GIPS JOURNAL WATCH, MAY-JUNE 2012

Am J Gastroenterol, May 2012

Cancer Risks for Relatives of Patients With Serrated Polyposis.
Win Ak, et al. Am J Gastroenterol 2012;.107(5):770-8.
The study shows that relatives of patients with serrated polyposis are at risk of colorectal and pancreatic cancer, suggesting a germline defect for this disorder.
http://www.ncbi.nlm.nih.gov/pubmed/22525305

The article is accompanied by an excellent editorial.
Serrated Polyposis: The Last (or Only the Latest?) Frontier of Familial Polyposis?
http://www.ncbi.nlm.nih.gov/pubmed/22552244

Gut, June 2012

Colorectal cancer: a tale of two sides or a continuum?
Yamauchi M, et al. Gut 2012;61:794-797
Commentary/leading article. Shuji Ogino and colleagues outline the two colon concept versus the colon continuum hypothesis. See Yamauchi et al. in the same issue of Gut.
Extract

Comparison between universal molecular screening for Lynch syndrome and revised Bethesda guidelines in a large population-based cohort of patients with colorectal cancer
Pérez-Carbonell L, et al. Gut 2012;61:865-872
Immuno studies for MMR proteins and/or MSI analysis were performed on >2000 patients with colorectal cancer. 486 patients (~23%) met some of the revised Bethesda criteria; in these, 12 germline mutations were identified. 180 patients of the total study group showed loss of some of the MMR proteins and/or MSI. Of these, 14 had a MMR germline gene mutation; however, two of these 14 did not meet Bethesda criteria. Routine molecular screening of all colorectal cancer patients using immunohistochemistry or MSI is proposed.
Abstract

Nat Genet, May 2012

Hereditary mixed polyposis syndrome is caused by a 40-kb upstream duplication that leads to increased and ectopic expression of the BMP antagonist GREM1.
Jaeger E, et al. Nat Genet. 2012;44(6):699-703.
Hereditary mixed polyposis syndrome (HMPS) is characterized is an autosomal dominant inherited polyposis that is characterized by polyps showing mixed features of hyperplastic, adenomatous and juvenile polyps. This study shows that HMPS is caused by duplication of the 3' end of the SCG5 gene. This leads to increased GREM1 expression and reduced bone

morphogenetic protein (BMP) pathway activity. The latter mechanism has also been implicated in juvenile polyposis.
http://www.ncbi.nlm.nih.gov/pubmed/22561515

Am J Clin Pathol, June 2012

Molecular Testing in Colorectal Cancer: Diagnosis of Lynch Syndrome and Personalized Cancer Medicine.
Shi C, Washington K. Am J CLin Pathol. 2012;.137(6):847-59.
Special article that reviews all the molecular aspects of colon cancer: major pathways, testing for Lynch syndrome, significance of EGFR and KRAS in treatment and prognostication of stage II disease.
http://www.ncbi.nlm.nih.gov/pubmed/22586043

Journal of Clinical Pathology, June 2012

Bateman AC, et al. Chronic gastric ulceration: a novel manifestation of IgG4-related disease?
After we thought we knew all the myriad manifestations of IgG-4-related disease, some unusual GI presentations including gastric ulcer are presented.
http://www.ncbi.nlm.nih.gov/pubmed/22259178

AJSP, June 2012

Malignant Gastrointestinal Neuroectodermal Tumor: Clinicopathologic, Immunohistochemical, Ultrastructural, and Molecular Analysis of 16 Cases With a Reappraisal of Clear Cell Sarcoma-like Tumors of the Gastrointestinal Tract
Stockman DL, et al. Am J Surg Pathol. 2012;36(6):857-868.
Sixteen cases (mean age 42y) of a new entity called "malignant gastrointestinal neuroectodermal tumor" are identified. Tumors arise in small bowel (10), stomach (4) and colon (2) with cells in sheets or nests; tumor cells stain for S-100, SOX10, and vimentin (100%), CD56 (70%), synaptophysin (56%), NB84 (50%), NSE (45%) and neurofilament protein (14%). Melanocytic, GIST, epithelial, and myoid markers are negative. Twelve cases (86%) show EWSR1 translocation with the partner ATF1 (46%, 6 cases), EWSR1 translocation with the partner CREB1 (23%, 3 cases), no rearrangement of either partner gene (2 cases) or extra copies of EWSR1 or chromosome 22 polysomy (1 case).

Phenotype and Polyp Landscape in Serrated Polyposis Syndrome: A Series of 100 Patients From Genetics Clinics
Rosty C, et al. Am J Surg Pathol. 2012;36(6):876-882.
Serrated polyposis syndrome (SPS) = hyperplastic polyposis and shows multiple serrated polyposis in the large intestine. The genetic basis is unknown. SPS patients over a 10-year period were included. Most of the polyps (83%) were serrated polyps, including microvesicular hyperplastic polyp, goblet cell hyperplastic polyp, SSA, SSA with cytologic dysplasia, and

traditional SA. Another 69 polyps were conventional adenomas. Overall, patients had a high polyp burden and a high rate of BRAF mutation (e.g., detected in 95% of SSA with dysplasia). The occurrence of colorectal cancer was associated with the presence of conventional adenoma.

