Anatomic pathology selected abstracts

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Surgical pathology of diffuse parenchymal lung disease in patients with psoriasis or psoriatic arthritis

January 2024—Diffuse parenchymal lung disease is a well-recognized complication of systemic connective tissue disease but rarely arises in patients with psoriasis or psoriatic arthritis, which are poorly understood. Therefore, the authors conducted a study to characterize diffuse parenchymal lung disease (DPLD) associated with psoriasis or psoriatic arthritis, with or without prior immunomodulation. Their pathology consultation files were searched for patients having psoriasis or psoriatic arthritis and DPLD. After excluding cases with active infection or smoking-related DPLD only, 44 patients (22 of whom were women; median age, 60 years; range, 23–81 years) were enrolled in the study. Clinical history and pathology slides were reviewed. Twenty-seven of 44 (61 percent) patients had psoriatic arthritis and the remainder had psoriasis alone. Most presented many years later with nonspecific respiratory symptoms. Nearly one-third had no prior immunosuppression, and most had no concomitant connective tissue disease. Radiographically, ground-glass opacities, consolidation, and/or reticulation were typical. Histologically, nonspecific interstitial pneumonia and unclassifiable fibrosis were seen in 24 (55 percent) patients and eight (18 percent) patients, respectively. Usual interstitial pneumonia and airway-centered fibrosis were rare. Superimposed acute lung injury was common, usually manifesting as organizing pneumonia. Lymphoplasmacytic infiltrates, lymphoid aggregates, and chronic pleuritis were frequent. Interstitial granulomas were seen in 17 (39 percent) patients but were usually rare, poorly formed, and nonnecrotizing. No histologic differences were apparent among patients with or without concomitant connective tissue diseases or prior therapy. The authors concluded that some patients who have psoriasis or psoriatic arthritis developed clinically significant DPLD, even without prior therapy. The histopathologic findings mirrored changes seen with other connective tissue diseases. Additional studies are warranted to clarify the association between psoriasis or psoriatic arthritis and DPLD.

Butt YM, Smith ML, Tazelaar HD, et al. Surgical pathology of diffuse parenchymal lung disease in patients with psoriasis or psoriatic arthritis. *Arch Pathol Lab Med*. 2023;147:525–533.

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Ability of apoptosis, crypt dropout, and IHC to indicate cytomegalovirus infection in IBD patients

Cytomegalovirus colitis superimposed on inflammatory bowel disease can be challenging to diagnose. Therefore, the authors conducted a study to determine which histologic clues and IHC utilization practices, if any, can help diagnose cytomegalovirus (CMV) superinfection in inflammatory bowel disease (IBD). Colon biopsies were reviewed for all patients with CMV colitis with and without IBD between 2010 and 2021 at one institution, as was a separate cohort of IBD patients with negative CMV IHC. Biopsies were assessed for histologic features of activity and chronicity, phlebitis, fibrin thrombi, basal crypt apoptosis, CMV viral cytopathic effect (VCE), and CMV IHC positivity. Features between groups were compared, with statistical significance set at $P < .05$. The study included 251 biopsies from 143 cases—21 CMV only, 44 CMV plus IBD, and 78 IBD only. The CMV plus IBD group was more likely than the IBD-only group to show apoptotic bodies (83 versus 64 percent; $P = .035$) and crypt dropout (75 versus 55 percent; $P = .045$). CMV was detected by IHC in 18 CMV plus IBD cases without VCE on H&E (41 percent). In the 23 CMV plus IBD cases in which IHC was performed on all concurrent biopsies, IHC was positive in at least one biopsy in 22 cases. Six individual CMV plus IBD biopsies with no VCE on H&E demonstrated equivocal IHC staining, five of which had evidence of CMV infection. The authors concluded that IBD patients with superimposed

CMV infection are more likely to demonstrate apoptotic bodies and crypt dropout compared with their noninfected counterparts. Equivocal IHC staining for CMV may indicate true infection in IBD patients, and staining multiple biopsies from the same accession can improve CMV detection.

Ono Y, Gonzalez RS. Apoptosis, crypt dropout, and equivocal immunohistochemical staining may indicate cytomegalovirus infection in inflammatory bowel disease patients. *Am J Surg Pathol*. 2023;47(8):933–941.

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Assessment of HER2 in gastric-type endocervical adenocarcinoma and its prognostic significance

