

Anatomic Pathology Selected Abstracts, 3/14

Anatomic pathology abstracts editors: Michael Cibull, MD, professor of pathology, University of Kentucky, Lexington; Rouzan Karabakhtsian, MD, attending pathologist, Department of Pathology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY; Thomas Cibull, MD, dermatopathologist, Evanston Hospital, NorthShore University HealthSystem, Evanston, Ill.; and Rachel Stewart, DO, resident physician, Department of Pathology and Laboratory Medicine, University of Kentucky.

Use of morphological parameters of LN in stereotactic 11-gauge vacuum-assisted needle core biopsy

Management of lobular in situ neoplasia when diagnosed on core biopsy remains controversial. The authors conducted a study to investigate the association between morphological parameters of lobular in situ neoplasia (LN) on vacuum-assisted needle core biopsy (VANCb) and the presence of malignancy (ductal carcinoma in situ, pleomorphic lobular carcinoma in situ, or invasive carcinoma) at surgical excision. The study included 14 pathology departments in Italy. Available slides from 859 cases of VANCb reporting an original diagnosis of flat epithelial atypia, atypical ductal hyperplasia, or LN, all with subsequent surgical excision, were reviewed. Overall, 286 cases of LN, pure or associated with other lesions, were identified, and a malignant outcome was reported at excision for 51 cases (17.8 percent). Among the 149 cases of pure LN, an increased risk of malignancy emerged in women in mammographic categories R4–R5 as compared with those in categories R2–R3 (OR, 2.46; $P=0.048$). In the series, a statistically significant decreased malignancy risk emerged among cases without determinant microcalcifications ($P=0.04$). The authors concluded that their results suggest that the diagnosis of pure LN on VANCb warrants followup excision because clinicopathological parameters do not allow the prediction of which cases will present carcinoma at surgical excision.

Bianchi S, Bendinelli B, Castellano I, et al; for VANCb Study Group. Morphological parameters of lobular in situ neoplasia in stereotactic 11-gauge vacuum-assisted needle core biopsy do not predict the presence of malignancy on subsequent surgical excision. *Histopathology*. 2013;63:83–95.

Correspondence: S. Bianchi at simonetta.bianchi@unifi.it

Outcome of pure MLL without atypia diagnosed on needle core biopsy

Guidelines recommend that mucocoele-like lesions of the breast diagnosed on needle core biopsy be categorized as a lesion of uncertain malignant potential (B3). However, data on the outcome of mucocoele-like lesions (MLL) diagnosed on needle core biopsy remain limited due to the rarity of the lesion. The authors conducted a study to assess the outcome of pure MLL without atypia diagnosed on needle core biopsy using a large series of cases and a review of the literature to provide evidence that can guide management. Patients who underwent diagnostic excision biopsy after a core biopsy diagnosis of MLL without atypia were identified from several medical centers. Two of 54 patients (four percent) with MLL without atypia on core biopsy had ductal carcinoma in situ in the subsequent excision specimen. This is similar to the rate in previous studies (four percent; four of 106). Previous studies found that when there is atypia in the core biopsy, the frequency of malignancy is much higher (21 percent; seven of 33). The authors concluded that their results provide evidence that pure MLL without atypia diagnosed on needle core biopsy is usually associated with a benign outcome.

Rakha EA, Shaaban AM, Haider SA, et al. Outcome of pure mucocoele-like lesions diagnosed on breast core biopsy. *Histopathology*. 2013;62:894–898.

