Anatomic Pathology Abstracts, 10/16

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Features of columnar-lined esophagus in gastroesophageal junction biopsies

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Features of columnar-lined esophagus in gastroesophageal junction biopsies

Inherent problems with the endoscopic and pathologic criteria for columnar-lined esophagus exist. Furthermore, the clinical and biological significance of an irregular squamocolumnar junction (SCJ) is unclear. The authors conducted a study to evaluate the association between histologic features in SCJ biopsies and columnar-lined esophagus (CLE) and to gain insight into the significance of an irregular SCJ. The study was a cross-sectional analysis of 2,176 mucosal biopsies of the SCJ from 544 patients in a large prospective community clinic-based study of gastroesophageal reflux disease in Washington state. Biopsy samples were evaluated blindly for a wide variety of histologic features, such as the presence and type of mucosal glands, submucosal glands and ducts, goblet cells, multilayered epithelium, inflammation, and buried columnar epithelium. Histologic findings were correlated with endoscopic findings (normal Z-line, irregular Z-line, or CLE) and evaluated by logistic regression and receiver operating characteristic analysis. Five histologic features were associated with CLE: pure mucous glands, multilayered epithelium, presence of goblet cells, 50 percent or more of crypts with goblet cells, and buried columnar epithelium. Pure oxyntic glands were inversely associated with CLE. The features most strongly related to CLE included biopsies with 50 percent or more of crypts with goblet cells, multilayered epithelium, and mucosal gland type (area under the curve, 0.71; 95 percent confidence interval, 0.66–0.76). Patients with an irregular Z-line were histologically similar to those with CLE. Certain histologic features in biopsies of the SCJ are associated with the presence of CLE. Irregularity of the Z-line is probably indicative of ultrashort segment CLE instead of being a potential variation of normal.

Soucy G, Onstad L, Vaughan TL, et al. Histologic features associated with columnar-lined esophagus in distal esophageal and gastroesophageal junction (GEJ) biopsies from GERD patients: a community-based population study. Am J Surg Pathol. 2016;40(6):827–835.

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Significance of Paneth cells in histologically unremarkable rectal mucosa

Paneth cell metaplasia of the rectal epithelium is a common histologic finding in patients with chronic inflammatory bowel disease. However, the clinical significance of isolated Paneth cells in otherwise unremarkable rectal mucosa

has not been examined extensively. The authors conducted a study in which they assessed the frequency and clinical correlates of rectal Paneth cells in 245 biopsies obtained from patients between the ages of two weeks and 20 years in a pediatric tertiary care facility from 2010 to 2011. The specimens comprised 193 endoscopic pinch biopsies and 52 rectal suction biopsies. All 245 cases were endoscopically and histologically unremarkable and did not have prominence of eosinophils, altered mucosal architecture, or inflammation. Paneth cells were present in 42 (17.1 percent) cases, which is higher than previous reports. Only one of 42 patients with rectal Paneth cells was subsequently diagnosed with Crohn disease. In the authors' study population, the finding of Paneth cells was associated with young age, and the incidence of Paneth cell cases decreased with increasing age (χ²=13.69; *P*=.0002). Constipation was the most common presenting symptom in patients with rectal Paneth cells and was highly associated with their presence (odds ratio, 4.5; 95 percent confidence interval, 2.2–9.0). The authors concluded that Paneth cells in otherwise unremarkable pediatric rectal biopsies frequently occur in common conditions, such as idiopathic constipation.

Pezhouh MK, Cheng E, Weinberg AG, et al. Significance of Paneth cells in histologically unremarkable rectal mucosa. *Am J Surg Pathol.* 2016;40:968–971.

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MicroRNA expression profile related to lymph node status in endometrial cancer

Conventional methods for the histologic classification and grading of endometrial cancer are not sufficient to predict lymph node metastases. MicroRNA signatures recently have been related to the pathologic characteristics or prognosis for endometrial cancer (EC). The authors conducted a study to evaluate whether microRNA profiles of grade 1–2 endometrioid adenocarcinomas can be related to nodal status and used as a tool to adapt surgical staging in early stage EC. MicroRNA expression was assessed in nine formalin-fixed, paraffin-embedded EC primary tumors with positive lymph node and in 27 formalin-fixed, paraffin-embedded EC primary tumors with negative lymph node, matched for grade, stage, and lymphovascular space involvement status. A microarray analysis showed a more than twofold significant difference in the expression of 12 microRNAs between the two groups. A quantitative RT-PCR assay was used to confirm these results. The expression levels of five microRNAs—microRNA-34c-5p, -375, -184, -34c-3p, and -34b-5p—were significantly lower in the EC primary tumors with positive lymph node compared with those with negative lymph node. A minimal P-value approach revealed that women with a microRNA-375-fold change of less than 0.30 were more likely to have positive lymph node (n=8; 53.3 percent) compared with those with a microRNA-375-fold change greater than 0.30 (n=1; 4.8 percent; P=.001). Furthermore, women with a microRNA-184-fold change of less than 0.30 were more likely to have positive lymph node (n=6; 60 percent) compared with those with a microRNA-184-fold change greater than 0.30 (n=3; 11.5 percent; P=.006). This microRNA expression profile provides a potential basis for further study of the microRNA function in EC and could be used as a diagnostic tool for nodal status.

