Results: A total of 355 patients had at least 1 positive result. Baseline characteristics and pathogens are shown in Table 1 and 2. Of the 53 bacterial pathogens identifiable by ME panel, 31 (58%) had discordant results – 29 positive by ME panel only and 2 by culture only (both *E.coli*). Patients with bacterial pathogens identified by ME panel only had lower CSF WBC and protein but higher CSF glucose (Table 3). Five patients with bacteria identified on ME panel only were not treated as meningitis given lack of pleocytosis, no antibiotic pretreatment and negative repeat cultures. Of these, 4 recovered without complications but one had hypoxic encephalopathy.

Two patients had HSV noted in ME panel but individual PCR negative. The first was a 13-day-old with typical skin lesions and positive surface swab. The other was a 6-day old only with CSF pleocytosis. Both had abnormal neuroimaging and were treated as true cases. Of 24 who had both EV PCR and ME panel, 7 were positive by ME panel only and 3 by PCR only.

Table 1: Baseline Characteristics of the Study Population

Total N = 355	N (%)
Age	
<30 days	153 (43%)
30-90 days	103 (29%)
>90 days	99 (28%)
Prematurity if <90 days (data available for n= 248)	28 (11%)
Female	169 (47%)
Immunization status	
UpToDate	281(79%)
None	42 (12%)
Delayed	12 (3%)
Prior Neurosurgical History	11* (3%)
Neurological symptoms at presentation	104 (29%)
Antibiotics before lumbar puncture (n =141)	
<24 hours prior	113 (32%)
>24 hours prior	28 (8%)
Traumatic taps (>1000 RBC/μL)	101 (28.3%)
Conventional PCR testing done	
HSV	59 (17%)
Enterovirus	24 (7%)

*- Patients with neurosurgical history included 7 with ventriculoperitoneal shunts, 2 untetherings, 1 shunt + untethering, 1 craniotomy with hematoma evacuation, 1 external ventricular drain placement.

Table 2: Pathogens identified via CSF Culture, ME panel or Conventional PCR

Pathogens identified	N
Bacterial pathogens included in ME panel (n = 53)	
Escherichia Coli (E. Coli)	15
Streptococcus pneumoniae (S. pneumoniae)	12
Streptococcus agalactiae (GBS)	**12**
Haemophilus influenzae (H. influenzae)	10
Listeria monocytogenes (L. monocytogens)	4
Bacterial pathogens NOT included in ME panel (n = 19)	
Staphylococcus aureus (S.aureus)	2
Staphylococcus epidermidis (S.epidermidis)	1
Enterobacter	2
Pseudomonas	1
*Enterococcus**	1
*Serratia**	1
Neiserria not meningitidis or gonorrhea	1
Bacteroides Fragilis	1
Streptococcus intermedius	1
Suspected contaminants†	8
Viral pathogens (n = 287)	
Enterovirus	174
Human Parechovirus	51
Human Herpes Virus 6 (HHV6)	46
HSV	14
Varicella Zoster virus	2
Fungal pathogens (n = 3)	
Cryptococcus neoformans‡	2
Candida parapsilosis	1

*- Two separate CSF cultures positive and hence, treated as true pathogen.

†- Suspected contaminants include: Staphylococcus hominis, Staphylococcus capitis, Bacillus, Micrococcus, Curtobacterium, Enterococcus, Corynebacterium.

‡ - One identified only by culture and the other only by ME panel.

Total more than N = 355 due to more than 1 pathogen identified in 14 patients.

Table 3: Characteristics of Discordant Results for Bacterial Pathogens Tested in ME panel

Variable	ME panel + CSF Culture + (n= 22)[a]	ME panel + CSF Culture - (n = 29)[b]	P value
Age, n (%) <30 days 30-90 days >90 days	 6 (27%) 3 (14%) 13 (59%)	 8 (28%) 9 (31%) 12 (41%)	0.31
Prematurity if <90 days, n (%)	1 (14%)	6 (46%)	0.33
Neurological symptom at presentation, n (%)	12 (55%)	12 (41%)	0.41
Any antibiotic before lumbar puncture, n (%)	10 (45%)	17 (59%)	0.41
Antibiotics >24 hour before lumbar puncture, n (%)	2 (9%)	4 (14%)	0.69
CSF with >1000 RBC/μL, n (%)	6 (21%)	5 (19%)	0.51
Blood Culture positive with same organism, n (%)	**15 (71%)**	**4 (14%)**	**0.0001***
Median CSF White count (range)	**927 (2-11976)**	**16 (0-8100)**	**0.0007***
Median CSF Glucose, mg/dL (range)	**21 (1-69)**	**46 (5-73)**	**0.005***
Median CSF Protein, mg/dL (range)	**200 (21-805)**	**68 (12-777)**	**0.004***
Treated as meningitis, n (%)	22 (100%)	24 (83%)[c]	0.062
Neurological impairment at discharge, n (%)	7 (32%)	3 (10%)	0.08
Death within 30 days	2 (9%)	0 (0%)	0.18

