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WHAT'S NEW IN PATHOLOGY?

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THE LATEST NEWS IN GI

By Dr. Raul S. Gonzalez

Below are several findings or discussions that have been published in recent literature. The AJCC Cancer Staging Manual, 8th edition has recently been released. Major changes (but not minor tweaks) will be mentioned under each organ specific heading. Additionally, gastrointestinal neuroendocrine neoplasms now each have an organ specific chapter (stomach, duodenum, etc.), and "pancreas (endocrine and exocrine)" has accordingly been split into separate exocrine and neuroendocrine chapters.

ESOPHAGUS

• Esophageal adenocarcinoma: CAP guidelines for reporting HER2 status have been published (Arch Pathol Lab Med 2015;139:618).

STOMACH

• *Helicobacter pylori*: The US GI Pathology Society has published guidelines for the use of ancillary staining in the detection of *H. pylori* (Am J Surg Pathol 2013;37:e12).

• Gastric adenocarcinoma: The Cancer Genome Atlas has published a molecular classification of gastric adenocarcinoma (Nature 2014;513:202). Surgical pathologists can roughly follow this classification scheme with the use of additional staining (Mod Pathol 2016;29:772).

• Gastrointestinal stromal tumor: Succinate dehydrogenase deficient GISTs have been established as a defined subtype of gastric GIST in younger patients, with unique morphology, loss of SDHB by immunohistochemistry, and good prognosis; conventional criteria do not adequately predict their behavior, and AJCC staging should not be applied (Am J Surg Pathol 2016 Jun 23, Epub).

AMPULLA

• Ampullary carcinoma: *ELF3* mutations appear to be a characteristic driver of ampullary carcinoma (Cancer Cell 2016;29:229). Additionally, a panel of immunostains may help distinguish pancreatobiliary type carcinoma from intestinal type carcinoma, which has treatment implications (Am J Surg Pathol 2014;38:1371). HER2 may prove to be a potential therapeutic target in some cases (Mod Pathol 2015;28:1123).

SMALL INTESTINE

• Well differentiated neuroendocrine tumors: Mesenteric deposits appear to be an adverse prognostic factor in small intestinal NETs, as they are in colorectal carcinoma (Am J Surg Pathol 2016 Sep 28, Epub); they have been incorporated into AJCC staging as N2 disease if > 2 cm. NKX6-1 is an immunohistochemical marker that appears fairly specific for duodenal and pancreatic NETs (Am J Surg Pathol 2015;39:850).

COLON

• Idelalisib induced enterocolitis: Much like the CTLA-4 inhibitor ipilimumab, the PI3K inhibitor idelalisib has been associated with enterocolitis (Am J Surg Pathol 2015;39:1653, Am J Surg Pathol 2015;39:1661).

• Lanthanum carbonate is a phosphate binding medication, used in dialysis patients, that can deposit in the gastrointestinal mucosa and mimic mucosal calcinosis (Am J Surg Pathol 2015;39:767).

• Ischemic colitis can rarely form an inflammatory mass that clinically resembles malignancy (Am J Surg Pathol 2015;39:1275).

• Hirschsprung disease: A staining panel including MAP2, calretinin, GLUT1 and S100 has been proposed to assist in the microscopic diagnosis of Hirschsprung disease (Histopathology 2015;66:824).

• CpG island methylation pathway: The "serrated pathway" to colorectal carcinoma has recently undergone increased molecular scrutiny. *BRAF* and *RNF43* mutations appear important to the development of sessile serrated adenoma and traditional serrated adenoma (Am J Surg Pathol 2016;40:1352; Gut 2016 Jun 21, Epub). Traditional serrated adenomas can also harbor *PTPRK-RSPO3* fusions (J Pathol 2016;239:133). HES1 loss by immunohistochemistry may help distinguish sessile serrated adenoma from hyperplastic polyp (Am J Surg Pathol 2016;40:113).

• Inflammatory bowel disease associated colorectal carcinoma has molecular changes distinct from non IBD associated cases: *IDH1* is mutated in carcinomas from Crohn's disease but not ulcerative colitis, while MYC amplification is seen in carcinomas from both (Gastroenterology 2016;151:278). IBD patients with biopsy findings "indefinite for dysplasia" are at risk of developing frank dysplasia or malignancy (Inflamm Bowel Dis 2015;21:378).

• Familial polyposis syndromes: New gene mutations have been described in novel forms of colorectal polyposis, including *POLE* and *POLD1* in polymerase proofreading associated polyposis (Hum Mol Genet

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2014;23:3506) and *NTHL1* (Nat Genet 2015;47:668).

• Colorectal carcinoma: New potential therapeutic targets in colorectal carcinoma include PD-1 / PD-L1 (particularly in medullary carcinomas and other mismatch repair deficient carcinomas) (N Engl J Med 2015;372:2509; Mod Pathol 2016 Jul 22, Epub) and HER2 (Cancer Discov 2015;5:832). Tumor budding is a poor prognostic indicator in colorectal carcinoma, particularly with ≥ 10 tumor buds per 20× field (Am J Surg Pathol 2015;39:1340).

