Anatomic pathology selected abstracts

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Clinical and histopathologic characteristics of recurrent sarcoidosis in post-transplant lungs

March 2024—Lung transplantation is the definitive therapy for end-stage pulmonary sarcoidosis. While several case reports have described recurrent sarcoidosis in allografts, the incidence and clinicopathologic characteristics remain unclear. The authors conducted a study in which they characterized the clinical and histopathologic features of recurrent sarcoidosis diagnosed in post-transplant lung surveillance transbronchial biopsies (TBBx). They identified 35 patients who underwent lung transplant for pulmonary sarcoidosis during the study period. Eighteen (51 percent) of the patients experienced recurrent sarcoidosis post-transplant—seven females and 11 males (mean age at recurrence, 51.6 years). The average time interval from transplant to recurrence was 252 days (22–984 days). All TBBx contained more than four pieces of alveolated lung tissue with no evidence of International Society for Heart and Lung Transplantation grade A2, A3, or A4 acute cellular rejection; chronic rejection; or antibody-mediated rejection. Thirty-three surveillance TBBx contained granulomatous inflammation, with a mean of 3.6 well-formed granulomas per TBBx (range, 1 to more than 20). Multinucleated giant cells were identified in 11 TBBx, and one of those cases contained asteroid bodies. While most of the granulomas were "naked," five cases showed prominent lymphoid cuffing and two showed evidence of fibrosis. One of the granulomas had focal necrosis. However, no infectious organisms were identified using special stains, and clinical correlation suggested that this case represented recurrent sarcoidosis. Biopsies of recurrent sarcoidosis usually show multiple well-formed granulomas with giant cells in more than half the cases, while lymphoid cuffing, fibrosis, asteroid bodies, and necrotizing granulomas are uncommon findings. The authors concluded that pathologists should be aware of these features, as sarcoidosis recurrence following lung transplant occurs in more than half of patients.

Lu L, Wein AN, Villanueva A, et al. Clinical and histopathologic characteristics of recurrent sarcoidosis in posttransplant lungs: 25 years of experience. *Am J Surg Pathol*. 2023;47(9):1034–1038.

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Utility of nuclear β-catenin expression patterns in determining the histotype of p53-abnormal endometrial carcinomas

Interobserver reproducibility is poor for histotyping within the p53-abnormal molecular category of endometrial carcinomas. Therefore, biomarkers that improve histologic classification are useful. β-catenin has been proposed to have prognostic significance in specific clinicopathologic and molecular contexts. The diagnostic utility of β-catenin expression patterns in determining the histotype of p53-abnormal endometrial carcinomas (ECs) has not been well studied. The authors identified ECs molecularly classified as p53 abnormal. The p53-abnormal classification was assigned when no *POLE* exonuclease domain hotspot mutations were identified, mismatch-repair protein expression was retained, and abnormal p53 expression (null or overexpression) was present. Morphology was re-reviewed and β-catenin immunohistochemistry was scored as abnormal (nuclear) or normal (membranous, non-nuclear). Eighty ECs were identified as p53 abnormal—27 (33.75 percent) uterine serous carcinomas and 53 (66.25 percent) nonserous histotype. Of the latter, 28 were uterine carcinosarcomas (35 percent), 16 endometrioid carcinomas (20 percent), two clear cell carcinomas (2.5 percent), and seven high-grade EC with ambiguous morphology (8.75 percent). The 27 uterine serous carcinomas demonstrated membranous β-catenin staining. Of the 53 nonserous ECs, 11 (21 percent) showed abnormal β-catenin expression—six endometrioid carcinomas, four uterine carcinosarcomas, and one high-grade EC with ambiguous morphology. The specificity of abnormal β-

catenin expression for nonserous EC is high (100 percent) but the sensitivity is low (21 percent), with positive and negative predictive values of 100 percent and 60 percent, respectively. The data show that abnormal β-catenin expression in the context of p53-abnormal EC is highly specific but not sensitive for nonserous ECs and may be of value as part of a panel for classifying high-grade EC, particularly for excluding uterine serous carcinoma when nuclear staining is present.

Keyhanian K, Yang EJ, Howitt BE. Nuclear β-catenin expression in the context of abnormal p53 expression indicates a nonserous histotype in endometrial carcinoma. *Int J Gynecol Pathol*. 2023;42(5):435–442.

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Diagnosing usual interstitial pneumonia vs. fibrotic hypersensitivity pneumonitis in transbronchial cryobiopsies

