Anatomic pathology selected abstracts

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Identification of autoimmune gastritis in a background of H. pylori infection

July 2022—*Helicobacter pylori*-associated gastritis and autoimmune gastritis may coexist in a subset of patients, necessitating treatment for both disorders. The authors conducted a study to identify autoimmune gastritis in the background of *H. pylori* infection. They examined cases involving patients with *H. pylori*-associated gastritis who had successful eradication therapy and subsequent biopsies diagnostic of autoimmune gastritis, as well as cases involving *H. pylori*-associated gastritis for which pathologists noted features of autoimmune gastritis during the original interpretation. Control subjects underwent *H. pylori* eradication and lacked evidence of autoimmune gastritis or *H. pylori* infection after 10 years of follow-up. Eight subjects had *H. pylori*-associated gastritis followed by *H. pylori*-negative sampling that showed autoimmune gastritis. A review of the original samples showed full-thickness inflammation of oxyntic mucosa in eight of eight cases and oxyntic gland loss in seven of eight cases. Enterochromaffin-like (ECL) cell hyperplasia, pyloric metaplasia, and intestinal metaplasia were present in four of eight, four of eight, and three of eight cases, respectively. Features of autoimmune gastritis were noted at the time of the original *H. pylori* diagnosis in 11 study subjects. Ten of 11 samples displayed full-thickness inflammation of oxyntic mucosa or partial loss of oxyntic glands, or both; eight of 11 had ECL cell hyperplasia (all tested cases); six of 11 showed pyloric metaplasia; and four of 11 harbored intestinal metaplasia. All of these features, except full-thickness inflammation of oxyntic mucosa, were absent in control cases. The authors concluded that full-thickness inflammation combined with oxyntic gland loss and ECL cell hyperplasia may help identify autoimmune gastritis in patients with concomitant *H. pylori* infection.

Choudhuri J, Hall S, Castrodad-Rodriguez CA, et al. Features that aid identification of autoimmune gastritis in a background of active *Helicobacter pylori* infection. *Arch Pathol Lab Med*. 2021;145(12):1536–1543.

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Analysis of familial adenomatous polyposis-associated traditional serrated adenoma of small intestine

Familial adenomatous polyposis is an inherited cancer-predisposition syndrome associated with numerous gastrointestinal tract adenomatous polyps, as well as gastric fundic gland polyps and pyloric gland adenomas in the upper gastrointestinal tract. Colonic familial adenomatous polyposis (FAP)-associated traditional serrated adenomas (TSAs) have been reported in a few studies, but small bowel FAP-associated adenomas with TSA morphology have not been characterized. The authors described the clinicopathologic and molecular findings of this type of adenoma in the small bowel of patients with FAP. They reviewed small bowel adenomas in 45 consecutive FAP patients to identify adenomas with zones showing slit-like serrations, cells with eosinophilic cytoplasm, ectopic crypt formation, and vesicular nuclei. They also reviewed sporadic small bowel adenomas from 51 consecutive patients for adenomas with the same features. An analysis of 177 polyps from 45 FAP patients and 60 polyps from 51 nonsyndromic patients identified 18 TSAs from nine FAP patients (20 percent) and 10 TSAs from the sporadic group (19.6 percent). FAP patients presented at a younger age than nonsyndromic patients (median, 43 versus 66 years; P=0.0048). FAP-associated TSAs were asymptomatic and smaller than sporadic TSAs (median size, 0.6 versus 2.5 cm; P=0.00006). Immunostaining for β-catenin and testing for *BRAF* and *KRAS* mutations were performed in a subset of the cohort. Nuclear β-catenin was seen in one FAP-associated TSA and three nonsyndromic TSAs. All TSAs (FAP associated and nonsyndromic) showed wild-type *BRAF*, while *KRAS* mutations

were identified only in the nonsyndromic setting. The authors concluded that small bowel FAP-associated and sporadic TSAs share a similar morphology, and the *BRAF*-serrated pathway does not contribute to their pathogenesis.

Alruwaii ZI, Chianchiano P, Larman T, et al. Familial adenomatous polyposis–associated traditional serrated adenoma of the small intestine: A clinicopathologic and molecular analysis. *Am J Surg Pathol*. 2021;45(12):1626–1632.

