

GIPS JOURNAL WATCH, SEP-OCT 2013

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.

Thiopurines are used for treatment of ulcerative colitis (UC) and have been associated with increase in the risk of lymphoma. In a retrospective analysis of more than 36,000 cases, this study shows that thiopurine use is associated with a 4x higher risk of lymphoma, which increases with each year of treatment and decreases with discontinuation of the drug.

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

Gastroenterology, Oct 2013

Central obesity in asymptomatic volunteers is associated with increased intrasphincteric acid reflux and lengthening of the cardiac mucosa.

Robertson EV, et al. Gastroenterology. 2013;145(4):730-9.

Most patients with adenocarcinoma of the GE junction and gastric cardia and gastroesophageal junction do not have GERD. This study shows that patients with central obesity have significantly longer cardiac mucosa, extension of gastric acid into the lower esophageal sphincter. We studied the gastroesophageal junction in asymptomatic volunteers with normal and large waist circumferences (WCs) to determine if central obesity is associated with abnormalities that might predispose individuals to adenocarcinoma. It is proposed that these findings may explain the increasing incidence of GE junction and cardia adenocarcinomas.

<http://www.ncbi.nlm.nih.gov/pubmed/23796455>

Gastroenterology, Sep 2013

Identification of molecular subtypes of gastric cancer with different responses to PI3-kinase inhibitors and 5-fluorouracil.

Lei Z, et al. Gastroenterology. 2013;145(3):554-65.

Gastric adenocarcinoma was divided into proliferative, metabolic, and mesenchymal subtypes based on gene expression in 248 tumors. The proliferative subtype was characterized by high levels of genomic instability, P53 mutations, and DNA hypomethylation. Tumors with metabolic subtype were more sensitive to 5-fluorouracil. Mesenchymal subtype tumors showed features of cancer stem cells, and cell lines of this subtype are particularly showed in vitro sensitivity to phosphatidylinositol 3-kinase-AKT-mTOR inhibitors.

<http://www.ncbi.nlm.nih.gov/pubmed/23684942>

Hum Pathol, Oct 2013

CD123 is a useful immunohistochemical marker to facilitate diagnosis of acute graft-versus-host disease in colon.

Lin J, et al. Hum Pathol. 2013;44(10):2075-80.

This study examines immunohistochemistry for CD123 and C4d in colon biopsies from patients with stem cell transplantation. CD123 was positive in 65% of acute GVHD compared to 15% of CMV colitis and no cases of patients on mycophenolate. There was no significant difference in C4d staining among these groups. It is suggested that CD123 may be useful in the diagnosis of acute GVHD.

<http://www.ncbi.nlm.nih.gov/pubmed/23791208>

Intestinal and pancreatobiliary differentiation in periampullary carcinoma: the role of immunohistochemistry.

Kumari N, et al. Hum Pathol. 2013; 44(10):2213-9.

This study examines the utility of CDX-2, MUC2, CK7 and CK17 for the distinction of intestinal and pancreatobiliary subtypes in periampullary carcinoma. CDX2 had high sensitivity and specificity (90% and 100% respectively) for intestinal adenocarcinoma. CK7, CK20 and MUC2 showed high specificity for pancreatobiliary origin (90%, 80% and 95% respectively, but the sensitivity was less than 50%. The survival in intestinal type was better than pancreatobiliary type and CDX2 expression was an independent favorable prognostic marker.

<http://www.ncbi.nlm.nih.gov/pubmed/23834763>

Gut, Oct 2013

The oesophageal string test: a novel, minimally invasive method measures mucosal inflammation in eosinophilic oesophagitis

Furuta GT et al. Gut 2013;62:

The esophageal string test, a minimally invasive technique using a capsule containing approximately 90 cm of string, was used to gather adherent secretions from the proximal esophagus. Eosinophil-derived proteins that bound to string were analyzed in comparison to mucosal pinch biopsies. This technique is reported to be predictive of eosinophilic inflammation on biopsy and also distinguished children from active EoE, treated EoE in remission, GERD, and normal esophagus. This could be a useful adjunct piece of information for pathologists evaluating esophageal biopsies for the question of EoE.

