Persistent SARS-CoV-2, COVID-19 Associated Acute Respiratory Distress Syndrome, Severe Coagulopathy and Massive Hemoptysis in a Renal Transplant Patient on Veno-Venous Extracorporeal Membrane Oxygenation

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Introduction:

Despite the official "end" of the COVID-19 pandemic, new hospitalizations for COVID-19 Acute Respiratory Distress Syndrome (CARDS) continue with approximately 200 deaths per day[1]. Solid organ transplant patients have increased risk of severe disease. Early suppression of viral replication is essential to prognosis, with unopposed corticosteroid administration a risk factor for persistent viral replication.

We relate the case of a young, chronically immunosuppressive patient who contracted COVID-19 and progressed to severe hypoxemic respiratory failure requiring VV-ECMO rescue. Novel components of this case included:

- Development of severe disseminated intravascular coagulation (DIC), GI and airway bleeding requiring massive blood product transfusion
- Persistently low COVID-19 cycle thresholds (CT)
- Immunomodulation with 1 x 10^9 novel allogenic invariant natural killer T cell (iNKT) infusion under emergency authorization (IND 30029)

OSH Presentation:

26-year-old male post cadaveric renal transplant at age 11, maintained on tacrolimus, mycophenolate and prednisone, presented to an OSH ED

- Positive for SARS-CoV-2 on home test 2 weeks ago
- Reported several days of worsening breathlessness
- O2 sats on arrival were 81% and CXR c/w ARDS
- Admitted on supplemental oxygen, continued immunosuppression but prednisone was increased to 40mg daily on hospital day (HD) 2 when he required high flow nasal cannula. Ultimately changed to dexamethasone 6 mg three times per day and dropped back to 5mg daily prednisone at discharge
- He was not treated with antivirals, IL-6 inhibitors or other immunomodulators
- He was discharged home on HD 10 with 2-4 liters per minute home oxygen with creatinine 4.6

Admission to UCLA:

- He presented to UCLA ED with worsening respiratory status 2 days after OSH discharge. Nasal swab + COVID-19 by polymerase chain reaction (C-PCR) with CT of 15.8
- Remdesivir, baricitanib and convalescent plasma given
- Required intubation on hospital day (HD) 2
- Developed worsening respiratory failure and required cannulation for veno-venous extracorporeal membrane oxygenation (VV-ECMO) on HD 5
- Continuous renal replacement therapy (CRRT) also initiated on HD 5

VV-ECMO on HD 5:

His oxygenation and hypercapnia rapidly stabilized after fem-fem VV-ECMO cannulation.

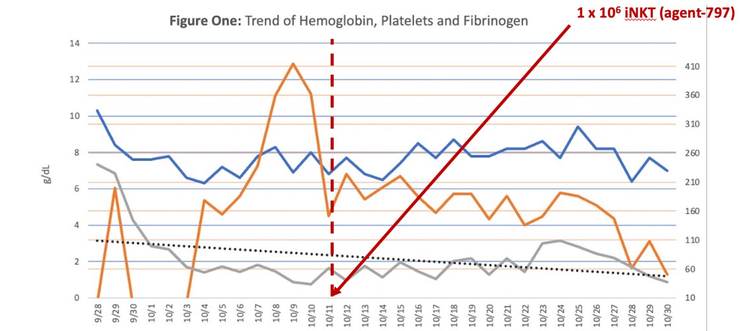
- ABG pre-cannulation 7.15/53/60 PEEP 15 FiO2 100%
- ABG post-cannulation 7.44/35/459 PEEP 8, FIO2 50%

GI Bleeding, Massive Hemoptysis and DIC beginning on HD 7:

EGD demonstrated diffuse bleeding from NG trauma. Massive hemoptysis developed and required emergent bronchoscopy with Fogarty Balloon placement .

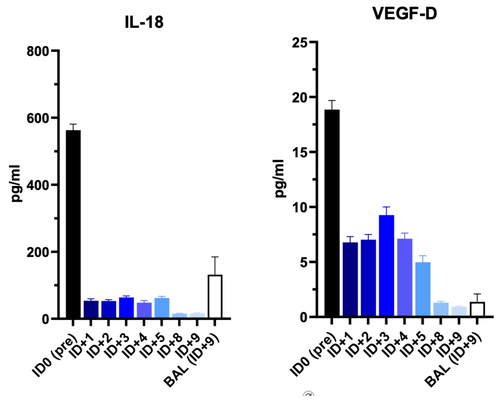
- Patient required 2-4 units of PRBC, FFP, cryoprecipitate and platelets daily
- Successfully extubated to high flow cannula on HD 37
- Decannulated from VV-ECMO on HD 47

Figure One: Trend of Hemoglobin, Platelets and Fibrinogen



	9/28	9/29	9/30	10/1	10/2	10/3	10/4	10/5	10/6	10/7	10/8	10/9	10/10	10/11	10/12	10/13	10/14	10/15	10/16	10/17	10/18	10/19	10/20	10/21	10/22	10/23	10/24	10/25	10/26	10/27	10/28	10/29	10/30
Hemoglobin	10.3	8.4	7.6	7.6	7.8	6.6	6.3	7.2	6.6	7.8	8.3	6.9	8	6.8	7.7	6.8	6.5	7.4	8.5	7.7	8.7	7.8	7.8	8.2	8.2	8.6	7.7	9.4	8.2	8.2	6.4	7.7	7
Fibrinogen	0	200	0	0	0	0	179	154	186	238	360	414	362	152	224	180	201	220	185	157	190	190	146	186	136	151	192	186	170	147	62	108	50
Platelet Count	241	225	145	100	94	63	54	64	55	67	56	37	34	62	40	65	46	72	56	43	74	78	50	78	55	104	109	99	87	79	63	48	37

Allogeneic Invariant Natural Killer T Cell Infusion on HD 13 (IND 30029):



- IL-18 is a pro-inflammatory cytokine that induces IFN-γ production
- IL-18 enhances NK cell activity and up-regulation of FasL expression
- IL-18 appears to regulate inflammation at multiple checkpoints
- IL-18 is associated with decreased survival in ARDS and an increased inflammatory infiltrate and more severe AKI

Conclusion:

The patient was transferred to the floor on HD 52 and discharged home on HD 60. On most recent follow up 6 months post UCLA hospitalization, the patient is off oxygen, off hemodialysis, back to baseline creatinine of 4.6, has returned to weight training and is independent in all daily activities.

- Immunosuppressed patients remain vulnerable to severe COVID-19 infection
- Unopposed corticosteroid administration without antiviral therapy can result in persistently low CTs
- The complex interplay between COVID-19, shear stress from VV-ECMO and potential disorders of coagulation such as disseminated intravascular coagulation (DIC) or acquired Von Willebrand's disease attributable to the VV-ECMO circuit itself
- Allogeneic iNKT therapy was safely administered with rapid decrease in IL-18 and other inflammatory cytokines and represents a novel potential therapy for COVID-19 associated ARDS that merits further study

References:

[1] As of 9/30/2023 https://covid.cdc.gov/covid-data-tracker/#trends_weeklydeaths_select_00

Hammond, T. C., Purbhoo, M. A., Kadel, S., Ritz, J., Nikiforow, S., Daley, H., ... &, M. A. (2024). A phase 1/2 clinical trial of invaExleyriant natural killer T cell therapy in moderate-severe acute respiratory distress syndrome. *Nature Communications*, *15*(1), 974.