a– Pathogens positive by both ME panel and culture included GBS (7), *S.pneumoniae* (5), *E.Coli* (4), *H.influenzae*(4) and *L.monocytogenes* (2)

b- Pathogens detected by ME panel only included *E.coli* (9), *S.pneumoniae* (7), GBS (5), *L. monocytogenes* (2), *H.influenzae* (6)

c- The 5 patients with positive results only by ME panel and NOT treated as meningitis include *E.Coli* (4) and *S.pneumoniae* (1)

*- statistically significant at p<0.05

Conclusion: More than half of bacterial pathogens identified by ME panel did not have a corresponding positive CSF culture. No difference was noted by antibiotic pretreatment. Treatment decisions based on positive ME panel should be made in the appropriate clinical context. Likewise, a negative ME panel does not rule out infection especially when atypical organisms are suspected.

Disclosures: **Krow Ampofo, MBChB**, **Merck** (Grant/Research Support)

51. A Review of Human Herpesvirus 6 and Central Nervous System Disease in Oncology Patients

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Session: O-10. CNS Infections

Background: Human herpesvirus 6 (HHV-6) infects most of the human population. With immunosuppression it can reactivate and cause clinical syndromes of central nervous system (CNS) dysfunction. Much of the literature describes cases after hematopoietic stem cell transplantation (HSCT), ranging from encephalitis to a defined post-transplant acute limbic encephalitis syndrome (PALE). Outside of HSCT, studies of HHV-6 encephalitis in cancer patients are limited to case reports.

Methods: In this retrospective review, we present data from all patients admitted to MD Anderson Cancer Center between March 2016 and December 2018 that met established definitions for encephalitis, aseptic meningitis or HHV-6 PALE with detectable HHV-6 DNA in the cerebrospinal fluid (CSF) detected using either the Viracor or Biofire® Meningitis Encephalitis (ME) Panel testing platforms and no other identified etiology. We extracted demographic features, known risk factors, imaging findings, CSF analysis, treatments and patient outcomes from medical records.

Results: 725 patients underwent HHV-6 testing during the study timeframe, with 19 (2.6%) cases of HHV-6 mediated CNS disease identified. Most patients, 13/19 (68%), had undergone HSCT. Median time to presentation was 31 days post-transplant.

Survival at 240 days after transplant was 62% often with long-term neurologic sequelae. CSF tended to have lymphocyte predominance and nearly all patients had peripheral lymphopenia. Other at risk populations identified included 2/19 (11%) patients who received chimeric antigen receptor (CAR) T-cell therapy, 2/19 (11%) who received biologic immunotherapy, and 2/19 (11%) who had non-HSCT hematologic malignancy. Notable discordance among testing platforms was found in 5/9 (55%) of patients receiving both testing platforms.

CSF and Laboratory Analytes

Median Values of CSF Analytes and Laboratory Findings

	HSCT Cohort (n=12)*	CART Cohort (n=2)	Non HSCT, CART Cohort (n=4)	Total Cohort (n=19)
LP Timing (Days)	4 (0-21)	3 (1-5)	4.5 (4-6)	4
CSF Protein mg/dL	68 (35-158)	106 (92-120)	49 (25-68)	68
CSF Glucose mg/dL	62.0 (44-115)	50.5 (32-69)	54.0 (45-73)	59.0
CSF WBC cells/µL	4.0 (0-58)	35.0 (25-45)	11.5 (0-24)	7.5
CSF % Lymph	67 (20-100)	75.5 (70-81)	77.5 (0-90)	72
CSF RBC cells/µL	3.5 (0-8800)	2.0 (2)	2.0 (0-25)	2.0
Peripheral WBC 1000 cells/µ	3.95 (0.1-10.7)	3.4 (3.3-3.5)	2.75 (0-6.9)	3.40
Peripheral ANC 1000 cells/µL	3.36 (1.39-9.84)	2.18 (1.92-2.45)	1.84 (0-3.74)	3.40
Peripheral ALC 1000 cells/µL	0.360 (0.09-1.180)	0.68 (0.66-0.70)	0.56 (0-1.40)	0.36

*Patient 13 excluded as LP was prior to symptom onset
*Patient 4 did not have a differential on CSF WBC analysis
*Patient 12 did not have glucose or protein analysis sent on initial LP