<http://gut.bmj.com/content/62/10/1395.full.pdf+html>

AJSP, Sept 2013

[Histologic Features in Colon Biopsies Can Discriminate Mycophenolate From GVHD-induced Colitis](#)

Star KV et al. Am J Surg Pathol. 37(9):1319-1328, Sep 2013.

The authors evaluate features that may help distinguish mycophenolate (MMF)-induced colitis from GVHD-induced colitis on biopsy. Key features to identify MMF colitis with combined

sensitivity of 76%, specificity of 93%, PPV of 81%, and NPV of 90% include lamina propria eosinophils >15 per 10 hpf, lack of endocrine cell aggregates in the lamina propria, and lack of apoptotic microabscesses.

[Acinar Cell Cystadenoma of the Pancreas: A Benign Neoplasm or Non-Neoplastic Ballooning of Acinar and Ductal Epithelium?](#)

Singhi AD et al. Am J Surg Pathol. 37(9):1329-1335, Sep 2013.

Eight acinar cell cystadenomas (ACA) of the pancreas are studied for detailed gross and microscopic findings. Based on clinical follow-up, none of the patients showed recurrence or malignant transformation. Over time as cysts increase in size, they fuse to form larger unilocular cysts. Five of seven cases with available data show random X-chromosome inactivation. The authors propose re-adoption of the term "acinar cystic transformation" till the non-neoplastic or neoplastic nature of these lesions can be confirmed.

[Gastrointestinal Histopathology in Chronic Granulomatous Disease: A Study of 87 Patients](#)

Alimchandani M et al. Am J Surg Pathol. 37(9):1365-1372, Sep 2013.

87 patients with CGD are analyzed, to include biopsy tissue and GI tissue from 15 autopsies. A minority of patients (4/87, 5%) had normal histology. Of the remaining 95%, colon was most commonly involved and esophagus was least commonly involved. Microgranulomas were present in 46% of colon biopsies, 23% of small bowel, and 6% of gastric. Pigmented macrophages and the presence of eosinophilia also are reported. GMS-positive fungal forms were present in four esophageal biopsies without associated tissue invasion or acute inflammation. For the most part, infectious etiologies were not identified. A subset of duodenal and ileal biopsies showed villous shortening.

AJSP, October 2013

[Loss of CDX2/CK20 Expression Is Associated With Poorly Differentiated Carcinoma, the CpG Island Methylator Phenotype, and Adverse Prognosis in Microsatellite-unstable Colorectal Cancer](#)

Kim JH et al. Am J Surg Pathol. 37(10):1532-1541, Oct 2013.

109 MSI-H samples of colorectal cancer were analyzed. Of those, 9 (8.3%) showed a CDX2-negative/CK20-negative phenotype. This combination is associated with age >56 years, higher stage (III or IV), deep invasion (T3 or T4), lymph node metastasis (N1 or N2), poor differentiation (nonmedullary/non-signet ring cell type), BRAF mutation, and CIMP-H status. This subset of patients showed worse overall and disease-free survival compared with patients with CDX2-positive and/or CK20-positive tumors (P<0.001).

[Characterization of Perineural Invasion As a Component of Colorectal Cancer Staging](#)

Ueno H et al. Am J Surg Pathol. 37(10):1542-1549, Oct 2013.

A multi-center review of 962 patients with stage I to III colorectal cancer (cohort 1) and 1883 patients (cohort 2) was performed to include detailed analysis of perineural invasion (Pn0, Pn1a – intramural PN, and Pn1b – extramural PN). Advanced perineural invasion status is a significant prognostic marker independent of T or N stage in both cohorts. The authors propose that

cancer staging could be enhanced by adding PN assessment based on location within the bowel.

[*Retrospective Evaluation of Elastic Stain in the Assessment of Serosal Invasion of pT3N0 Colorectal Cancers*](#)

Liang W-Y et al. Am J Surg Pathol. 37(10):1565-1570, Oct 2013.

