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Session: P-53. Infections in Immunocompromised Individuals

Background. Acute leukemia patients are at risk for cytomegalovirus (CMV) retinitis following hematopoietic stem cell transplantation, though the disease can also occur in non-transplant adult leukemia patients. Emerging data suggest a shift to pediatric-inspired chemotherapy regimens in adults with acute lymphoblastic leukemia (ALL) can lead to increasing cytopenias and impaired functional immunity, placing these patients at risk for this opportunistic infection. Here we describe a case of CMV retinitis in an ALL patient following a lower-intensity regimen during maintenance chemotherapy.

Methods. Chart review.

Results. A 55-year-old male with ALL presented to his optometrist with complaints of visual changes including "fogginess" and "floaters". The patient had completed 8 cycles of dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (EPOCH-R) and achieved complete remission. He had been on maintenance chemotherapy with 6-mercaptopurine, vincristine, methotrexate, and prednisone (POMP) for 2 months at the time of symptom onset. He was referred to his local ophthalmologist who had concerns for bilateral, zone 1 CMV retinitis based on fundoscopic exam (Figure 1). Vitreous aspiration was performed and CMV DNA PCR returned positive at 1.6 million IUs/ml. Peripheral blood CMV DNA PCR was also positive at 1133 IU/ml. He was started on combination therapy with intravitreal ganciclovir injections and oral valganciclovir 900 mg twice daily (Figure 2). The patient received 14 intravitreal injections with resultant stability of his eye exam, though he remained on induction valganciclovir for 5 months due to persistent blood CMV DNAemia. Letermovir was added to help suppress his peripheral CMV DNAemia and he attained partial vision recovery.

Figure 1. Fundoscopic images

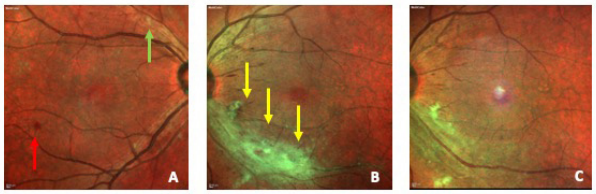

Figure 1A, 1B, 1C: Multicolor images (Heidelberg Engineering, SPECTRALIS®) of the both eyes. 1A: Small cotton wool spots (green arrow) and intraretinal hemorrhages (red arrow) noted in the macula of the right eye. 1B: Retinal whitening and hemorrhages noted along the infererotemporal arcade vessels (yellow arrow) in the left eye. Distribution of necrosis follows the vasculature, consistent with hematogenous spread of viral retinitis. 1C: Multicolor image of left eye after induction of intravitreal ganciclovir 4 mg/0.1 mL after four weeks. Retinal whitening and intraretinal hemorrhages improve with treatment.

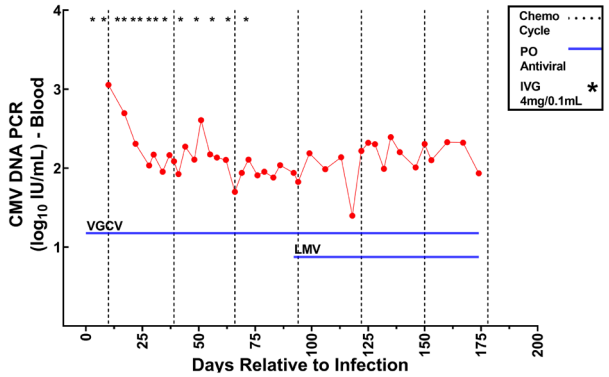

Figure 2 – Peripheral CMV DNAemia and systemic antiviral course. Peripheral CMV DNAemia relative to initial diagnosis of CMV retinitis. All CMV DNA PCR values (red) are in IU/mL and $\log_{10}$ transformed for graphical purposes. Maintenance chemotherapy (dotted lines), systemic antivirals (blue lines), and bilateral intravitreal antiviral administration dates (asterisks) are also shown. Of note, the patient also received bilateral prophylactic laser retinopexy both eyes to lattice degeneration on Days 8 and 119 post-infection. CMV=cytomegalovirus, IVG=intravitreal ganciclovir, VGCV=valganciclovir, LMV=letermovir

