Disclosures. All authors: No reported disclosures.

2586. Human Breast Milk Inhibits the Replication of Parechovirus-A3
Ryohi Irumizu, MD, PhD; Kazuki Kon, MS; Yuta Aizawa, MD, PhD; Kanako Watanabe, PhD; Akihiko Saitoh, MD, PhD; Niigata University, Niigata, Japan
Session: 268. Neonatal Infections - non CMV/HSV
Saturday, October 5, 2019: 12:15 PM

Background: Parechovirus-A3 (PeV-A3) is an emerging pathogen causing sepsis and meningoencephalitis in neonates and young infants. We previously reported that maternal antibodies against PeV-A3 are important to protect neonates and young infants from the infection. Recent studies showed that (1) breastfeeding had a protective effect against enterovirus, which is closely-related virus to PeV-A, and (2) human breast milk (HBM) neutralized enterovirus in vitro. Currently, no report is available related to the antiviral effect of HBM against PeV-A3.

Methods: HBM (colostrum, 3–5 days after childbirth; mature milk, 1 month after childbirth) and serum (within ± 1 week of child’s birthday) samples were obtained from mothers at obstetrics clinic in Niigata, Japan. Neutralizing antibody titers (NATs) against PeV-A3 were measured using the Vero cells.

Results: The anti-PeV-A3 NATs of colostrum (n = 32) ranged from 1:8 to 1:2048, those ≥1:32 was 59% (19/32). Whereas, the anti-PeV-A3 NATs of mature milk ranged from 1:8 to 1:96, and those ≥1:32 was 20% (2/20) (P < 0.001). The median NATs anti-PeV-A3 was higher in colostrum (1:32) compared with mature milk (1:8) (P > 0.001). There was a strong positive correlation between the NATs of colostrum and serum (r = 0.604, P < 0.001).

Conclusion: This study showed that HBM had high NATs against PeV-A3, which was correlated with serum NATs. Further studies are necessary to investigate which components of HBM has antiviral effects against PeV-A3.

Disclosures. All authors: No reported disclosures.

2587. Etiology and Outcome of Acute Neonatal Infectious Encephalitis
Craig Frankel, MD1; Hilary Whyte, MD2; Yann Chau, MD2; Daune MacGregor, MD2; Sanjay Mahant, MD2; Helen Branson, MD2; Aaron Campigotto3; Ari Bitun2, MD2; 3Western University, London, ON, Canada; 1Hospital for Sick Children, Toronto, ON, Canada
Session: 268. Neonatal Infections - non CMV/HSV
Saturday, October 5, 2019: 12:15 PM

Background: There are very few studies on acute encephalitis with onset during the neonatal period. The objectives of this study were to investigate the etiology and salient clinical features of neonatal encephalitis.

Methods: Neonates with possible infectious encephalitis (IE) were prospectively enrolled. Inclusion criteria included encephalopathy (altered/fluctuating level of consciousness ≥24 hours) plus ≥2 of: fever/temperature instability; seizure(s); focal neurologic findings; CSF pleocytosis; EEG abnormalities consistent with encephalitis; neuroimaging abnormalities consistent with encephalitis. Neonates with a clear diagnosis of post-perinatal encephalopathy or asphyxie pre or perinatal events were excluded. Results shown as absolute numbers, proportions or medians [interquartile range] as appropriate.

Results: Fifty-nine neonates fulfilled the inclusion/exclusion criteria (June 2013–November 2018). Empirical acyclovir was initiated in 49 (83.1%) cases. An infectious etiology was identified in 25 (42.4%): enteroviruses (n = 15), HSV (n = 5), HHV6 (n = 2), parainfluenza 3 (n = 1), influenza A (n = 1), CMV (n = 1). A noninfectious cause was confirmed in 20 (33.9%): missed hypoxic-ischemic encephalopathy (n = 10), genetic/metabolic disorders (n = 7), ischemic/hemorrhagic stroke (n = 3). No specific etiology was identified in 14 (23.7%). Thirteen (52%) neonates with IE either died (n = 7) or suffered neurologic sequelae (n = 6). Deaths were attributable to HSV (n = 4), enteroviruses (n = 2) and HHV6 (n = 1). Neurocognitive sequelae were documented in one case each of enterovirus, HSV2, HHV6, CMV, parainfluenza 3 and influenza A. Differences between neonates with and without IE, respectively, included age in days of symptom onset (7 [6, 10] vs. 1 [0, 3]; P < 0.001), gestational age (37.0 [36.0, 39.0] vs. 36.6 [37.6, 40.0]; P = 0.045), peripheral leukocyte count (10.5 [8.9, 14.6] vs. 8.1 [7.7, 21.7]; P = 0.008) and CSF glucose (2.80 [2.3, 3.2] vs. 3.10 [2.8, 3.8]; P = 0.003).