Correspondence: E. A. Rakha at emadrakha@yahoo.com

Perineural invasion in T1 oral squamous cell carcinoma and aggressive elective neck dissection

Observation versus elective neck dissection for cN0 neck is controversial for the treatment of T1-2 oral squamous cell carcinoma (OSCC). Perineural invasion has been recognized as a poor prognostic factor for OSCC. However, its significance in T1 OSCC remains unclear. A detailed histologic re-evaluation of perineural invasion was carried out in 307 patients with T1-2 OSCC who underwent surgical treatment between June 2001 and January 2009. The authors found that perineural invasion correlated with cervical lymph node metastasis in T1 and T2 OSCC, with a lower perineural invasion-positive rate in T1 (17.1 percent versus 36.6 percent; $P < 0.001$). Importantly, observation for cN0 neck was used twice as often in T1 as in T2 patients (47.4 percent versus 22.8 percent; $P < 0.001$). Although patients with T1 OSCC achieved significantly better outcomes, perineural invasion correlated with neck recurrence and poor disease-specific survival in T1 (P

Tai SK, Li WY, Yang MH, et al. Perineural invasion in T1 oral squamous cell carcinoma indicates the need for aggressive elective neck dissection. *Am J Surg Pathol*. 2013;37(8):1164-1172.

Correspondence: S. K. Tai at sktai@vghtpe.gov.tw

Atypical Spitz tumors with chromosomal copy number aberrations and conventional melanomas in children

Death due to melanoma in childhood (up to 20 years of age) is a rare event, with an average of 18 cases reported annually in the United States. In this study, the authors evaluated two subgroups of high-risk melanocytic neoplasms in childhood, specifically atypical Spitz tumors with chromosomal copy number changes and conventional melanomas. They analyzed the clinical, histologic, and molecular features of all cases and performed the Fisher exact test, logistic regression, and multivariate analysis to evaluate features associated with aggressive clinical behavior in these cases. Among the atypical Spitz tumors, all of which had one or more chromosomal copy number aberrations, the presence of homozygous 9p21 deletions and a positive sentinel lymph node were found to be correlated with tumor extension beyond the sentinel lymph node ($P = 0.046$ and 0.01 , respectively). Two patients with atypical Spitz tumors that had homozygous 9p21 deletions developed brain metastasis, and one died of disease. Among the 21 patients with conventional melanomas, three patients developed distant metastasis and died of disease. Chromosomal copy number aberrations evaluated by fluorescence in situ hybridization were present in the majority of the cases (16 of the remaining 18). Among the conventional melanomas, the authors did not identify any clinical, histologic, or molecular features associated with aggressive behavior. The presence of 8q24 gains was seen almost exclusively in six amelanotic small cell melanomas in children, one of whom died of disease. The authors concluded that characteristic chromosomal copy number aberrations may occur in specific subtypes of melanocytic neoplasms in children and may help with the classification and prognostication of these rare tumors.

Gerami P, Cooper C, Bajaj S, et al. Outcomes of atypical Spitz tumors with chromosomal copy number aberrations and conventional melanomas in children. *Am J Surg Pathol*. 2013; 37:1387-1394.

Correspondence e-mail address not provided.

Value of methylene blue-assisted lymph node dissection technique in colorectal cancer cases

Lymph node staging is of paramount importance for estimating prognosis and stratifying therapy for colorectal cancer. A high number of harvested lymph nodes is associated with improved outcome. Methylene blue-assisted lymph node dissection improves the lymph node harvest and ensures sufficient staging. The authors investigated the effect of the advanced lymph node dissection technique on node positivity rate and stage-related outcome. The study cohort consisted of 669 colorectal cancer cases of all stages with advanced lymph node dissection

collected between 2007 and 2012. A historical collection of 663 cases investigated with conventional techniques between 2002 and 2004 served as the control. The authors found that lymph node harvest was dramatically improved in the study group, with mean lymph node numbers of 34 ± 17 versus 13 ± 5 ($P < 0.001$) and sufficient staging rates of 98 percent versus 62 percent ($P < 0.001$). However, neither the rate of nodal positive cases (37 percent versus 37 percent; $P = 0.98$) nor N2 cases differed between the two groups (14 percent versus 13 percent; $P = 0.80$). Furthermore, no differences in outcome were noted between the groups. The authors concluded that the advanced lymph node dissection technique guarantees adequate histopathological lymph node staging in virtually all cases of colorectal cancer and is, therefore, extremely helpful. However, the hypothesis that it also provides a higher sensitivity in detecting metastases could not be proved.