IgG4-related Sclerosing Disease of the Small Bowel Presenting as Necrotizing Mesenteric Arteritis and a Solitary Jejunal Ulcer
Wong DD, et al. Am J Surg Pathol. 2012;36(6):929-934.
Case report. The authors present the first case of IgG4-related sclerosing disease involving the small bowel. The patient had jejunitis with an isolated chronic ulcer, necrotizing mesenteric arteritis, and abundant IgG4+ plasma cells in the wall of the bowel and mesenteric artery. Serum IgG4 level was highly elevated (>800 mg/dL, normal 8-140 mg/dL).

Duodenal Gastrinoma With Multiple Gastric Neuroendocrine Tumors Secondary to Chronic Helicobacter pylori Gastritis
Grin A, et al. Am J Surg Pathol. 2012;36(6):935-940.
Case report. *Helicobacter pylori* (HP) gastritis is associated with ECL-cell tumors and duodenal gastrinomas as separate findings. This is a case of a patient with both HP-associated gastrinoma in the duodenum and ECL cell hyperplasia in the stomach with progression to microcarcinoids and well-differentiated neuroendocrine tumors; parietal cell hypertrophy also is present.

Histopathology, June 2012

The connective tissue changes of Crohn's disease.
Golda Shelley-Fraser G et al. Histopathol. 2012;60(7):1034-44.
This review summarizes the pathology of fat, smooth muscle changes, collagen and fibrosis, neural pathology, and vascular changes in Crohn disease, including gross and microscopic findings. These findings are discussed in the context of "chronic" or long-term Crohn disease.
Abstract

Mucinous differentiation in colorectal cancer – indicator of poor prognosis?
Langner C, et al. Histopathol. 2012;60(7):1060-70.
Two pathologists reviewed 381 colorectal mucinous adenocarcinomas and adenocarcinomas with a mucinous component. Mucinous differentiation was associated significantly with mismatch repair protein deficiency, but did not affect patient outcome. Factors significantly associated with outcome were: tumor grade, vascular and perineural invasion, tumor border configuration, and budding. Venous invasion and tumor budding as independent predictors of outcome are discussed in additional detail. Their recommendation: extent of mucinous differentiation may be used as an indicator of mismatch repair deficiency, but not for prognostic stratification.
Abstract

Arch Pathol Lab Med, May 2012

Predictors of Response to Targeted Therapies for Gastrointestinal Stromal Tumors

Andrea M, et al. Arch Path Lab Med. 2012; 136(5):483-9.
This is a review of GIST and KIT or PDGFRA status as a predictor of response to treatment. Patients with a KIT exon 11 mutation benefit from imatinib treatment, but patients without detectable KIT or PDGFRA mutations (i.e., patients with "wild-type" GIST) generally do not respond to imatinib.
Abstract

Targeted Therapies and Predictive Markers in Epithelial Malignancies of the Gastrointestinal Tract
McIntire M, Redston M. Arch Path Lab Med. 2012; 136(5):496-503.
This is a review of currently available targeted therapies and predictors of response in GI tumors. Major topics include EGFR inhibition, VEGF inhibition, BRAF inhibition, PI3K inhibition, and anti-HER2/neu treatment specifically in gastric cancer.
Abstract

Human Pathology, May 2012

Gastric Schwannoma: a clinicopathologic study of 51 cases.
Voltaggio L, et al. Hum Pathol. 2012;43(5):650-9.
The study highlights the typical features of gastric schwannoma including micorotrabecular architecture, peritumoral lymphoid aggregates and focal nuclear atypia. Typical features of tissue schwannoma such as encapsulation, nuclear palisading and hyalinized vessels are usually absent. No malignant examples were seen.
http://www.ncbi.nlm.nih.gov/pubmed/22137423

Modern Pathology, May/June 2012

HER-2 testing in gastric cancer: a practical approach.
Ruschoff J, et al. Mod Pathol. 2012;25(5):637-50.
We are increasingly being asked by oncologists to obtain HER-2 tests on advanced esophageal and gastric adenocarcinomas based on the results of the TOGA trial that demonstrated 13.8 vs. 11.2 month survival advantage in patients treated with Herceptin. The patient selection for treatment is based on HER-2 status. It is recommended that immunohistochemistry be used as the initial testing modality. The article discusses the practical aspects of testing in detail and emphasizes that recommendations specifically devised for gastric adenocarcinomas should be used for interpretation.
http://www.ncbi.nlm.nih.gov/pubmed/22222640

The molecular basis of EPCAM expression loss in Lynch syndrome-associated tumors.
Huth C, et al. Mod Pathol. 2012;25(6):911-6.
Epithelial cell adhesion molecule (EPCAM) gene is located upstream of the MSH2 gene. Germline deletions of EPCAM leading to silencing of MSH2 gene has been reported as a novel mechanism leading to Lynch syndrome. These cases show MSH2 loss by immunohistochemistry, but do not show MSH2 gene mutations. This study shows that EPCAM expression by

immunohistochemistry is lost in these cases if the EPCAM deletion is biallelic, i.e., the second hit that inactivates the MSH2 gene also includes the upstream EPCAM gene. EPCAM expression is preserved if the EPCAM gene is not involved in the second hit. EPCAM loss can be seen in adenomas in cases with biallelic inactivation.
http://www.ncbi.nlm.nih.gov/pubmed/22388758

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