Conclusion. CMV retinitis is an uncommon and highly morbid infection that can occur during maintenance chemotherapy in adult non-transplant ALL patients. Early identification of the disease is imperative as delay can result in blindness or further systemic CMV disease. Treatment is challenging, involving systemic and intravitreal antiviral therapy, serial ophthalmologic exams, serum CMV monitoring, and close coordination with the treating hematologist.

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925. Infectious Complications Following Chimeric Antigen Receptor (CAR) T-cell Therapy

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Background. Chimeric antigen receptor (CAR-T) T-cell therapy is a novel immunotherapy for cancer treatment in which patients are treated with targeted, genetically-modified T-cells. Common side effects include cytokine release syndrome, neurotoxicity, hypogammaglobulinemia, and increased susceptibility to infections. Long-term infectious outcomes are poorly characterized.

Methods. We retrospectively examined patients who received CAR-T therapy at BIDMC & MGH from July 2016 to March 2020 and evaluated bacterial, fungal, viral, and parasitic infections at 3 months intervals to 1 year following cell infusion. The incidence, timing, and outcomes of the infectious complications were evaluated.

Results. In total, there were 47 patients; averaging 61.4 years of age (±12 years). Primary indications for CAR-T therapy included diffuse large b-cell lymphoma (65%) and multiple myeloma (25%), chronic lymphocytic leukemia (2%) and mantle cell lymphoma (2%). Patients had received an average 4 ± 2.9 lines of chemotherapy prior to CAR-T infusion; 19 subjects (40%) had a history of prior autologous stem cell transplant. All patients received acyclovir for antiviral prophylaxis and most received either trimethoprim-sulfamethoxazole (24/47; 51%) or atovaquone (16/47; 34%) for pneumocystis prophylaxis. In the first year, 35/47 (74.5%) of subjects experienced at least one infection with an infection rate of 84.4/10,000 person days. Median time to first infection was 59 days (range 1-338 patient days). 31/47 (66.0%) subjects had at least one bacterial infection, with pulmonary (42/113; 37.2%) sources being the most common site of infection. 13/47 (27.7%) of patients had a viral infection (predominantly respiratory viral infections) and 6/47 (12.8%) had a proven or probable fungal infection. Death attributed to infection was noted in 2 subjects (4.3%), both related to COVID-19. Baseline IgG levels were significantly lower in the group with infections (p=0.028), while white blood cell count and absolute neutrophil counts were comparable.

Table 1. Baseline Demographic, Clinical Characteristics, and Outcomes of 47 Recipients of CAR-T Cell Therapy by Infection Status

Table 1. Baseline characteristics

Characteristic	Without order set (n=176)	With order set (n= 52)	P-Value
Age – year	36.1 ± 10.5	35.7 ± 9.9	0.767
Male – no. (%)	174 (98.9)	47 (90.4)	0.008
Gender identity – no. (%)			0.256
Male	136 (77.3)	37 (71.2)	
Female	1 (0.6)	1 (1.9)	
Transgender Male to Female	0 (0)	1 (1.9)	
Transgender Female to Male	1 (0.6)	0 (0)	
Not specified	38 (21.6)	13 (25)	
Race – no. (%)			0.724
White	108 (61.4)	36 (69.2)	
Black	7 (4.0)	2 (3.9)	
Asian	18 (10.2)	5 (9.6)	
Other/Unknown	43 (24.4)	9 (17.3)	
Ethnicity – no. (%)			0.362
Hispanic or Latino	55 (31.3)	14 (26.9)	
Non-Hispanic nor Latino	117 (66.5)	35 (67.3)	
Unknown	4 (2.3)	3 (5.8)	
Prescriber type – no. (%)			0.629
Attending	128 (72.7)	37 (71.2)	
Resident	45 (25.6)	13 (25.0)	
Other	3 (1.7)	2 (3.9)	
Prescription type – no. (%)			0.001
New start	110 (62.5)	19 (36.5)	
Refill	66 (37.5)	33 (63.5)	
Drug – no. (%)			0.138
TDF/FTC	165 (93.8)	45 (86.5)	
TAF/FTC	11 (6.2)	7 (13.5)	
Indication – no. (%)			0.129
MSM	169 (96.0)	48 (92.3)	
Heterosexual male/female	4 (2.3)	4 (7.7)	
Not specified	3 (1.7)	0 (0)	