APPENDIX

• Low grade appendiceal mucinous neoplasm: The Peritoneal Surface Oncology Group International recently released consensus and classification guidelines for mucinous appendiceal neoplasia (Am J Surg Pathol 2016;40:14). Proximal margin involvement in LAMNs appears not to predict recurrence (Arch Pathol Lab Med 2015;139:518). Cecal / appendiceal endometriosis with intestinal metaplasia can mimic LAMN (Am J Surg Pathol 2014;38:698). SATB2 staining can help distinguish between primary ovarian neoplasms and spread of appendiceal disease (Am J Surg Pathol 2016;40:419). *GNAS* mutation is common in LAMNs (Hum Pathol 2014;45:1737). AJCC staging now classifies these lesion as Tis(LAMN).

• Sessile serrated adenoma: Unlike their colonic counterparts, appendiceal serrated lesions often have *KRAS* mutations but not *BRAF* mutations (Hum Pathol 2014;45:227).

LIVER

• Primary biliary cirrhosis has been renamed "primary biliary cholangitis," as not all patients progress to cirrhosis (Hepatology 2015;62:1620).

• Congestive hepatopathy: A scoring system has been proposed for this form of outflow obstruction (Mod Pathol 2014;27:1552).

• Fibrolamellar hepatocellular carcinoma is characterized by a specific *DNAJB1-PRKACA* mutation (Mod Pathol 2015;28:822) and also shows LFABP loss by immunohistochemistry (Mod Pathol 2016;29:607).

• Combined hepatocellular cholangiocarcinoma: Among cHC-CC with stem cell features, *ARID1A* mutations are seen in the cholangiocellular type, and *TERT* promoter mutations are seen in the intermediate cell type (Histopathology 2016 Sep 16, Epub).

• Hepatic small vessel neoplasm is a recently described benign vascular neoplasm that can mimic angiosarcoma and that may be a variant of anastomosing hemangioma (Hum Pathol 2016;54:143).

• Ipilimumab induced hepatitis: This type of drug induced liver injury resembles autoimmune hepatitis and can also cause endothelialitis (Am J Surg Pathol 2015;39:1075).

PANCREAS

• Pancreatic cysts: The American Gastroenterological Association has released a recommendation for clinical approach to asymptomatic pancreatic cysts (Gastroenterology 2015;148:819). Molecular testing on cyst fluid can also assist in diagnosis (Gastroenterology 2015;149:1501).

• Pancreatic intraepithelial neoplasia is now classified as low grade (formerly PanIN 1a, 1b, and 2) or high grade (formerly PanIN 3) (Am J Surg Pathol 2015;39:1730).

• Pancreatic ductal adenocarcinoma: *RMB10* mutations and *KRAS* Q61 allele mutations appear to confer improved survival (Nat Commun 2015;6:6744). AJCC T category staging now relies almost entirely on tumor size; extrapancreatic extension has been removed.

• Pancreatic well differentiated neuroendocrine tumors: Histologically well differentiated neuroendocrine tumors can have a grade 3 mitotic or Ki67 rate; this does not make them carcinomas (Am J Surg Pathol 2016;40:1192; Am J Surg Pathol 2015;39:683). PHH3 may be a more reproducible method of grading than Ki67 (Ann Surg Oncol 2016 Mar 28, Epub). Poor prognostic factors include alternative telomere lengthening and *DAXX / ATRX* loss (Clin Cancer Res 2016 Jul 12, Epub; Clin Cancer Res 2016 Sep 23, Epub).

• Intraductal oncocytic papillary neoplasm appears to be genetically distinct from intraductal papillary mucinous neoplasm and harbors an overall better prognosis (Mod Pathol 2016;29:1058, J Am Coll Surg 2015;220:839).

• Undifferentiated carcinoma with osteoclastic giant cells has a better prognosis than previously believed (Am J Surg Pathol 2016;40:1203).

• The Pancreatobiliary Pathology Society officially formed in 2016 and is accepting new members.

EXTRAHEPATIC BILE DUCTS

• Extrahepatic bile duct carcinoma: AJCC T category staging of distal bile duct carcinomas now depends on measured depth of invasion, rather than anatomic extent of invasion.

MEET THE AUTHOR

Raul S. Gonzalez, M.D., is an Assistant Professor and codirector of the Gastrointestinal Pathology fellowship at the University of Rochester Medical Center. He earned his M.D. from the Medical College of Georgia, then completed residency training in Anatomic and Clinical Pathology at Emory University and fellowship training in Surgical Pathology and Gastrointestinal Pathology at Vanderbilt University.

Dr. Gonzalez has authored a liver pathology textbook, has published more than 30 peer reviewed journal articles, has served as a peer reviewer for several journals, and is on the editorial board of *Archives of Pathology & Laboratory Medicine*. He has been invited to speak at multiple national conferences, maintains active Facebook and Twitter pages dedicated to gastrointestinal pathology, and was named one of the American Society for Clinical Pathology's "40 Under Forty" for 2016.