The use of elastic stain (all cases) or CK7 immunostain (subset of 169 cases) was evaluated on one block per case from 244 consecutively resected pT3N0 colorectal cancers. Of 101 cases with identifiable elastic lamina, 60 cases (24.6%) showed elastic lamina invasion. This finding was associated with worse 5-year disease-free survival ($P < 0.001$, 5-year disease-free survival = 60%) and worse overall survival ($P = 0.01$, 5-year overall survival = 66.7%) compared with patients lacking elastic lamina invasion (5-year disease-free survival = 87.8%, overall survival = 92.7%). CK7 was comparatively less useful to identify serosal invasion. The authors propose using a single elastic stain routinely in pT3N0 cases.

[*BRAFV600E Immunohistochemistry Facilitates Universal Screening of Colorectal Cancers for Lynch Syndrome*](#)

Toon CW et al. Am J Surg Pathol. 37(10):1592-1602, Oct 2013.

The authors propose a universal Lynch syndrome screening protocol for colorectal cancer using reflex IHC for BRAFV600E and MMR proteins; in their hands, BRAF IHC is highly concordant with two commonly used PCR-based BRAFV600E assays and performs well in identifying *MLH1* mutation carriers from a large Australian patient registry; all cases of proven Lynch syndrome were identified in the study group.

Histopathology, Sept 2013

[*Improving the standard of lymph node retrieval after gastric cancer surgery \(pages 316–324\)*](#)

Hanna GB et al. Histopathology 2013, 63, 316-324.

114 gastrectomy specimens were analyzed by manual node dissection and systematic fat blocking, the latter of which resulted in higher total node counts and identified more small positive lymph nodes (less than 5 mm).

[*Immature squamous metaplasia \(focal atypical epithelial hyperplasia\) of the pancreatic duct—immunohistochemical distinction from intraductal carcinoma \(pages 343–350\)*](#)

Mochizuki K et al. Histopathology 2013, 63, 343-350.

A combination of CK5/6 and Ki67 is found to differentiate immature squamous metaplasia of the pancreatic duct (ISMPD) from intraductal carcinoma of the pancreas (ICP, used interchangeably with PanIN-3 and CIS). 20 ISMPD and 10 ICP samples were analyzed. Mean Ki67 is 1.0% in ISMPD and 18.5% in ICP. 95% of ISMPD expressed CK5/6 in contrast to none of the ICP.

Histopathology, Oct 2013

[*Oesophageal hyperkeratosis: clinicopathological associations \(pages 463–473\)*](#)

Taggart M et al. *Histopathology* 2013, 63, 463-473.

The authors identify hyperkeratosis in approximately 2% of studied esophageal biopsies and were able to divide them into cases occurring in the setting of Barrett esophagus/adenocarcinoma or outside this setting. In the former case, lesions have no clinical significance and are often identified incidentally as a single small focus, often endoscopically undetectable. In the latter case (outside of Barrett esophagus/adenocarcinoma), hyperkeratosis is associated with esophageal squamous neoplasia/disease of the head and neck. Background risk factors (smoking, alcohol, and possibly reflux) are discussed.

Arch Pathol Lab Med, Sept 2013

The Clinical Significance of Duodenal Lymphocytosis With Normal Villus Architecture

Hammer STG and JK Greenson. *Arch Pathol Lab Med* 2013; 137, 1216-1219.

The Marsh I lesion is described in detail with the authors' approach to signing out such cases, a range of which represent celiac disease (9-40%).

[Abstract](#)

Classic Versus Type II Enteropathy-Associated T-Cell Lymphoma: Diagnostic Considerations

Arps DP and LB Smith. *Arch Pathol Lab Med* 2013; 137, 1227-1231.

Review article focusing on the two forms of enteropathy-associated T-cell lymphoma.

[Abstract](#)

Modern Pathology, Sept 2013

Peutz-Jeghers syndrome: a critical look at colonic Peutz-Jeghers polyps

Julie Y Tse, et al. *Mod Pathol. Sep*; 26(9):1235-40.