Conclusion: Enteroviruses and HSV are the predominant causes of neonatal IE. Outcome of neonatal IE is poor with approximately half dying or suffering neurologic sequelae.

Disclosures. All authors: No reported disclosures.

2588. Acute Toxoplasmosis among Pregnant Arab Women in Northern Israel: to Screen or Not?
Alona Paz, MD1,2; Asela Potasman, MD2; Tamar Stam, PhD2; Israel Potasman, MD2; Bnai Zion Medical Center, Haifa, Israel; 3Medical Faculty, Technion, Haifa, Israel; 4Hadassah, Haifa, Israel; 5Bnai Zion Medical Center, Haifa, Israel; 6Hadassah, Haifa, Israel; 7Meuhedet HMO, Haifa, Haifa, Israel
Session: 268. Neonatal Infections - non CMV/HSV
Saturday, October 5, 2019: 12:15 PM

Background: The seroprevalence of toxoplasmosis among Israeli Arabs is high. Yet, the regulation of the Israeli Ministry of Health suggests not screening pregnant women for toxoplasmosis. During 2017/8 we have seen a surge in cases of acute toxoplasmosis in pregnancy in Northern Israel. We aimed to explore this surge and compare the rates of acute toxoplasmosis in pregnancy in Northern Israel among Jews and Arabs.

Methods: The database of the lab of Meuhedet HMO (Northern Israel only) was retrospectively screened for all tests for Toxoplasma serology during 2013–2017. We focused on women of childbearing age and compared rates of seropositivity in Jews and Arabs. IgG and IgM were carried out using Abbott Architect, and IgG avidity by Vidas, BioMerieux. Birth rates were retrieved from the central computer of Meuhedet HMO.

Results: In 2017, Northern Israel had 1,397,833 citizens of whom 53% were Arabs. Of this population, 13% were insured by Meuhedet HMO, and of these 60% were Arabs (Muslims or Christians). During the 5-year period 16,044 serology tests have been requested (both sexes), of which 26% returned IgG positive. 88% of the positive ones were of Arab citizens (P < 0.0001). Excluding duplicates, we found 118 women of childbearing age with a positive IgM test (2.8%). Of the latter, 57 had a low/medium avidity test (31.4%). 112 of the women were Arabs, while only 6 were Jews (P < 0.0001). Two-thirds of the women had a positive JHC1G test at the same time. During this 5-year period there were 23,074 live births in this HMO (11,512 Arab newborns). Thus, all of these women delivered an infected newborn, the rate of congenital toxoplasmosis in the Arab population (97.2/10,000) was 19-fold higher than among the Jewish (5.2/10,000; P < 0.00001). Interview of 35 acute cases during 2017/8 revealed that most of the women had consumed raw meat called “Kibbe Niyye”—a popular dish unique to Northern Israeli Arabs (Galilee) and served on festive occasions.

Conclusion: We found that Northern Israeli Arab women are at a high risk to contract toxoplasmosis during pregnancy due to consumption of traditional raw meat. This finding calls for awareness among women as well as doctors. We believe that the regulation not to screen pregnant women in the Arab sector should be reevaluated.

Disclosures. All authors: No reported disclosures.