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Clinicopathological findings in patients with COVID-19-associated ischemic enterocolitis

COVID-19 has been recognized as predominantly a respiratory tract infection, but some patients manifest severe systemic symptoms or coagulation abnormalities. The authors conducted a study to evaluate the impact of severe COVID-19 infection on the gastrointestinal tract. They examined clinicopathological findings in 28 resected ischemic bowels from 22 patients with severe COVID-19. Most patients required intubation preoperatively and presented with acute decompensation shortly before surgery. D-dimer levels were markedly elevated in all measured cases (mean, 5,394 ng/mL). Twenty-five cases (19 patients) showed histologic evidence of acute ischemia with necrosis. The most characteristic finding in this group was small vessel fibrin thrombi (24 of 25 cases, 96 percent), which were numerous in 64 percent of cases. Patients with COVID-19 were significantly more likely than a control cohort made up of 35 subjects with non-COVID-19–associated acute ischemic bowels to show isolated small intestine involvement (32 versus six percent, $P<0.001$), small vessel fibrin thrombi (100 versus 43 percent, $P<0.001$), submucosal vessels with fibrinous degeneration and perivascular neutrophils (90 versus 54 percent, $P<0.001$), fibrin strands within submucosal vessels (58 versus 20 percent, $P=0.007$), and histological evidence of pneumatosis (74 versus 34 percent, $P=0.010$). Three cases in this cohort had histopathological findings normally seen with chronic ischemia, notably prominent fibroblastic proliferation affecting the outer layer of the muscularis propria. The authors described the histopathological findings in COVID-19–associated ischemic bowels and postulated a relationship with the hypercoagulable state seen in patients with severe COVID-19 infection. Additional experience with these cases may further elucidate specific features or mechanisms of COVID-19–associated ischemic enterocolitis.

Zhang ML, Jacobsen F, Pepe-Mooney BJ, et al. Clinicopathological findings in patients with COVID-19–associated ischaemic enterocolitis. *Histopathology*. 2021;79:1004–1017.

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Feasibility of frozen sections for detecting spread through air spaces in pulmonary adenocarcinoma

Tumor spread through air spaces has been associated with worse prognosis in sublobar resections of lung adenocarcinoma. It was recently proposed that spread through air spaces (STAS) detected on frozen sections may be an indication for lobectomy over sublobar resection. The authors undertook a study to evaluate the reliability of STAS assessment on frozen sections compared to permanent sections, as well as the associations among STAS, tumor grade, and recurrence-free survival after sublobar resection. The study comprised 163 stage I lung adenocarcinoma resections with frozen sections identified retrospectively. For each case, the presence or absence of STAS, percentage of each histological growth pattern, and tumor grade were recorded for frozen and permanent sections. When compared to permanent sections, the detection of STAS on frozen sections had low sensitivity (55 percent), low positive predictive value (48 percent), and fair agreement ($\kappa = 0.34$) but higher specificity (80 percent) and negative predictive value (85 percent). The accuracy was 74 percent. Tumor grade assessment on frozen sections showed higher sensitivity (77 percent), positive predictive value (90 percent), agreement ($\kappa = 0.72$), specificity (94 percent), and accuracy (87 percent), and the same negative predictive value (85 percent). High-grade histology on frozen sections was associated with shorter recurrence-free survival ($p = 0.02$)

compared to STAS on frozen sections ($p = 0.47$). The authors' results suggest that the intraoperative detection of STAS has low sensitivity and positive predictive value. False-positive results may lead clinicians to overtreat lung cancer patients. The determination of tumor grade on frozen sections offers better sensitivity and specificity and, unlike STAS on frozen sections, is associated with recurrence-free survival. The authors concluded that further study is needed to explore the utility of assessing tumor grade on frozen sections.

Zhou F, Villalba JA, Sayo TMS, et al. Assessment of the feasibility of frozen sections for the detection of spread through air spaces (STAS) in pulmonary adenocarcinoma. *Mod Pathol*. 2022;35(2):210–217.

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Tumor spread through air spaces in NSCLC: evidence supportive of an in vivo phenomenon

Tumor spread through air spaces is associated with locoregional recurrence in patients undergoing limited resection for non-small cell lung cancer. The authors hypothesized that spread through air spaces (STAS) in the initial limited resection specimen and additional resection specimens from the same patient, when the specimens were processed using different knives, provides evidence that STAS is an in vivo phenomenon that contributes to locoregional recurrence. The authors retrospectively identified patients with NSCLC—nine adenocarcinoma and one squamous cell carcinoma—who underwent limited resection, had STAS in that specimen, and underwent additional resection in the form of lobectomy or limited resection. The limited resection and additional resection specimens from each patient were processed at different times using different tissue-processing knives. All specimens were analyzed for STAS. All 10 patients underwent limited resection with negative margins (R0). All additional resection specimens had STAS: Eight patients had STAS clusters in their completion lobectomy specimens and two had STAS in their additional limited resection specimens. In two patients, STAS was found in the completion lobectomy specimen only after extensive sampling (more than 10 sections) from the staple line adjacent to the initial limited resection. STAS in the limited resection and additional resection specimens processed using different knives supports the concept that STAS is an in vivo phenomenon rather than an artifact from tissue processing. This observation indicates that occult STAS tumor cells can be present in the lung tissue of the remaining unresected lobe after limited resection and supports the concept that STAS is a contributing factor for locoregional recurrence following limited resection.

Gross DJ, Hsieh M-S, Li Y, et al. Spread through air spaces (STAS) in non-small cell lung carcinoma: evidence supportive of an in vivo phenomenon. *Am J Surg Pathol*. 2021;45(11):1509–1515.

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