Anatomic pathology selected abstracts

Editors: Rouzan Karabakhtsian, MD, PhD, professor of pathology and director of the Women's Health Pathology Fellowship, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY; Shaomin Hu, MD, PhD, staff pathologist, Cleveland Clinic; S. Emily Bachert, MD, breast pathology fellow, Brigham and Women's Hospital, Boston; and Amarpreet Bhalla, MD, assistant professor of pathology, Albert Einstein College of Medicine, Montefiore Medical Center.

Adenomatous polyposis-associated foveolar-type adenoma of the stomach

August 2023—Gastric foveolar-type adenoma is a rare benign neoplasm that occurs sporadically or presents in patients with familial adenomatous polyposis. The molecular features of foveolar-type adenoma (FA) and the relationship between sporadic and syndromic lesions remain unclear. The authors conducted a study in which they performed clinicopathological, immunohistochemical, and genetic analyses of 18 sporadic and 30 familial adenomatous polyposis (FAP)-associated FAs. The majority of sporadic and FAP-associated FAs were located in the upper or middle third of the stomach on a background of fundic gland mucosa. Most lesions were low grade, but three had a high-grade component. Sporadic FAs included two morphologically distinct subtypes—that is, flat and raspberry-like FAs—which the authors distinguished based on endoscopic features. Seven lesions were considered to be flat FAs and appeared as large, slightly elevated lesions measuring 11 to 87 mm. Conversely, 10 raspberry-like FAs were small bright-red polyps measuring 2 to 8 mm in size. FAP-associated FAs, particularly larger lesions, exhibited morphologic features resembling flat FAs but varied significantly in size (2–103 mm). Mutation analysis identified *APC* and *KRAS* mutations in all flat FAs but not in raspberry-like FAs. Remarkably, somatic *APC* and *KRAS* mutations were also detected in 19 (63 percent) and 27 (90 percent) FAP-associated FAs, respectively. This indicates that FAP-associated FAs are genetically equivalent to sporadic flat FAs. This study showed that sporadic FA includes at least two morphologically and genetically distinct subtypes—flat and raspberry-like FA. Furthermore, flat FA represents a sporadic counterpart of FAP-associated FA.

Naka T, Hashimoto T, Cho H, et al. Sporadic and familial adenomatous polyposis-associated foveolar-type adenoma of the stomach. *Am J Surg Pathol*. 2023;47:91–101.

Correspondence: Dr. Shigeki Sekine at ssekine@ncc.go.jp

Intraoperative lymph node assessment via touch preparation for metastatic breast cancer

Touch preparation alone is discouraged for intraoperative lymph node assessment in the neoadjuvant setting because of its overall low sensitivity in detecting metastatic breast cancer. The authors conducted a study to compare the sensitivity, specificity, and negative predictive value of intraoperative lymph node assessment via touch preparation and examine potential causes of discrepancies, as well as the clinical, radiologic, and pathologic parameters in the neoadjuvant setting (NAS) and non-neoadjuvant setting (NNAS). They identified 99 lymph nodes from 47 neoadjuvant patients and 108 lymph nodes from 56 non-neoadjuvant patients. Discordant cases were reviewed retrospectively to reveal the reasons for discrepancy. Clinical, radiologic, and pathologic data were obtained from chart review and the CoPath system database. The authors found that the sensitivity, specificity, and negative predictive value of touch preparation in NAS and NNAS were 34.2 versus 37.5 percent, 100 versus 100 percent, and 70.9 versus 90.2 percent, respectively. In NAS, the reasons for discrepancy were interpretation challenges due to lobular histotype, poor touch preparation quality secondary to therapy-induced histomorphologic changes, and undersampling due to small tumor deposits (2 mm or less). The latter was the major reason for discrepancy in NNAS. More cases with macrometastasis were missed in NAS than in NNAS (14 of 25 versus one of 10). The parameters associated with discrepancy were lobular histotype, histologic grade 2, estrogen receptor positivity, HER2 negativity, and multifocality, as well as pathologic tumor size greater than 10 mm in NAS and lymphovascular space involvement and pathologic tumor size greater than 20 mm in NNAS. The authors concluded

that in NAS, intraoperative touch preparation alone should be used cautiously owing to a high false-negative rate for macrometastasis, especially for patients with invasive lobular carcinoma and known axillary lymph node metastasis before neoadjuvant therapy.