Canlorbe G, Wang Z, Laas E, et al. Identification of microRNA expression profile related to lymph node status in women with early-stage grade 1–2 endometrial cancer. *Mod Pathol.* 2016;29:391–401.

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Plasma cells in melanoma: prognostic significance and possible role of IgA

Melanoma is not only one of the most immunogenic cancers but also one of the cancers most effective at subverting host immunity. The role of T lymphocytes in tumor immunity has been extensively studied in

melanoma, whereas less is known about the importance of B lymphocytes. The effects of plasma cells, in particular, are still obscure. The authors conducted a study to characterize the pathological features and clinical outcome of primary cutaneous melanomas associated with plasma cells. Moreover, they investigated the origins of the melanoma-associated plasma cells. Finally, they studied the outcome of patients with primary melanomas with plasma cells. The authors reviewed 710 melanomas to correlate the presence of plasma cells with histological prognostic markers. Immunohistochemistry for CD138 and heavy and light chains was performed in primary melanomas and locoregional lymph nodes, both metastatic and nonmetastatic. In three primary melanomas and nine lymph nodes with frozen material, VDJ (variable, diversity, joining) rearrangement was analyzed by GeneScan analysis. Survival analysis was performed on a group of 85 primary melanomas greater than 2 mm in thickness. Forty-one (3.7 percent) cases showed clusters or sheets of plasma cells. Plasma cell-rich melanomas occurred at an older age and were thicker, more often ulcerated, and more mitotically active (P<.05). Plasma cells were polyclonal and often expressed IgA in addition to IgG. In lymph nodes, clusters or sheets of IgA+ plasma cells were found in the sinuses and subcapsular areas. Analysis of VDJ rearrangements showed the IgA to be oligoclonal. Subjects with melanomas with clusters or sheets of plasma cells had a significantly worse survival rate compared to those with melanomas without plasma cells, while, interestingly, melanomas with sparse plasma cells were associated with a better clinical outcome (P=.002). The authors concluded that melanomas with sheets or clusters of plasma cells are associated with worse prognosis. IgG and IgA are the isotypes predominantly produced by these cells. IgA oligoclonality suggests an antigen-driven response that facilitates melanoma progression by a hitherto unknown mechanism.

Bosisio FM, Wilmott JS, Volders N, et al. Plasma cells in primary melanoma. Prognostic significance and possible role of IgA. *Mod Pathol.* 2016;29:347–358.

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Human epidermal growth factor receptor 2 testing in invasive breast cancer

The recent American Society of Clinical Oncology/College of American Pathologists guidelines for human epidermal growth factor receptor 2 testing in breast cancer recommend repeat testing based on tumor grade, tumor type, and hormone receptor status. The authors conducted a study to test the value of these criteria. Human epidermal growth factor receptor 2 (HER2) status was concordant in the core biopsies and excision specimens in 392 of 400 invasive carcinomas. The major reasons for discordance were amplification around the cutoff for positivity and tumor heterogeneity. Of 116 grade 3 carcinomas that were HER2 negative in the core biopsy, four were HER2 positive in the excision specimen. Three of these four showed borderline negative amplification in the core biopsy or were heterogeneous. None of the 55 grade 1 carcinomas were HER2 positive. Review of repeat testing of HER2 in routine practice suggested that it also may be of value for multifocal tumors and if recommended by the person assessing the in situ hybridization. The authors concluded that mandatory repeat HER2 testing of grade 3 HER2-negative carcinomas is not appropriate. This is particularly true if repeat testing is performed after borderline negative amplification in the core biopsy or in HER2-negative heterogeneous carcinomas.

Rakha EA, Pigera M, Shin SJ, et al. Human epidermal growth factor receptor 2 testing in invasive breast cancer: should histological grade, type and oestrogen receptor status influence the decision to repeat testing? *Histopathology.* 2016;69:20–24.

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