As the most common type of human papillomavirus-independent endocervical adenocarcinoma, gastric-type endocervical adenocarcinoma accounts for approximately 10 percent of all endocervical adenocarcinomas. However, data about HER2 expression and amplification in endocervical adenocarcinoma (ECA), including gastric-type endocervical adenocarcinomas (GEAs), are limited and inconsistent. The limited data regarding HER2 in GEAs and ECAs vary considerably and are likely due to differences in tumor type selection, testing methods, and scoring criteria. The authors conducted a study to systematically investigate HER2 overexpression and amplification in GEAs to set the foundation for eventually developing HER2 scoring recommendations for GEAs. They also examined the prognostic value of HER2 overexpression and amplification and their association with other known and potential prognostic factors. The authors selected 58 GEA cases for the purpose of analyzing HER2 status using IHC and FISH. When strong complete or lateral/basolateral membranous reactivity in 10 percent or more of tumor cells was used to define HER2 positivity, a relatively high prevalence of HER2 overexpression (10 of 58 [17.2 percent]) and amplification (nine of 58 [15.5 percent]) and a high IHC-FISH concordance rate (nine of 10 [90 percent]) were found in GEAs. A lateral/basolateral staining pattern (U shaped) was observed, at least focally, in most HER2-positive (3+) and equivocal (2+) tumors. Considerable heterogeneity of HER2 expression was observed in HER2-positive and equivocal cases (80 and 83.3 percent, respectively). HER2 overexpression and amplification were associated with worse progression-free survival (P=.047 and .032, respectively). Programmed death-ligand 1 expression was also associated with worse progression-free survival (P=.032), whereas mutant-type p53 demonstrated no prognostic significance. The authors concluded that their findings create a solid foundation for the eventual development of a standard HER2-testing guideline for GEAs.

Wang S, Zhou X, Niu S, et al. Assessment of HER2 in gastric-type endocervical adenocarcinoma and its prognostic significance. Mod Pathol. 2023. https://doi.org/10.1016/j.modpat.2023.100148

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Clinical impact of testing for biomarkers in gastric cancer patients

HER2 was the first biomarker for guided therapy registered for clinical use in gastric cancer. Considering the recent approvals of immune checkpoint blockade in gastro-oesophageal cancers, it is increasingly important to test for mismatch repair deficiency (dMMR), Epstein–Barr virus (EBV), and PD-L1 combined positive score (CPS). The authors conducted a study in which they assessed biomarker testing performed in daily clinical practice and its impact on therapeutic choices, with the intent of proposing a practical approach to assessing biomarkers in gastric cancer patients. The study included patients diagnosed with gastric cancer between 2017 and 2021. Biomarker results were retrieved from patients' EMR files. PD-L1 CPS was determined retrospectively on dMMR and EBV-positive (EBV+) tumors. Data on genomic sequencing were analyzed separately. Of 363 patients identified, 45 percent had metastatic disease. At least one biomarker was tested in 335 (92 percent) patients. The prevalence of HER2+, dMMR, and EBV+ tumors was 10 percent (32 of 319), seven percent (20 of 294), and one percent (three of 235), respectively. Of the dMMR and EBV+ tumors, 95 percent had a PD-L1 CPS of five or more. Therapeutic strategy was adjusted in 31 of 55 (56 percent) patients and consisted of anti-HER2 therapies and immune checkpoint blockade in clinical trials. Genomic alterations were found in 44 of 60 (73 percent) of the patients. *TP53* (73 percent) and *PIK3CA* (21 percent) were the most common mutations, followed by *KRAS* (11 percent) and

amplification of the *KRAS* gene (11 percent). The authors concluded that in this real-world cohort, testing for HER2, dMMR, and EBV status affected treatment decisions in 56 percent of patients. Although most dMMR and EBV+ tumors had a PD-L1 CPS of five or more, not all patients with a high probability of treatment response were identified. Based on these results, the authors propose a stepwise diagnostic strategy.

Van der Sluis K, van Sandick JW, van Dieren JM, et al. The clinical impact of testing for biomarkers in gastric cancer patients: a real-world cohort. *Histopathology*. 2023;82(6):826–836.

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Fibrosis progression in nonalcoholic fatty liver disease among people with and without diabetes

Data are limited regarding progression of fibrosis in biopsy-proven nonalcoholic fatty liver disease among people with type 2 diabetes mellitus compared with people without the latter disease. The authors conducted a large, multi-center study to assess the time to fibrosis progression and regression in people with and without type 2 diabetes mellitus (T2DM) who had paired liver biopsies. The study included 447 adult participants (64 percent of whom were female) with nonalcoholic fatty liver disease who had paired liver biopsies more than one year apart. A central pathology committee blinded to clinical data systematically assessed liver histology. The primary outcome was the cumulative incidence of a one-stage or greater increase in fibrosis among participants with T2DM compared with participants without T2DM. The mean age of participants was 50.9 years (standard deviation [SD], 11.5 years) and mean body mass index (calculated as weight in kilograms divided by the square of the height in meters) was 34.7 (SD, 6.3). The median time between biopsies was 3.3 years (interquartile range, 1.8–6.1 years). The authors found that participants with T2DM had a significantly higher cumulative incidence of fibrosis progression at four years (24 versus 20 percent), eight years (60 versus 50 percent), and 12 years (93 versus 76 percent) ($P = .005$). Using a multivariable Cox proportional hazards model adjusted for multiple confounders, T2DM remained an independent predictor of fibrosis progression (adjusted hazard ratio, 1.69; 95 percent confidence interval, 1.17–2.43; $P = .005$). The cumulative incidence of fibrosis regression by one stage or more was similar in participants with and without T2DM ($P = .24$). The authors concluded that fibrosis progressed faster in participants with versus without T2DM and that these findings have important implications for clinical practice and trial design.

Huang DQ, Wilson LA, Behling C, et al. Fibrosis progression rate in biopsy-proven nonalcoholic fatty liver disease among people with diabetes versus people without diabetes: A multicenter study. *Gastroenterology*. 2023;165(2):463–472.

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