Findings and Outcomes in HSCT Patients

Findings and Outcomes

Patient	Days from HSCT to CNS dysfunction	Initial Symptoms	Electroencephalogram (EEG)	MRI foci of T2/FLAIR/DWI hyperintensity	Plasma HHV-6 DNA copies/mL†	CSF HHV6 Test	CSF HHV-6 DNA Peak copies/mL	CSF HHV-6 Testing Discordant	Etiology	Prophylactic Antivirals	Antiviral Treatment	Outcome
1	28	Confusion Mutism Nausea/Vomiting	Multifocal intermittent epileptiform discharges, bitemporal region dysfunction	Bilateral posterior occipitoparietal regions	600	Viracor HHV-6 PCR	106	N/A	HHV-6 PALE	Valacyclovir -> Foscarnet day 20 (HHV-6 viremia)	Foscarnet 21d -> Cidofovir Brincidofovir	Died day 85 from disseminated adenovirus
2	25	Anterograde amnesia Retrograde amnesia	Diffuse disturbance of cerebral activity with theta wave bursts	Medial temporal lobe	Detected <188	Viracor HHV-6 PCR	143	N/A	HHV-6 PALE	Valacyclovir	Foscarnet 21d	Alive day 1148, moderate cognitive recovery, but persistent memory dysfunction. Remains no evidence of malignant disease
3	31	Anterograde amnesia Retrograde amnesia Non-sensical Speech	Diffuse disturbance of cerebral activity with epileptiform waveforms	Bilateral hippocampi	29500	Viracor HHV-6 PCR	211000	N/A	HHV-6 PALE	Valacyclovir	Foscarnet 34d	Died day 68 from respiratory failure, no microbiologic diagnosis, HHV-6 DNA 1700 copies/mL in bronchoalveolar lavage
4	10	Confusion Fever Rash	Mild generalized slowing	Known myelomic disease without new findings	1000	Viracor HHV-6 PCR	Detected <81	N/A	Confirmed HHV-6 Encephalitis	Valacyclovir	None	Died day 491 from retropharyngeal abscess and diskitis, encephalitis resolved after engraftment before HHV-6 testing resulted. Relapsed malignant disease
5	19	Headache Fever	ND	None	5500	Viracor HHV-6 PCR	59400	N/A	HHV-6 Aseptic Meningitis	Valacyclovir	Foscarnet 14d	Alive day 905, remains in clinical remission
6	32	Anterograde amnesia Retrograde amnesia Non-sensical Speech	Normal, repeat EEG day 4 with diffuse disturbance of cerebral activity and left temporal lobe epileptogenicity	Bilateral hippocampi, parietal cortices	15500	Viracor HHV-6 PCR	135000	N/A	HHV-6 PALE	Valacyclovir	Foscarnet 15d IVIG (1 dose)	Alive day 908, persistent memory and neurocognitive deficits up to 12 months but returned to normal function, remains no evidence of malignant disease
7	1265	Headache Fever Nausea/Vomiting Photophobia Syncope	ND	6mm right frontal subdural hematoma without other foci	600	Viracor HHV-6 PCR Biofire® MEP	1100	No	HHV-6 Aseptic Meningitis	Valacyclovir	Foscarnet 43d IVIG (6 doses) Valganciclovir 23d	Died day 1850 from *Escherichia coli* bacteremia, relapsed malignant disease
8	711	Episodic confusion Impaired hand-eye coordination Word finding difficulty	Diffuse disturbance of cerebral activity	Punctate right clivus	2900	Viracor HHV-6 PCR	Detected <81	N/A	Possible HHV-6 Encephalitis	Valacyclovir	None	Died day 737 from relapsed and progressive extramedullary disease, encephalitis resolved prior to HHV-6 testing resulted
9	43	Fever Lethargy Rash	ND	ND	Detected <188 ++	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	Possible HHV-6 Encephalitis	Valacyclovir	Foscarnet 14d	Alive day 850, no residual neurocognitive deficits, relapsed malignant disease, repeat HSCT 12/2019.
10	19	Episodic somnolence Slowed speech	Diffuse disturbance of cerebral activity	Right cerebellum	Not Detected	Viracor HHV-6 PCR Biofire® MEP	Detected <81	No	Confirmed HHV-6 Encephalitis	Valacyclovir -> Acyclovir -> Foscarnet day 15 for presumed resistant oral HSV lesion	Foscarnet 38d	Died day 110 from multiorgan failure due to disseminated adenovirus, RSV pneumonia and steroid refractory GVHD
11	24	Headache Rash Seizure	Diffuse disturbance of cerebral activity	Bilateral supratentorial, cerebellum and right splenium of corpus callosum	12700	Viracor HHV-6 PCR Biofire® MEP	4700	No	HHV-6 PALE	Valacyclovir -> Foscarnet day 19 for HHV-6 viremia	Foscarnet 21d	Alive day 717, moderate cognitive recovery, some difficulty with concentration and writing 1 month after discharge but returned to normal function
12	43	Headache Nausea/Vomiting Exacerbated facial nerve palsy	ND	None	Detected <188 +++	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	HHV-6 Aseptic Meningitis	Valacyclovir, Letermovir -> Foscarnet day 11 for 14d for HHV-6 viremia -> cidofovir day 25 for adenovirus viremia -> Valacyclovir	Foscarnet 15d	Died day 198 from *Staphylococcus aureus* bacteremia. Meningitis resolved but developed BK viuria and adenovirus viremia with seizures. Treated with cidofovir
13	195	Fever Headache Nausea/Vomiting	Diffuse disturbance of cerebral activity with epileptigenic potential	ND	6700	Viracor HHV-6 PCR Biofire® MEP	4200	No	HHV-6 PALE	Valacyclovir -> Valganciclovir day 174 for 4d for CMV reactivation -> Foscarnet day 178 for 14d for detected HHV-6 in CSF -> Valacyclovir	Foscarnet 14d	Died day 200 from *Streptococcus viridans* and *Enterococcus* bacteremia and sepsis. HHV-6 detected initially in CSF when taken prior to intrathecal chemotherapy before symptoms developed

