in 11% of UC control patients, a statistically significant finding ($P < .05$), but a finding judged by the authors to be of poor sensitivity and specificity for reliably detecting *C. difficile* infection in patients with UC.
<http://www.ncbi.nlm.nih.gov/pubmed/24225751>

Modern Pathology, Dec 2013

Very well-differentiated gastric carcinoma of intestinal type: analysis of diagnostic criteria
Ushiku T, et al. Mod Pathol 2013 Dec;26(12):1620-1631.

In this study the histologic, immunohistochemical, and clinical features of 21 cases of the so called very well differentiated gastric adenocarcinoma of intestinal type were examined to determine key diagnostic features. Histologic features found to be characteristic include: pit and glandular anastomosis (described as W, H, Y, and X shapes); spikey glands; distended glands; discohesive cells; abortive glands; and glandular outgrowth. At least three of these features were present in all cases and 86% of the cases had four or more. In half of cases, the biopsies showed diagnostic features of very well-differentiated adenocarcinoma were present but in only half of these cases was a malignant diagnosis given (36% adenocarcinoma, 14% suspicious for adenocarcinoma); the remainder of these biopsies were judged to be indeterminate (26%) or reactive (24%).

<http://www.ncbi.nlm.nih.gov/pubmed/23723017>

MET overexpression assessed by new interpretation method predicts gene amplification and poor survival in advanced gastric carcinomas

Ha S, et al. Mod Pathol 26 Dec;26(12) 1632-1641; advance online publication, June 28, 2013; doi:10.1038/modpathol.2013.108

This study evaluates immunohistochemistry for MET proto-oncogene as a prognostic indicator and possible target for specific inhibitors. The authors concluded that MET overexpression correlated with shorter overall survival and disease free survival; however, this association was only found in cases with membranous and cytoplasmic staining. In a previous study on gastric cancers using the same antibody, but only looking at membranous staining, no clinical significance was identified.

Inflammatory Bowel Diseases, Dec 2013

The Correlation Between Endoscopic and Histological Inflammation in Ulcerative Colitis
Theede K, et al. Volume 19 Supplement 1 pgs. S1-S132 December 2013

Mucosal healing has become a treatment goal in ulcerative colitis because it is associated with a better outcome. This study evaluates two scoring systems for endoscopic mucosal inflammation in cases of ulcerative colitis. The more commonly used Mayo Endoscopic Score (MES) was found to correlate with the newer Ulcerative Colitis Endoscopic Score of Severity (UCEIS). Both systems (described in detail in the paper) had good predictive value for the presence of histologic inflammation, but 5-8% of the cases judged to have mucosal healing endoscopically did have some weak activity. The paper notes that some reports do state that histologic inflammation without endoscopically visible lesions can occur and are associated with a worse prognosis, independent of the endoscopic findings.

[no pub med link available]

Gastroenterology Clinics of North America, Dec 2013

Anal squamous intraepithelial neoplasia.

Bejarano PA, et al. *Gastroenterol Clin North Am.* 2013 Dec;42(4):893-912.

This clinically based review article discusses the general epidemiology, terminology, association with HPV, and current diagnosis and treatment topics of anal dysplasia and its possible progression to squamous cell carcinoma. Most importantly the new recommendations from the Lower Anogenital Squamous Terminology Standardization Project for HPV-Associated Lesions (LAST) are discussed and put into historical perspective with explanations of why low and high grade squamous intraepithelial lesions correspond to AIN 1 and AIN 2 and 3 respectively.

<http://www.ncbi.nlm.nih.gov/pubmed/24280406>

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