Anatomic Pathology Selected Abstracts, 5/14

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.

Impact of operator techniques and specimen-preparation checklist on bone marrow assessment

Successful bone marrow assessment is essential to the diagnosis and staging of hematologic malignancies. The authors conducted a study to determine whether specific operator techniques or use of a specimen-preparation checklist, or both, could impact the quality of bone marrow assessment by reducing the frequency of obtaining nonspicular aspirates, small cores, and nondiagnostic samples. All bone marrow biopsies performed at the Dana-Farber Cancer Institute from April 2012 to September 2012 were eligible for inclusion in the study. Six operator techniques were linked with specimen quality in a preintervention cohort. Next, a specimen-preparation checklist was implemented, and outcomes were compared from the preintervention and postintervention cohorts. In total, 830 procedures performed by 41 operators were prospectively observed and analyzed. In the preintervention cohort (n=413), no operator technique was associated with specimen quality in multivariable models accounting for patient characteristics and operator. Compared with the preintervention cohort, in multivariable analyses, the postintervention cohort (n=417) had decreased odds of nondiagnostic specimens (odds ratio, 0.49; 95 percent confidence interval [CI], 0.28–0.87; P=0.01) and core lengths of 1 cm or less (odds ratio, 0.67; 95 percent CI, 0.50–0.90; P=0.009), but there was no significant difference in spicularity. The authors concluded that variation in the operator techniques studied did not influence specimen quality, but implementation of a specimen-preparation checklist significantly improved core length and the frequency of obtaining diagnostic samples.

Odejide OO, Cronin AM, DeAngelo DJ, et al. Improving the quality of bone marrow assessment: impact of operator techniques and use of a specimen preparation checklist. *Cancer.* 2013;119:3472–3478.

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Basal cell carcinoma of the anal region compared with basaloid squamous cell carcinoma

Basal cell carcinoma of the anal region is rare and morphologically difficult to distinguish from basaloid squamous cell carcinoma, particularly on biopsies. The distinction has therapeutic and prognostic implications. The authors reviewed morphological features of nine basal cell carcinomas and 15 basaloid squamous cell carcinomas from the anal region diagnosed from 1993 to 2011. They then determined the utility of Ber-EP4, BCL2, TP63, CK5/6, CDKN2A, and SOX2 as diagnostic tools. Immunostains were scored in a semi-quantitative manner (1+, one to 10 percent; 2+, 11 to 50 percent; 3+, more than 50 percent). All basal cell carcinomas were located in the perianal region, while all basaloid squamous cell carcinomas originated in the anal canal or anorectum. Nodular subtype of basal cell carcinoma was the most common subtype. Retraction artifact was the only significant distinguishing histological feature of basal cell carcinoma compared with basaloid squamous cell carcinoma (88 percent versus 26 percent; P=0.04). Atypical mitoses were more common in basaloid squamous cell carcinomas (71 percent versus 11 percent; P=0.05). An in situ component was present only in basaloid squamous cell carcinomas and was noted in six of 15 cases. Basal cell carcinomas had 2–3+ Ber-EP4 (basal cell carcinoma 100 percent versus basaloid squamous cell carcinoma 40 percent; P<0.001) and BCL2 immunoreactivity (basal cell carcinomas 100 percent versus basaloid squamous cell carcinoma 33 percent; P<0.001). Diffuse CDKN2A and SOX2 expression was seen only in basaloid squamous cell carcinomas (basal cell carcinoma zero versus basaloid squamous cell carcinoma 93 percent; P<0.001). No difference in TP63 and CK5/6 expression was found. Perianal location, retraction artifact,

and lack of atypical mitoses are histological features that help distinguish basal cell carcinoma from basaloid squamous cell carcinoma. An in situ component supports the diagnosis of basaloid squamous cell carcinoma. Immunostains are extremely helpful as diffuse Ber-EP4 and BCL2 expression is a feature of basal cell carcinoma, and basaloid squamous cell carcinoma is typified by diffuse CDKN2A and SOX2 expression.

Patil DT, Goldblum JR, Billings SD. Clinicopathological analysis of basal cell carcinoma of the anal region and its distinction from basaloid squamous cell carcinoma. *Mod Pathol.* 2013;26:1382–1389.