The study shows that the characteristic feature of arborizing smooth muscle, usually seen in small bowel PJPs, was seen in only a minority of the colonic polyps (41%). In addition the arborizing pattern was not specific to PJPs and was seen to a certain degree in including prolapse type polyps, hyperplastic polyps, tubular adenomas with prolapse change, ganglioneuromatous polyps, and juvenile polyps. Instead of arborization of smooth muscle, a lobular organization of crypts surrounded by a layer of smooth muscle (in some cases only identified by desmin immunohistochemistry) was specific to PJPs and, although not completely sensitive (68%).

<http://www.ncbi.nlm.nih.gov/pubmed/23599156>

Immunohistochemical stains for CD3 and CD8 do not improve detection of gluten-sensitive enteropathy in duodenal biopsies

Rachel Hudacko, et al. *Mod Pathol Sep*; 26: 1241-1245.

In a study of 200 duodenal biopsies, the study shows that slightly more lymphocytes were identified by immunohistochemistry (mean of 2.1 ± 0.1 intraepithelial lymphocytes per 20 enterocytes by H&E, compared with 3.2 ± 0.1 CD3-positive and 2.1 ± 0.1 CD8-positive intraepithelial cells), but that none of the cases reached the threshold for significant

lymphocytosis. The authors concluded that immunohistochemistry does not add to the identification of gluten sensitive enteropathy over normal evaluation by H&E.

www.ncbi.nlm.nih.gov/pubmed/23558576

Methylene blue-assisted lymph node dissection technique is not associated with an increased detection of lymph node metastases in colorectal cancer

Bruno Märkl, et al. *Mod Pathol* 26: 1246-1254

Methylene blue-assisted lymph node dissection, the technique of injecting dye into fresh colorectal cancer resection specimens followed by fixation and manual dissection, has been advocated as a means to increase lymph node harvests for adequate staging of colorectal cancer. In this study 669 prospectively collected colorectal cancer resections that were evaluated by methylene blue assisted lymph node dissection were compared to a historic control group with conventional lymph node dissection. Although the study group had a dramatic increase in the mean number of lymph nodes harvested with the technique, the percentage of nodal positivity as well as the rate of N2 cases were similar in both groups. In addition, there was no difference in stage matched outcomes. The authors conclude that although methylene blue assisted lymph node dissection was helpful in identifying lymph nodes, this study did not support the hypothesis that it might have an impact on clinical staging or outcome.

www.ncbi.nlm.nih.gov/pubmed/23599158

Modern Pathology, Oct 2013

Clinicopathological analysis of basal cell carcinoma of the anal region and its distinction from basaloid squamous cell carcinoma.

Deepa T Patil, et al. *Mod Pathol* 26: 1382-1389

Basal cell carcinoma of the perianal region, although rare, can enter the differential diagnosis of basaloid squamous cell carcinoma of the anal canal, particularly in biopsies in which exact anatomic location is difficult to identify. In this study, retraction artifact and lack of atypical mitoses favor basal cell carcinoma. An in situ component, when present, favors basaloid squamous cell carcinoma. BerEP4 +/BCL2+/ CDKN2A (p16)-/ SOX2 – phenotype was associated with basal cell carcinoma while basaloid squamous cell carcinoma was CDKN2A+/SOX2+.

www.ncbi.nlm.nih.gov/pubmed/23599161

Gastroenterology Clinics of North America, Sept 2013

Real-time Histology in Colonoscopy.

Martin Goetz. *Gastroenterology Clinics – Sep 2013, Volume 42, Issue 3 , Pages 567-575,*

This review article discusses recent advancements in gastrointestinal endoscopy techniques that move from macroscopic assessment of architecture to techniques that enable real time evaluation of histologic features. High definition endoscopy with filter techniques and

autofluorescence, techniques that can evaluate architectural features at the crypt level are discussed as well as newer techniques such as endocytoscopy, which reveals cellular detail after application of a topical dye, and endomicroscopy, which involves laser scanning devices that can elucidate cellular detail at and below the mucosal surface.

www.ncbi.nlm.nih.gov/pubmed/23931860

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