ND = not done; RSV = respiratory syncytial virus; GVHD = graft versus host disease
†Peak plasma level within 7 days before or after dysfunction onset
++ Was 23500 26 days prior to presentation
+++ Was 27400 55 days prior to presentation

Findings and Outcomes in Non-HSCT Patients

Findings and Outcomes

Patient	Initial Presentation	Electroencephalogram (EEG)	MRI foci of T2/FLAIR/DWI hyperintensity	Plasma HHV-6 DNA copies/mL	CSF HHV-6 Test	CSF HHV-6 DNA Peak copies/mL	CSF HHV-6 Testing Discordant	Etiology	Prophylactic Antivirals	Antiviral Treatment	Outcome
14	Confusion Disorientation Hallucinations	Mild diffuse generalized slowing	Periventricular and subcortical white matter	Not Detected	Viracor HHV-6 PCR	Detected <81	N/A	Confirmed HHV-6 Encephalitis	Valacyclovir	None	Alive day 1028 after presentation, improved before testing resulted. Remains no evidence of malignant disease
15	Fever Seizure	Left temporal and frontal region dysfunction with epileptiform discharges	Right hippocampus/parahippocampal gyrus, right putamen, bilateral posterior medial thalami and right middle frontal gyrus	2100	Viracor HHV-6 PCR Biofire® MEP	Detected <81	Yes, only Viracor positive	HHV-6 Limbic Encephalitis	Valacyclovir	Foscarnet 7d	Died day 80 after presentation from *Enterobacter*, *Staphylococcus aureus*, rhinovirus, enterovirus pneumonia. After foscarnet, did not recover neurologically, repeat lumbar puncture for fever and CSF HHV-6 DNA up to 241 copies/mL, foscarnet restarted until death
16	Headache Neck Stiffness Nausea/Vomiting	ND	Left suprasellar cistem	Not Detected	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	HHV-6 Aseptic Meningitis	Valacyclovir	Foscarnet 7d	Alive day 495 after presentation, symptoms improved after foscarnet. HHV-6 DNA in plasma rose to 32,100 copies/mL and repeat CSF check day 314 without symptoms with 1000 copies/mL of HHV-6 DNA. Underwent HSCT day 243 after presentation
17	Fever Seizure Left Eye Deviation	Mild diffuse generalized slowing	Bilateral cerebral hemisphere white matter	60900	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	HHV-6 Limbic Encephalitis	Valacyclovir	Foscarnet 11d -> Ganciclovir/ Valganciclovir 15d -> Foscarnet 7d -> discontinued at discharge	Unknown, discharged to hospice day 47 after presentation due to progressive HLH refractory to ruxolitinib, rituximab, clofarabine
18	Fall Lethargy Mutism	Mild diffuse generalized slowing	Bilateral periventricular and deep white matter	24200	Viracor HHV-6 PCR	20600	N/A	Confirmed HHV-6 Encephalitis	N/A	Foscarnet 14d	Alive day 783 after presentation, moderate neurologic recovery but continued memory difficulty. Nivolumab stopped after HHV-6 episode and remains on clinical surveillance
19	Anterograde Amnesia Retrograde Amnesia Fever Headache Non-sensical Speech Hyponatremia	Mild diffuse generalized slowing	ND	7800	Viracor HHV-6 PCR	22300	N/A	Confirmed HHV-6 Encephalitis	N/A	Foscarnet 11d -> Valganiclovir for planned 28d	Unknown, discharged with significant neurologic recovery but lost to follow-up