*Plus-minus values are means ± SD. Percentages may not total 100 because of rounding. Abbreviations = TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; TAF/FTC, tenofovir alafenamide/emtricitabine; MSM, men who have sex with men.

Notes. BMI: body mass index; DLBCL: diffuse large B-cell lymphoma; CLL: chronic lymphocytic leukemia; Flu/Cy: Fludarabine/cyclophosphamide; IVIG:

intravenous immunoglobulin; WBC: white blood cell count; ANC: absolute neutrophil count; ALC: absolute lymphocyte count.

Table 2. Characteristics of the 113 Infections in the 35 Subjects Who Developed Infections

Total Infections by Category*	113 Total Infections
Bacterial (Total #,% infections)	77 (68.1)
Proven bacterial infections	34
Gram positive (# infections, % proven bacterial)	12 (35.3)
Gram negative (# infections, % proven bacterial)	19 (55.9)
Other+ (#infections, % proven bacterial)	3 (8.8)
Proven bacterial infections by body site	
Pulmonary (# infections, % proven bacterial)	19 (55.9)
Urinary (# infections, % proven bacterial)	17 (50.0)
Sinus (# infections, % proven bacterial)	14 (41.2)
Other (# infections, % proven bacterial)	27 (35.1)
Probable bacterial infection+	43
Viral (Total #, % infections)	27 (23.9)
Proven viral infections	20
Non-respiratory virus (# infections,% proven viral)	5 (25.0)
Respiratory virus (# infections,% proven viral)	15 (75.0)
Proven viral infections by body site	
Pulmonary (# infections,% proven viral)	22 (81.5)
Urinary (# infections,% proven viral)	0 (0)
Skin (# infections,% proven viral)	1 (3.7)
Other (# infections,% proven viral)	4 (4.8)
Probable viral infections	7
Fungal (Total #, % infections)	9 (8.0)

*Patients could have more than one infection in each group and could have infections in each of the categories. Gram positive organisms included the following: Enterococcus faecium, Enterococcus spp, Staphylococcus spp, Coagulase negative Staphylococcus, Staphylococcus epidermidis. Gram negative organisms included: Klebsiella pneumoniae, Escherichia coli, Enterobacter spp, Stenotrophomonas, Acinetobacter spp, Citrobacter spp, Pseudomonas aeruginosa, Salmonella spp, Serratia marcescens. +Additional bacterial infections included Clostridium difficile infection and Lyme disease (Borrelia burgdorferi). Non-respiratory viruses included: included human papillomavirus and Cytomegalovirus. Respiratory viruses included: Coronavirus (non-SARS-CoV2), SARS-CoV2, Enterovirus, Human metapneumovirus, Influenza, Parainfluenza, Rhinovirus. Fungal infections included: Aspergillus spp, Cryptococcus spp, Candida glabrata. +Probable bacterial infections were treated with systemic antibiotics but did not have a confirmed pathogen.

Conclusion. Infectious complications, particularly of bacterial etiology, are common in the first year following CAR-T therapy. These data may inform future prophylactic strategies in this patient population.