2589. Two Cases of Congenital Babesiosis
Kevin Hachey, MD, MPH1; Deirdre Lewis, MD2; Juliesta L. Rodriguez, MD1; Matthew W. Richardson, MD2; Alicia M. Johnston, MD2; 1Baystate Medical Center, Springfield, Massachusetts; 2Baystate Children’s Hospital, Northampton, Massachusetts; 3Baystate Children’s Hospital/UUMMS, Springfield, Massachusetts
Session: 268. Neonatal Infections - non CMV/HSV
Saturday, October 5, 2019: 12:15 PM

Background: Babesiosis is caused by Babesia microti and often transmitted via Ixodes scapularis. To the best of our knowledge, only 9 cases of vertical transmission have been reported. The spectrum of clinical presentation and optimal therapy for this population remains unknown.

Methods: Case 1 is a 4 week old female admitted with fever and irritability for 2 days. She was pancytopenic with Hgb of 9.2 g/dl, Plt of 57 k/mm3, and absolute
neutrophil count (ANC) of 500/mm³. Thin smear revealed 2.5% parasitemia. Mother was diagnosed with acute Lyme disease in the seventh month of pregnancy. Maternal serologies were positive for B. microti (IgM 1:100 and IgG ≥ 1:320). The infant received 1 PRBC transfusion and was treated with 10 days of atovaquone and azithromycin. Case 2 is a 5 week old female twin A admitted with 2 days of pallor, fatigue and poor feeding. Twin A was treated with atovaquone and azithromycin for 10 days. The mother had an acute, self-limited febrile illness at 23 weeks gestation. At infant's presentation, maternal serology revealed negative B. microti IgM and positive IgG (1:160). Placental tissue from both twins was positive for B. microti DNA by PCR. Twin B was asymptomatic, had negative B. microti blood PCR, a negative B. microti IgM, positive IgG at 1:30 fold to represent placental maternal antibody, and did not require treatment.

Results: Both infants were successfully treated without relapse.

Conclusion: Congenital babesiosis is rare and may cause profound hematologic disturbances. We report 2 cases exhibiting neutropenia in addition to anemia and thrombocytopenia, supporting recent assertions by Wormser et al. that this is a common finding. In addition, Case 2 presented with a severe hemolytic anemia significantly worse than previously reported. Finally, we demonstrated successful treatment in neonates without exchange transfusion, even with severe anemia.

Disclosures. All authors: No reported disclosures.

2590. Streptolysin O Enhances Binding of the Group A Streptococcal NAD+-Glycohydrolase Toxin to Oropharyngeal Keratinocytes

Jorge J. Velarde, MD, PhD; Nicola Lynskey, PhD; Alessandro Fiaz, PhD; James Chou, PhD; Michael Wessels, MD; Boston Children's Hospital, Boston, Massachusetts; Harvard Medical School, Boston, Massachusetts

Session: 269. Pathogenesis and Host-Response Interactions
Saturday, October 5, 2019: 12:15 PM

Background: Streptolysin O (SLO) and the NAD+-glycohydrolase (NADase) are co-toxins secreted by group A Streptococcus (GAS) that play a significant role in virulence. NADase requires SLO for translocation into the host cell cytoplasm, a process termed cytolsin-mediated translocation (CMT). Recently, we noted that interaction of the two toxins mutually increased their stability. Although NADase is predicted to bind to the host cell surface, this interaction is incompletely understood. Here, we investigate potential mechanisms by which NADase binds to oropharyngeal keratinocytes.

Methods: The amino terminal region of NADase has been implicated in CMT, but the nature of the native translocation domain has not been characterized. We determined the solution structure of this domain by NMR spectroscopy. We used flow-cytometry and confocal microscopy to investigate whether NADase could interact directly with oropharyngeal keratinocytes. Finally, since we expect that NADase and SLO are co-expressed from the same operon, are secreted in a coordinated fashion, and interact in solution, we tested whether SLO affects NADase binding to host cells.