Ersoy E, Elsayad M, Pandiri M, et al. Intraoperative lymph node assessment (touch preparation only) for metastatic breast carcinoma in neoadjuvant and non-neoadjuvant settings. *Arch Pathol Lab Med*. 2023;147(2):149–158.

Correspondence: Dr. Esma Ersoy at ersoye@mskcc.org

Rb1, cyclin D1, and p16 IHC expression to distinguish lung carcinomas

Large-cell neuroendocrine carcinoma of the lung and small-cell lung cancer are high-grade neuroendocrine tumors and share several fundamental features. Because the tumors may respond to different treatment modalities and show unique molecular alterations, it is clinically relevant to distinguish between the two. However, this can be challenging due to sampling and fixation issues and shared morphological features. To address this issue, the authors conducted a study in which surgically resected primary small-cell lung cancer (SCLC; n = 129) and large-cell neuroendocrine carcinoma (LCNEC; n = 27) were immunohistochemically stained with Rb1, cyclin D1, and p16 using tissue microarrays. Expression patterns of the proteins were compared between the two tumors to identify the discriminatory pattern. All markers had high diagnostic accuracy, with Rb1 being the highest, followed by p16 and cyclin D1. The majority of SCLC were Rb1−/p16+/cyclin D1−, and more than half of LCNEC were Rb1+/p16−/cyclin D1+. Overall, the expression pattern Rb1− and cyclin D1− was strongly associated with the diagnosis of SCLC, while the pattern Rb1+ and/or cyclin D1+ was strongly associated with LCNEC. The use of this simplified expression pattern led to a diagnostic accuracy of 97.3 percent. P16 did not further discrimination. The heterogeneity in Rb1, cyclin D1, and p16 expression was insignificant in SCLCs compared with LCNECs. The authors concluded that use of Rb1, cyclin D1, and p16 IHC can distinguish the two tumors with a high degree of accuracy. Notably, the Rb1−/cyclin D1− pattern in a given tumor sample would confirm the diagnosis of SCLC. The results could be extrapolated and applied to routine diagnostic samples, such as biopsies and cytology samples.

Papaxoinis G, Bille A, McLean E, et al. Comparative study of Rb1, cyclin D1 and p16 immunohistochemistry expression to distinguish lung small-cell carcinoma and large-cell neuroendocrine carcinoma. *Histopathology*. 2022;81:205–214.

Correspondence: Dr. D. Nonaka at dnonaka@msn.com

Histomorphological and molecular analysis of acinar cystic transformation of the pancreas

Acinar cystic transformation of the pancreas, previously called acinar cell cystadenoma, is a poorly understood and rare pancreatic cystic lesion. The authors conducted a study that focused on the clinicopathologic and molecular characterization of acinar cystic transformation (ACT). Their research cohort included 25 patients with pancreatic ACT for whom they described the clinicopathological features and molecular profile of ACT using next-generation sequencing. The authors noted that ACT arose more often in women (female/male ratio, approximately 2:1) and in the body-tail region. The mean size was approximately 4 cm. At the latest follow-up, all patients were alive and disease free. Histologically, a typical acinar epithelium lined all cysts, intermingled with ductal-like epithelium in 11 of 25 (44 percent) cases. All cases lacked evidence of malignancy. Three ACT showed peculiar features: one showed an extensive and diffuse microcystic pattern and the other two harbored foci of low-grade pancreatic intraepithelial neoplasia (PanIN) in the ductal-like epithelium. Next-generation sequencing revealed two pathogenic/likely pathogenic mutations in two different cases—one with ductal-like epithelium and one with PanIN—affecting *KRAS* (c.34G>C, p.G12R) and *SMO* (c.1685G>A, p.R562Q) genes, respectively. The other case with PanIN was not available for sequencing. Overall, the authors' findings indicate that ACT is a benign entity that potentially arises from a heterogeneous condition or background, including acinar microcysts, malformations, an obstructive/inflammatory setting, or genetic predisposition, or it may have a neoplastic origin. Although all indications point to ACT being benign, the potential occurrence of driver mutations suggests the need to discuss

the possibility of surveilling these patients over the long term.

Luchini C, Mattiolo P, Basturk O, et al. Acinar cystic transformation of the pancreas: Histomorphology and molecular analysis to unravel its heterogeneous nature. *Am J Surg Pathol*. 2023;47(3):379–386.

Correspondence: Dr. Claudio Luchini at claudio.luchini@univr.it or Dr. Aldo Scarpa at aldo.scarpa@univr.it