ND = Not done; MEP = Meningitis Encephalitis Panel

Conclusion: In addition to HSCT patients, HHV-6 reactivation leading to CNS disease also occurs in settings such as following adoptive T cell therapy or biologic immunotherapy. Significant diagnostic discordance exists between testing platforms.

Disclosures: Rodrigo Hasbun, MD, MPH, Biofire (Consultant)

52. A Nationwide Analysis of the Trends and Outcomes of Cryptococcal Meningitis in the United States

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Session: O-10. CNS Infections

Background: Cryptococcal Meningitis (CM) is the most common presentation of invasive cryptococcosis. Seen in patients with and without HIV, CM is associated with significant morbidity and mortality. We present findings from a nationwide analysis of patients admitted with CM in the United States between 2007 and 2016.

Methods: The national inpatient sample (NIS) database was queried for all inpatient visits for Cryptococcal Meningitis between January 2007 and December 2016. Logistic regression models were used to determine risk factors for mortality, prolonged admissions, and delays in obtaining an initial lumbar puncture.

Results: The number of admissions for CM decreased during the study interval, from 3590 in 2007 to 2830 in 2016. Mortality did not change over this period (9.9%), however length of stay and inpatient cost significantly increased ($P = 0.003$ and $P < 0.001$ respectively). The proportion of patients with HIV declined from 70.7% to 54.0% ($P < 0.001$). HIV patients had a lower risk of mortality (OR = 0.77, CI 0.68–0.86, $P < 0.001$), whereas Africa-American, Hispanic and Native American ethnicities had a significantly increased association with mortality. Delay in lumbar puncture beyond the first 24 hours was independently associated with mortality, with an OR of 1.55 (CI 1.31–1.82, $P < 0.001$). . Patients admitted on a weekend, those of African-American ethnicity, and those without a known history of HIV were more likely to have delays in obtaining an early LP.

Conclusion: Inpatient mortality for patients with CM continues to remain high, with an increasing proportion of patients without underlying HIV infection. We found significant deviations in management of CM from IDSA guidelines, and an independent association of delay in early lumbar puncture with worsened patient outcomes.

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53. Incidence of Bloodstream Infections and Outcomes in Patients with Severe COVID-19 Pneumonia

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Session: O-11. COVID-19 Clinical Calls and Indicators 1

Background: Coronavirus disease 19 (COVID-19) leading to acute respiratory distress syndrome is associated with need for intensive care (IC), mechanical ventilation (MV), and prolonged recovery. These patients are thus predisposed to blood stream infections which can worsen outcomes. This risk may be aggravated by adjunctive therapies.

Methods: We reviewed the medical records of all adults admitted to Stony Brook University Hospital, NY, from March 1 to April 15, 2020 with severe COVID-19 pneumonia (requiring high-flow O_2). Patients who received MV or died within 24h were excluded. Patients were followed until death or hospital discharge. We reviewed positive blood cultures (PBC) for pathogenic microorganisms, and calculated the incidence of bacteremia, rates of infective endocarditis (IE), and impact on mortality. Microbes isolated only once and belonging to groups defined as commensal skin microbiota were labelled as contaminants. We also examined the impact of adjunctive therapies with immunosuppressive potential (steroids and tocilizumab), on bacteremia.

Results: A total of 469 patients with severe COVID-19 pneumonia were included (**Table 1**). Of these, 199 (42.4%) required IC and 172 (36.7%) MV. Median length of stay was 13 days (8–22) and 94 (20.0%) had PBC. Of these, 43 were considered true pathogens (bacteremia), with predominance of *E. faecalis* and *S. epidermidis,* and 51 were considered contaminants (**Table 2**). The incidence of bacteremia (43/469, 9.2%) was 5.1 per 1000 patient-days (95%CI 3.8–6.4). An echocardiogram was performed in 21 patients, 1 had an aortic valve vegetation (IE) by methicillin sensitive *S. aureus*. Bacteremia rates were nonsignificantly higher with steroids (5.9 vs 3.7 per 1000 patient-days; P=0.057). Use of tocilizumab was not associated with bacteremia (5.8 vs 4.8 per 1000 patient-days;