Transbronchial cryobiopsy is increasingly used in diagnosing fibrosing interstitial pneumonias, but there are few detailed descriptions of the pathologic findings in such cases. It has been proposed that a combination of patchy fibrosis and fibroblast foci with an absence of alternative features is diagnostic of usual interstitial pneumonia (UIP), the pathologic pattern of idiopathic pulmonary fibrosis (IPF), in transbronchial cryobiopsy. The authors reviewed 121 transbronchial cryobiopsies in which a diagnosis of fibrotic hypersensitivity pneumonitis (FHP; n=83) or IPF (n=38) was made at a multidisciplinary discussion to determine which pathologic features are found in transbronchial cryobiopsy UIP/IPF and FHP cases and which can be used to separate these entities. Patchy fibrosis was found in 65 of 83 (78 percent) biopsies from FHP and 32 of 38 (84 percent) biopsies from UIP/IPF cases. Fibroblast foci were present in 47 of 83 (57 percent) FHP and 27 of 38 (71 percent) UIP/IPF cases. A combination of fibroblast foci and patchy fibrosis did not favor either diagnosis. Architectural distortion (large blocks of fibrosis that render the underlying lung architecture indiscernible) was found in 54 of 83 (65 percent) FHP and 32 of 38 (84 percent) UIP/IPF cases (odds ratio [OR] for FHP, 0.35; P=.036). Honeycombing (large blocks of fibrosis with spaces lined by bronchiolar epithelium) was present in 18 of 83 (22 percent) and 17 of 38 (45 percent), respectively (OR, 0.37; P=.014). Airspace giant cells/granulomas were present in 13 of 83 (20 percent) FHP and one of 38 (2.6 percent) UIP/IPF cases (OR for FHP, 6.87; P=.068) and interstitial giant cells/granulomas in 20 of 83 (24 percent) FHP and zero of 38 (0 percent) UIP/IPF (OR, 6.7×10^6; P=.000). The authors concluded that patchy fibrosis plus fibroblast foci can be found in transbronchial cryobiopsies from FHP and UIP/IPF. The complete absence of architectural distortion and honeycombing favors a diagnosis of FHP, as does the presence of airspace or interstitial giant cells/granulomas, but these measures are insensitive, and many cases of FHP cannot be separated from UIP/IPF on transbronchial cryobiopsy.

Churg A, Tazelaar H, Matej R, et al. Pathologic criteria for the diagnosis of usual interstitial pneumonia vs fibrotic hypersensitivity pneumonitis in transbronchial cryobiopsies. *Mod Pathol*. 2023. https://doi.org/10.1016/j.modpat.2023.100221

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Pathological features associated with metastasis in early invasive colorectal carcinoma in colorectal polyps

Complete endoscopic resection alone can, in many cases, sufficiently treat colorectal carcinoma arising in a colorectal polyp with invasion limited to the submucosa. Histological features of colorectal carcinoma, including tumor size, vascular invasion, and poor tumor differentiation or evidence of de-differentiation, such as tumor budding, are associated with a higher risk for metastasis, thereby supporting the recommendation for oncological resection. However, most malignant polyps with these features do not have lymph node metastases at the time of resection, necessitating better refinement of the histological risk features. The authors investigated the predictive value of known and potentially novel pathological factors in a cohort of pT1 colorectal carcinomas enriched for those with lymph node metastases and those that underwent endoscopic polypectomy. In the 466-person study group, there were 437 consecutive colorectal polyps with submucosal invasive carcinoma from a single center, 57

of which had metastatic disease, supplemented by 30 cases of known metastatic disease from two additional centers. Clinical and histological features of the polyp cancers were reviewed to determine the differences between 87 cancers that were metastatic and the remaining cases without metastasis. A subgroup of 204 polyps removed intact was also analyzed to ensure maximum histological accuracy. This study confirmed larger invasive tumor size, vascular invasion, and poor tumor differentiation as adverse predictive features. Other prominent adverse features included peritumoral desmoplasia and high cytological grade. A predictive logistic-regression model utilizing the presence of any form of vascular invasion, presence of high tumor budding (BD3), width of invasive tumor component greater than 8 mm, depth of invasive tumor greater than 1.5 mm, and findings of prominent expansile desmoplasia within and beyond the deep invasive edge of the carcinoma showed excellent performance in predicting metastatic disease.

Brown I, Zammit AP, Bettington M. Pathological features associated with metastasis in patients with early invasive (pT1) colorectal carcinoma in colorectal polyps. *Histopathology*. 2023;83(4):591–606.

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Use of Texas Red-filtered microscopy to increase specificity of Congo red stain for amyloid

The diagnosis of amyloidosis via tissue biopsy is traditionally suggested by H&E stain and confirmed by Congo red stain, both of which are used in routine light microscopy. False-positive and false-negative congophilia are well documented, limiting the sensitivity and specificity of Congo red stain for diagnosing amyloidosis. Using Texas Red-filtered fluorescence microscopy (TRFM) to examine Congo red-stained tissue is known to enhance amyloid-specific congophilia, thereby increasing diagnostic sensitivity. The authors conducted a study to determine whether TRFM can mitigate the false positivity seen with light microscopy and thus improve the specificity of Congo red stain in detecting amyloid deposits in histology sections from a variety of tissue types. Ninety-two tissue samples were selected for the study and categorized into three groups. Group one included 15 samples with tissue deposition of amyloid. Group two consisted of 63 samples in which amorphous eosinophilic structures reminiscent of amyloid were seen on H&E-stained tissue sections. Group three included 14 samples in which amyloid and amyloid-like tissue were seen side by side. Clinicopathologic correlation was used to rule in or rule out amyloidosis in each case. The congophilic areas in each case were identified by light microscopy and then examined by TRFM. TRFM confirmed the diagnosis of amyloidosis in all group one cases by enhancing the congophilic areas. Enhancement was not seen in 52 of the 63 group two cases. TRFM enhanced amyloid-specific congophilia, but not nonspecific congophilia, in all group three cases. The authors concluded that TRFM increases the diagnostic yield and specificity of Congo red-stained tissue sections for detecting amyloid.

Shehabeldin A, Hussey C, Aggad R, et al. Increased diagnostic specificity of Congo red stain for amyloid: The potential role of Texas Red–filtered fluorescence microscopy. *Arch Pathol Lab Med*. 2023;147(8):907–915.

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