Märkl B, Schaller T, Krammer I, et al. Methylene blue-assisted lymph node dissection technique is not associated with an increased detection of lymph node metastases in colorectal cancer. *Mod Pathol*. 2013;26:1246-1254.

Correspondence: Dr. B. Märkl at bruno.maerkl@klinikum-augsburg.de

Use of TP53 and CDKN2A to distinguish ovarian high-grade serous carcinoma from low-grade serous ovarian tumors

Low-grade serous carcinomas and serous borderline tumors, jointly referred to as low-grade serous tumors herein, show distinct molecular alterations and clinical behaviors compared with high-grade serous carcinomas. Differentiating between low-grade serous tumors and high-grade serous carcinomas using small tissue samples, such as cell blocks of paracentesis fluid or biopsies from omental disease, can be challenging. The authors conducted a study to test the ability of TP53 and CDKN2A immunohistochemistry to distinguish between high-grade serous carcinomas and low-grade serous tumors on small tissue samples. Tissue microarrays containing 582 high-grade serous carcinomas, 45 low-grade serous carcinomas, and 49 serous borderline tumors confirmed by contemporary histopathological review were stained for TP53 and CDKN2A (DO7 and E6H4 antibody clones, respectively). TP53 was scored as completely absent, wild-type pattern, or overexpressed (more than 60 percent). CDKN2A was scored as negative/patchy (fewer than 90 percent) or block expression (more than 90 percent). The combination of TP53 wild-type pattern and CDKN2A patchy expression had sensitivity for low-grade serous tumors of 89 percent, specificity of 93 percent, positive predictive value of 68 percent, and negative predictive value of 98 percent. The authors concluded that these markers can be used on small biopsies or cell blocks to refute a diagnosis of low-grade serous tumors. These findings may influence emerging neoadjuvant therapeutic strategies in advanced ovarian cancers and may be crucial to future clinical trials on molecular-based therapies.

Altman AD, Nelson GS, Ghatage P, et al. The diagnostic utility of TP53 and CDKN2A to distinguish ovarian high-grade serous carcinoma from low-grade serous ovarian tumors. *Mod Pathol*. 2013;26(9):1255-1263.

Correspondence: Dr. M. Köbel at martin.koebel@cls.ab.ca

Use of immunohistochemical stains for CD3 and CD8 in detecting gluten-sensitive enteropathy in duodenal biopsies

Patients with gluten-sensitive enteropathy usually have increased numbers of duodenal intraepithelial lymphocytes, even if the villous architecture is normal. Some authors advocate the use of CD8 and CD3 immunohistochemical stains to improve detection of intraepithelial lymphocytosis, yet the added value of immunohistochemistry when biopsies appear normal remains unproven. The authors conducted a study to evaluate the utility of CD3 and CD8 immunostains in detecting intraepithelial lymphocytosis among duodenal biopsies originally interpreted to be normal based on routine evaluation. They identified 200 duodenal biopsies from 172 patients, all of which were accompanied by a clinical question of gluten-sensitive enteropathy. Five well-oriented villi from each biopsy were assessed. Intraepithelial lymphocytes present in hematoxylin-and-eosin-stained slides were counted and compared with the number of CD3 and CD8 immunopositive cells present in the villous epithelium. Results were expressed as the mean number of intraepithelial lymphocytes or

immunopositive cells present per 20 villous tip enterocytes. Review of H&E-stained slides revealed a mean of 2.1 ± 0.1 intraepithelial lymphocytes, compared with 3.2 ± 0.1 CD3-positive and 2.1 ± 0.1 CD8-positive intraepithelial cells (P=

Hudacko R, Kathy Zho X, Yantiss RK. Immunohistochemical stains for CD3 and CD8 do not improve detection of gluten-sensitive enteropathy in duodenal biopsies. *Mod Pathol*. 2013;26:1241-1245.

Correspondence: Dr. R. K. Yantiss at rhy2001@med.cornell.edu