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Reproducibility of histological cell type in high-grade endometrial carcinoma

Subclassifying endometrial carcinoma according to histological type shows variable interobserver agreement. The authors conducted a study to assess the interobserver agreement of histological type in high-grade endometrial carcinomas recorded by gynecological pathologists from five academic centers across Canada. A secondary aim of the study was to assess the agreement of consensus diagnosis with immunohistochemical marker combinations, including six routine (TP53, CDKN2A [p16], estrogen receptor [ER], progesterone receptor [PGR], Ki67, and VIM) and six experimental (PTEN, ARID1A, CTNNB1, IGF2BP3, HNF1B, and TFF3) immunohistochemical markers. The paired interobserver agreement ranged from κ 0.50 to 0.63 (median, 0.58) and the intraobserver agreement from κ 0.49 to 0.67 (median, 0.61). Consensus about histological type based on morphological assessment was reached in 72 percent of high-grade endometrial carcinomas. A seven-marker immunohistochemical panel differentiated FIGO grade 3 endometrioid from serous carcinoma with a 100 percent concordance rate compared with the consensus diagnosis. More practically, a three-marker panel including TP53, ER, and CDKN2A (p16) can aid in differentiating FIGO grade 3 endometrioid from endometrial serous carcinoma. The authors concluded that their study demonstrates that the inter- and intraobserver reproducibility of histological type based on morphology alone is mostly moderate. Ancillary techniques, such as immunohistochemical marker panels, are likely needed to improve the diagnostic reproducibility of histological types within high-grade endometrial carcinomas.

Han G, Sidhu D, Duggan MA, et al. Reproducibility of histological cell type in high-grade endometrial carcinoma. *Mod Pathol.* 2013;26:1594–1604.

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Basis of the International Society of Urological Pathology Vancouver Classification of Renal Neoplasia

The classification working group of the International Society of Urological Pathology consensus conference on renal neoplasia made recommendations regarding expanding and changing the World Health Organization Classification of Renal Tumors (2004). Members of the group performed an exhaustive literature review, assessed the results of a preconference survey, and participated in a consensus conference discussion and polling activities. On the basis of the input received, the group reached a consensus that five entities should be recognized as new distinct epithelial tumors within the classification system: tubulocystic renal cell carcinoma (RCC), acquired cystic disease-associated RCC, clear cell (tubulo) papillary RCC, the MiT family translocation RCCs (in particular t[6;11] RCC), and hereditary leiomyomatosis RCC syndrome-associated RCC. Three rare carcinomas were considered emerging or provisional new entities: thyroid-like follicular RCC, succinate dehydrogenase B deficiency-associated RCC, and ALK translocation RCC. Additional reports of these entities are required to better understand the nature and behavior of these highly unusual tumors. The working group also introduced a number of new concepts and suggested modifications to the existing World Health Organization 2004 categories. Within the clear cell RCC group, it was agreed upon that multicystic clear cell RCC is best considered a neoplasm of low malignant potential. There was agreement that subtyping of papillary RCC is of value and that the oncocytic variant of papillary RCC should not be considered a distinct entity. The hybrid oncocytic chromophobe tumor, an indolent tumor that occurs in three

settings, namely Birt-Hogg-Dubé syndrome, renal oncocytosis, and as a sporadic neoplasm, was placed, for the time being, in the chromophobe RCC category. Recent advances related to collecting duct carcinoma, renal medullary carcinoma, and mucinous spindle cell and tubular RCC were elucidated. Outside the epithelial category, advances in understanding angiomyolipoma, including the epithelioid and epithelial cystic variants, were considered. In addition, the apparent relationship between cystic nephroma and mixed epithelial and stromal tumor was discussed, with the consensus that these tumors form a spectrum of neoplasia. Finally, it was thought that synovial sarcoma should be removed from the mixed epithelial and mesenchymal category and placed in the sarcoma group. The new classification was deemed the International Society of Urological Pathology Vancouver Classification of Renal Neoplasia.

Srigley JR, Delahunt B, Eble JN, et al; The ISUP Renal Tumor Panel. The International Society of Urological Pathology (ISUP) Vancouver Classification of Renal Neoplasia. *Am J Surg Pathol.* 2013;37(10):1469–1489.

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