been associated with adverse outcomes even in immunocompetent patients, with sepsis. Study objective was to evaluate the association between incidence of CMV reactivation and immune alteration in sepsis-induced immunosuppression in patients with prolonged sepsis.
Methods: Prospective observational study, which included consecutive patients admitted to hospital ICU, with severe sepsis and length of stay > 48 hours. Patients with other causes of immune-suppression and anti-CMV treatment were excluded. Blood samples were collected on enrolment and further weekly until 21 days or death/discharge. Quantification of CMV viremia was done using RT-PCR (qPCR). Markers used to evaluate immune suppression using Flow Cytometry were i) lymphocyte subsets (CD3+,CD19+,CD16+CD56+,CD4+,CD8+ and regulatory T cells - CD25+ CD127-), ii) surface receptor expression of HLA-DR on monocytes, and Programmed Death marker expression (PD-1) on T lymphocyte, iii) Measurement of pro-inflammatory(IL-6,TNF-a,IFN-g) and anti-inflammatory cytokines(IL-4,IL-10) by Cytometric Bead Array (CBA) assay.
Results: A total of 25 CMV IgG positive patients and 11 healthy controls were analyzed. CMV reactivation occurred in 20 patients. Median time for reactivation was 7 days. Patients with CMV reactivation had significant T-cell lymphopenia ($p<0.01$). PD-1 expression on both CD4+ and CD8+ T cells in these patients was markedly elevated as compared to non-reactive group. HLA-DR expression was significantly low on monocytes in all sepsis patients ($p<0.01$) vs healthy controls; however it did not show any significant correlation. Levels of IL-6 showed marked elevation from day 7 while, IL-10 was observed to be significantly higher from day 0 in CMV reactivated group as compared to the CMV non-reactive group of patients.
Conclusion: Our study evidence suggests that monitoring lymphocyte subsets, PD-1expression on T lymphocyte, and levels of IL-6/IL-10 using flow cytometry, may serve as indicators for reactivation of CMV. Individualized immune therapy such as PD-1 receptor blockade drugs can be used to optimize treatment of patients with severe sepsis.

International

False Negative Rate (2%) of Lynch Syndrome Screening Utilizing A Two-Antibody (PMS2/MSH6) Immunohistochemistry Panel: Failure To Detect a Subset of MSH2-Deficient Endometrial Carcinomas.

R. Wood[1], S. Murray[1], S. Offman[1], M. Carter[1]; [1]Pathology, Nova Scotia Health Authority/Dalhousie Medicine, Halifax, Nova Scotia, CANADA|

Introduction/Objective: Lynch syndrome (LS) is an inherited condition caused by defective DNA mismatch repair (MMR), leading to a higher incidence of cancers of multiple sites. Screening for LS is now recommended for new diagnoses of endometrial cancer (EC) using either two- (PMS2, MSH6) or four-antibody (2/4Ab) (PMS2, MSH6, MSH2, MLH1) immunohistochemical (IHC) panels. The 2Ab panel assumes consistent loss of expression of the minor dimer component, PMS2 or MSH6, when the major component, MLH1 or MSH2, respectively, is lost due to mutation. Recent studies have indicated that 2Ab testing may lead to underdiagnosis of MSH2-deficient tumors in cases where MSH6 staining is weak or focal, potentially leading to underdiagnosis of LS.
Methods: We conducted a retrospective study using archived slides for 293 cases of EC (identified via LIS search from 2016-2019) that were screened using the 2Ab panel (expanded to 4Ab when PMS2 or MSH6 were negative). MSH6 expression was reviewed; if weak, focal (less than 10% staining), or both, MSH2 IHC was performed. When a previously undetected loss of MSH2 expression was found, the attending clinician was informed such that referral to medical genetics could be arranged.
Results: Results Overall, 68 (23.2%) tumors were MMR deficient, with 54 (18.4%) showing MLH1/PMS2 loss, 7 (2.4%) with MSH2/MSH6 loss, 2 (0.7%) with isolated PMS2 loss, 4 (1.4%) with isolated MSH6 loss, and 6 (2.0%) with isolated MSH2 loss (i.e. intact but weak/focal MSH6, seen in biopsy and hysterectomy specimens). Interestingly, 1 tumor (1.5%) demonstrated loss of MSH6, MLH1 and PMS2. Two tumors (0.7%) with isolated MSH2 loss were previously unrecognized as MMR-deficient and hence at high risk for LS. Both cases were evaluated by PCR for microsatellite instability (MSI) and confirmed to have high-degree MSI.
Conclusion: This study identifies the frequency of mismatch repair deficient endometrial cancers in Atlantic Canada, highlights a potential pitfall of using two-stain IHC screening for Lynch syndrome, and supports emerging recommendations for universal Lynch syndrome screening in EC.

