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1170. CSF HSV PCR Testing in Adults and Children with Meningitis and Encephalitis

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Background. Herpes simplex virus (HSV) is a common treatable cause of meningitis and encephalitis. Delayed antiviral therapy is associated with worse clinical outcomes in HSV encephalitis.

Objectives. To determine the utilization of a cerebrospinal fluid (CSF) HSV polymerase chain reaction (PCR) and identify predictors for a positive HSV PCR result.

Methods. A retrospective review of 751 adults and children with meningitis and encephalitis at 9 hospitals in Houston TX from January 1 2005 to December 31 2010.

Results. Of 751 patients, 331 (44%) underwent CSF HSV PCR testing. Adults were more commonly tested than children (84% vs. 69%, P < 0.0001). Additionally, patients with more comorbidities and clinical findings of encephalitis (e.g., altered mental status, focal neurological findings, seizures) were more commonly tested for HSV (P < 0.001). Patients tested for HSV were also more likely to be evaluated for West Nile Virus, receive empiric acyclovir and have worse outcomes (P < 0.001). In total, 48 of 331 (14.5%) patients tested had a positive CSF HSV PCR. Predictors for a positive CSF HSV PCR on logistic regression analysis were stiff neck (odds ratio [OR], 2.181 [1.090–4.366]; P = 0.028, lymphocytic pleocytosis >50% lymphocytes (OR, 6.187 [1.412–27.11] P = 0.016, and CSF protein >100mg/dl (OR, 3.279 [1.105–9.731] P = 0.032.

Conclusion. CSF HSV PCR is underutilized in community acquired meningitis and encephalitis and is done more frequently in adults and in those with an encephalitis presentation.

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1171. The Expression of hsp-miRNA-200b-3p and -200c-3p in Human Cytomegalovirus-infected Formalin-Fixed, Paraffin-Embedded Tissues

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Background. Human cytomegalovirus (HCMV), which exist as asymptomatic latent status, can cause the tissue invasive disease through reactivation in various immunocompromised conditions. Hsp-microRNA has a specific function of post transcriptional suppression through binding with 3' untranslated region (UTR) of mRNA. In previous study, hsp-miR-200b-3p and -200c-3p had high probability of conjugation with 3'UTR of mRNA encoded by HCMV UL 122–123 region, which translate the immediate early protein 2 (IE2) protein. IE2 (pp86) plays an essential role to initiate and regulate viral early (E) gene activation as well as propagate the subsequent steps of HCMV lytic replication. This study was aimed to evaluate whether HCMV-infected tissue had a lower expression level of hsp-miR-200b-3p and -200c-3p.

Methods. We had collected the formalin-fixed, paraffin-embedded tissues (FFPEs) with cytopathic pathologic findings as well as positive immunohistochemical stain (IHC) test for HCMV (N = 111). The HCMV-uninfected normal tissues (N = 77) were selected among FFPEs with neither infection nor inflammation as well as negative HCMV IHC test. We performed TaqMan MicroRNA real-time RT-PCR to measure the expression levels of hsp-miR-200b-3p and -200c-3p and TaqMan[®] real-time PCR for HCMV UL83 region to measure HCMV viral load in each FFPE. We utilized the standard curves consisting of mirVanaTM miRNA mimics corresponding to each of two miRNAs, ranging from 10⁶ to 10¹ copies/μL and HCMV NIBSC 09/162 strain, ranging from 5 X 10⁶ to 5 X 10¹ IU/mL.

Results. The levels of hsp-miR-200b-3p and -200c-3p were strongly correlated with r=0.844 (P < 0.001). The expressions levels of hsp-miR-200b-3p in HCMV-infected FFPEs (\log_{10} 3.50 ± 0.13 copies/μL) were significantly lower than normal tissues (\log_{10} 5.24 ± 0.12 copies/μL of input RNA, P < 0.001). Also, HCMV-infected FFPEs were significantly lower levels of hsp-miR-200c-3p compared than normal tissues (\log_{10} 5.28 ± 0.18 vs. 7.81 ± 0.11 copies/μL of input RNA, P = 0.025). The levels of miR-200b-3p and -200c-3p had the significant inverse correlation with HCMV VL (200b-3p, spearman r=-0.392, P < 0.001 and 200c-3p, spearman r=-0.355, P < 0.001).

Conclusion. The low expression of hsp-miRNA-200b-3p and -200c-3p could play a pathophysiological role of development of HCMV tissue-invasive disease.