Results: The solution structure of the NADase translocation domain revealed a β-sandwich fold with an elongated N-terminal intrinsically disordered region. Structural homology searches (DALI) identified a potential carbohydrate binding module, suggesting the translocation domain could play a role in glycan binding. We also demonstrated by flow-cytometry that purified recombinant NADase toxin is significantly enriched in keratinocyte lines, compared to the same lines transfected with control constructs. With the cell surface, resulting in a 5-fold increase of the geometric mean fluorescence intensity. We further demonstrate by flow-cytometry that purified recombinant NADase toxin is significantly enriched in keratinocyte lines, compared to the same lines transfected with control constructs. With the cell surface, resulting in a 5-fold increase of the geometric mean fluorescence intensity. Importantly, interaction with SLO significantly enhanced the association of NADase to host cells. Finally, since we expect that NADase and SLO are co-expressed from the same operon, are secreted in a coordinated fashion, and interact in solution, we tested whether SLO affects NADase binding to host cells.

Conclusion: The solution structure of the NADase translocation domain reveals a potential carbohydrate binding module, which may mediate binding of the toxin to a cell-surface glycan. Binding of NADase to host cells is markedly enhanced by its interaction with SLO. We conclude that interaction of the two toxins contributes to the CMT process by functionally increasing the local concentration of NADase at the cell surface.

Disclosures. All authors: No reported disclosures.

2591. The Role of Neutralizing Antibodies (nAb) Against Cytomegalovirus (CMV) Epithelial Cell-entry in Patients with Self-limited (SL) CMV infection after Hematopoietic Cell Transplantation (HCT)

Danielle Zamora, MD; Margaret Green, MD, MPH; Jo Tono, BS; Rachel Blazevic, BS; Bradley Edmison, BS; Terry Stevens-Ayers, MSc; Adam Gehrle, MD; Michael Roeckh, MD, PhD; University of Washington, Seattle, Washington; Fred Hutchinson Cancer Research Center, Seattle, Washington; University of Washington/Fred Hutch, Seattle, Washington; Fred Hutchinson Cancer Research Center/University of Washington, Seattle, Washington

Session: 269. Pathogenesis and Host-Response Interactions
Saturday, October 5, 2019: 12:15 PM

Background: CMV transmission after HCT occurs in 20–30% of CMV-seronegative recipients with CMV-seropositive donors (i.e., CMV D+/R−) and a distinct subset develops transient CMV DNAemia without progression to culture positivity in the absence of antivirals (BMT 1992; 9:221; J Med Virol 2019; 91:1128). The mechanism of SL CMV infection is unknown but may involve nAb, which have been implicated in primary viral clearance, including nAb that inhibit viral epithelial and endothelial cell-entry via CMV pentameric complex (PC). We aimed to describe viral kinetics and the influence of nAb on CMV infection progression in SL CMV-infected patients and controls within a unique cohort from the pre-antiviral era.

Methods: Weekly serum samples from 456 CMV D+/R− allogeneic HCT patients collected between 1978–95 were screened using quantitative CMV DNA PCR. Patients with CMV DNAemia in the first 100 days after HCT followed by a sustained return to undetectable levels without positive surveillance CMV cultures were defined as having SL CMV infection. SL CMV-infected patients were matched 1:1 to CMV-infected controls (patients with CMV infection by culture in the same period after HCT ± 14 days) and non-infected controls (patients without CMV DNA or culture positivity) to compare viral kinetics and nAb. A modified nAb assay was used to evaluate serum nAb activity against CMV PC-mediated cell entry (Vaccine 2008; 26:5769; JID 2019; in press).

Results: We identified 9 patients with SL CMV infection and baseline demographics are shown (Table 1). SL CMV-infected patients had a median of 21 days (range 7–54 days) until detectable CMV DNAemia. The median peak CMV DNAemia was 94.2 IU/mL (range 40.2–225.9 IU/mL) and 46.18 IU/mL (range 1,132–284,362 IU/mL) in SL CMV-infected and CMV-infected controls respectively. There was no difference in nAb titers between groups at infection day 0 or in the preceding 4 weeks (Figure 1, Figure 2).

Conclusion: nAb against CMV PC-mediated cell entry did not appear to play a critical role in viral clearance in SL CMV infection after CMV D+/R− allogeneic HCT. Our study illustrates the potential for clearance of relatively low CMV DNAemia after HCT without the addition of antivirals. CMV-specific T-cell immunity or innate immune mechanisms may be more important in early viral control.

Disclosures. All authors: No reported disclosures.