Importance of the Second Opinion in Surgical Breast Pathology and Its Therapeutic Implications

A. Ibarra[1], K. Baksai[1], M. Vial[1]; [1]Pathology, Clinica las Condes, Santiago, CHILE|

Introduction/Objective: Histopathological diagnosis determines surgical management and complementary therapies in patients with breast cancer. There has been reported significant diagnostic divergences, between 7.8 and 26%, and in tumor markers between 3.4 and 41%. We evaluate the agreement between diagnoses of general

DOI: 10.1093/ajcp/aqaa161

pathologists and specialists of our center, in which serious discrepancies could have therapeutic repercussions.
Methods: Method: A retrospective study from 2012 to 2019. The cases were classified in benign and malignant. The atypical lesions were included with benign. Major disagreements were considered when there was a change in diagnosis from benign to malignant or vice versa, variation from intraepithelial to microinvasive carcinomas, infiltrating to intraductal carcinomas or vice versa. When necessary, we repeat routine stains and/or immunostains, or add new immunostains.
Material: 295 cases. 294 women and 1 man. 228 biopsies and 67 immunostains of prognostic-predictive factors.
Results: We found diagnostic differences in 46/295 cases (15.6%). Major discrepancies in 32 cases (10.8%). In morphological diagnoses 11/228 (4.8%) and in immunodeterminations 20/67 (29.9%). In diagnostic changes, they highlighted 3 cases of ductal carcinoma in situ (DCIS) to benign, 2 cases of benign lesions to DCIS, 1 benign to invasive ductal carcinoma (IDC), 1 DCIS to IDC and 1 IDC to DCIS.
Conclusion: We found serious diagnostic divergences in 32 of 295 cases, 10.8%, which could have varied the therapeutic approach. In morphological interpretation 4.8% and in immunohistochemical results 29.9%. This should motivate multidisciplinary teams to routinely use the second opinion in surgical breast disease

Evaluation of Renal Biopsy for Transplant: The Significance of Whole Slide Imaging (WSI) in Telepathology

S. Sonawane[1], E. Borys[1], D. Borys[1], M. Picken[1]; [1]Pathology, LUMC, Lombard, Illinois, UNITED STATES|

Introduction/Objective: Percutaneous Renal biopsy remains a gold standard technique to provide diagnostic and prognostic information post kidney transplantation. Recently Whole slide imaging (WSI) telepathology systems have been widely used for clinical, education and research purposes. Our aim was to examine reliability and accuracy of WSI telepathology service in the pathology diagnosis of biopsy specimens from transplanted kidney.
Methods: At our institution we have two renal pathologists. They utilize WSI telepathology service with Aperio scanner for rapid initial assessment of the transplant renal biopsy specimens. We retrospectively reviewed reports of all transplant renal biopsies which were examined remotely utilizing WSI telepathology service and compared the results for initial versus final diagnoses.
Results: In period from Jan 2019 to April 2020 total 160 renal transplant biopsies were evaluated remotely utilizing the WSI scanner. The diagnosis was divided in 4 subcategories as reperfusion injury, rejection (Antibody mediated or T cell mediated), mixed inflammation-favor infection and Polyoma virus infection. There were 48 cases of reperfusion injury; 5 cases of polyoma virus infection, 37 cases of rejection and 28 cases with mixed inflammation and 42 cases with no significant histopathologic findings. There was no discrepancy between the preliminary and final diagnosis for all 160 cases. The ancillary studies including special stains and electron microscopy added to the final diagnosis or confirmed the preliminary diagnosis.
Conclusion: WSI telepathology is a reliable and simple method to rapidly review transplant kidney biopsies. The ability to transmit images from hospitals to pathologists with WSI scanner has the potential for not only an accurate assessment of the rejection but also for additional histopathological findings. Digital pathology enhances the clinical usefulness of immediate assessments of transplant biopsy samples and also provides a platform to share the scanned images with clinicians which also can be utilized for education of trainees.

Mesenteric Cysts: A Retrospective Review. Its Not All That Simple

M. Bourgeau[1], V. Avadhani[1]; [1]Pathology, Emory University, Atlanta, Georgia, UNITED STATES|

Introduction/Objective: Mesenteric cysts are rare intra-abdominal lesions in adults. However, with the advanced imaging techniques and laparoscopic techniques, they are more often being identified and resected when clinically significant. There is a lack of detailed information in histopathology (except as case reports) since mesentery is generally neglected in our organ-based textbooks. The aim of our study is to highlight the importance of identifying and classifying mesenteric cystic lesions; they are not all that simple.
Methods: We performed a retrospective search on all mesenteric cysts submitted as excisions in our electronic database from 2013-2019. We classified them as per the de Perrot (PMID: 11053936) classification with modification.
Results: Our search showed: A. Lymphatic origin-11 (lymphangioma-10, Lymphangioma hamartomatous-1, associated with LAM-0), B. Mesothelial origin-68 (Benign mesothelial cysts-57, multilocular mesothelial cyst-11), C. Enteric origin- 3, D. Urogenital origin (Urachal cyst, mullerian inclusion cyst)-9, E. Mature cystic teratom-2, F. Pseudocyst-12, G. Epithelial cyst (not urogenital)- 11 (a/w LAMN-3, MCN-4, Mucinous cystadenoma-4), H. Associated with carcinoma-2.
Case illustration: A 61-year-old male presented with worsening dysphagia, emesis and hiccups. A CT scan

DOI: 10.1093/ajcp/aqaa161

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