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1172. Human Adenovirus (HAdV) Viremia in Immunocompetent Children with HAdV Infection in Respiratory Specimens: Does Viremia Predict Severity of Illness?

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Background. The interpretation of HAdV PCR from upper respiratory tract (RT) specimens can be challenging due to prolonged low grade viral shedding. We hypothesized that HAdV detection in the blood (viremia) is more common in acute HAdV infection with high respiratory viral burden (VB) compared with those with low VB in the RT. We sought to determine the frequency of HAdV viremia in immunocompetent children who have detectable HAdV in the RT.

Methods. We prospectively identified + HAdV in RT specimens from emergency department or inpatients using semi-quantitative real-time PCR (Ct < 40) or multiplex respiratory viral PCR (FILMARRAY RESPIRATORY PANEL v1.7) and prospectively collected available whole blood from 8/2013 to 2/2015. Blood was considered positive for HAdV if Ct was < 40 in whole blood. We compared virologic, including HAdV type from the RT and blood, and clinical characteristics between viremic and non-viremic groups using Mann-Whitney or chi-square as appropriate.

Results. There were 196 unique patients with + HAdV in RT specimens as well as available blood for PCR (median age=1.3 years old). Blood and RT samples were obtained on the same calendar day in 78% of patients. Among these 196 patients, 163 (83%) were hospitalized and 58 (36%) were admitted to PICU. HAdV was detected in the blood in 33% of patients. Upper respiratory tract infections were more common (P = 0.026) and the duration of fever at the time of enrollment was longer in the viremia group (3 vs. 2 days, P = 0.043). There was no difference in ICU admission between two groups. Coinfections with bacterial pathogens from sterile sites were only found in the non-viremic group (4%); these included S. aureus or pneumococcal bacteremia, E. coli urinary tract infections, or pneumococcal pneumonia. HAdV VB in RT were significantly higher in the viremia group (Ct median 25.01 vs. 36.38, P < 0.0001). Species C was more predominant in the viremia group compared with non C (A, B/E, D, F) (P = 0.018). RT type was 100% concordant with blood type.

Conclusion. HAdV viremia is relatively common in immunocompetent children with HAdV infection in the RT. Subjects with viremia had significantly higher VB in the RT, but this didn't seem to be correlated with disease severity. HAdV viremia may be useful tool to add further evidence of acute HAdV infection.

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1173. Molecular Epidemiological Investigation of Human Parainfluenza 3 Virus Outbreak in a Pediatric Bone Marrow Transplantation Unit

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Background. Human parainfluenza virus 3 (hPIV3), a common cause of respiratory infections in children, can cause nosocomial outbreaks in patients undergoing hematopoietic stem cell transplantation, resulting in significant morbidity and mortality. Between July and August 2016, an increased number of hPIV3 infections were noted in a pediatric bone marrow transplant unit (BMT). Two patients were identified in late July and 4 patients in August. We undertook molecular typing of hPIV3 to determine whether cases represented multiple introductions of community virus strains or patient to patient transmission of a single strain. Previous reports of molecular typing have targeted either the F (fusion protein) gene or HN (hemagglutinin-neuraminidase) gene. We compared results using both methods direct from clinical specimens.

Methods. Nasopharyngeal (NP) swabs from 6 patients in BMT ward and 6 patients hospitalized on other wards had hPIV3 detected by the Luminex NxTAG Respiratory Pathogen Panel over 2 months. For the F gene a single pair of primers were used to first amplify then sequence a 278 basepair (bp) region by reverse-transcriptase PCR (RT-PCR). For HN gene a 1719 bp region was amplified using nested RT-PCR, then sequenced with 6 sets of overlapping primers. The resulting contigs were assembled manually with ContigExpress. Phylogenetic analysis of assembled sequences was performed in MEGA7 using the maximum likelihood method.

Results. For the HN gene sequence of 1715 bp was obtained for 10 of 12 patients (5 in each group). Phylogenetic analysis of HN sequences indicated 2 distinct hPIV3 lineages (Figure 1). The 5 BMT patients differed by a maximum of 1bp, while 5 samples from other wards differed by 14 to 57 bp. For the F gene only 98 bp of common sequence was obtained for 7 patients, all of whom had HN gene sequences available. Phylogenetic analysis of F gene sequence also supported the presence of 2 distinct lineages.

Conclusion. Molecular typing of hPIV3 suggests there was transmission of a single hPIV3 strain within the BMT unit despite protective isolation of all BMT patients in positive pressure single rooms and the use of contact and droplet precautions for infected cases. We found sequencing the HN gene more informative than sequencing the F gene.