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926. COVID-19 Infections After SARS-CoV-2 Vaccination in Solid Organ Transplant Recipients

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Background. Solid organ transplant recipients (SOTR) have lower humoral responses following SARS-CoV-2 vaccination. Whether this equates to reduced vaccine effectiveness in SOTR or impacts disease severity is not yet known. We used the IDSA Emerging Infections Network (EIN) to identify SARS-CoV-2 cases in vaccinated SOTR. We describe their clinical characteristics and outcomes.

Methods. On 4/7/21, we requested case reports via the EIN listserv of COVID-19 infection following SARS-CoV-2 vaccination in immunocompromised individuals. Case reports were collected until June 7th. Online data collection included patient demographics, dates of SARS-CoV-2 vaccine administration and clinical data related to COVID-19 infection. We performed a descriptive analysis of these patient factors and compared differences between early onset (< / = 21 days after completing vaccine series) and late onset infection (> 21 days after completing vaccine series).

Results. As of 6/7/21, 34 cases of COVID-19 infection after vaccination in SOTR were submitted. Most cases (79%) occurred in individuals who were fully vaccinated. Only 3 cases (8.5%) occurred in SOTR within their first year after transplantation. Clinical characteristics are listed in Table 1. The vaccine administration date was known for 26 SOTR among whom symptoms occurred a median of 26.5 days (IQR 21.75 days, range 5-79 days) after completing the COVID-19 vaccine series. Twenty-three SOTR (68%) required hospitalization of which 12 had critical illness. Outcome data was available for 29 individuals of whom 20 (69%) demonstrated improvement. When comparing SOTR with early versus late onset COVID-19 infection in relation to vaccination timing, there were no differences in disease severity (80% vs 75% with severe or critical disease, p=NS) or outcome (30% vs 31% died or deteriorating, p=NS).

Table 1: Characteristics of Solid Organ Transplant Recipients with COVID-19 Infection Following SARS-CoV-2 Vaccination

Characteristics	N=34 (%)
Gender	
Female	13 (38%)
Male	10 (29%)
Unknown	11 (32%)
Age Group	
18-44	4 (12%)
45-64	10 (29%)
65-74	14 (41%)
75-84	5 (15%)
Unknown	1 (3%)
Vaccine Administered	
Pfizer/BioNTech	21 (62%)
Moderna	10 (29%)
Janssen	1 (3%)
Unknown	2 (6%)
Completed Vaccine Series	
Yes	27 (79%)
No	2 (6%)
Unknown	5 (15%)
Organ Transplanted	
Lung	10 (29%)
Heart	7 (21%)
Kidney	12 (35%)
Liver	1 (3%)
Dual	4 (12%)
Time from Transplant to COVID-19 Infection	
< 1 year	3 (9%)
1-5 years	15 (44%)
>5 years	13 (38%)
Unknown	3 (9%)
Disease Severity	
Mild/Moderate	11 (32%)
Severe	11 (32%_
Critical	12 (35%)
Outcomes	
Improving/Recovery	20 (59%)
Died/Deteriorating	9 (26%)
Unknown	5 (15%)

Conclusion. SARS-CoV-2 infections after vaccination are occurring in SOTR, including cases of critical illness, suggesting reduced vaccine effectiveness within this vulnerable population. We did not appreciate any correlation between time from vaccination and COVID-19 disease severity or outcome. Further studies evaluating the true incidence of and risk factors for breakthrough infections among vaccinated SOTR are needed.

Disclosures. **Matthew Kuehnert, M.D.**, **American Association of Tissue Banks** (Board Member)**ICCBBA** (Board Member)**Musculoskeletal Transplant Foundation** (Employee) **John W. Baddley, M.D.**, **Eli Lilly** (Consultant)**Pfizer** (Consultant)**R-Pharm** (Consultant)**Viela Bio** (Consultant)

927. Clinical Characteristics and Outcomes of Norovirus Infection in Patients with Hematologic Malignancies: A Retrospective, Single Center Study

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