

Clinical presentation and outcomes of COVID-19 following hematopoietic cell transplantation

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Background

- As of January 2021, more than 1,300 cases of SARS-CoV-2 infection have been reported to CIBMTR¹
- Yet, one year into the pandemic published data on HCT recipients with COVID-19 is limited

Objectives

- To report clinical presentation and outcomes of HCT patients with COVID-19 at our center.

Methods

- Retrospective single center study adult HCT recipients with RT-PCR-confirmed SARS-CoV2 infection, diagnosed from Mar 2020 to Dec 2020
- Primary end points: maximum COVID-19 severity and all-cause mortality
- Follow up: median of 59 days (IQR, 40-88).
- Definitions: COVID-19 severity was defined as mild (no pneumonia on imaging), moderate (pneumonia on imaging) and severe (Acute respiratory distress syndrome (ARDS), mechanical ventilation or shock). Virological clearance was defined as one negative PCR (without subsequent tests; routine swabbing until negativity was not done) or two consecutive negative PCRs. Superimposed infections were defined as infections other than SARS-CoV2 diagnosed by the treating physician during admission for COVID-19.

Results 1

Clinical presentation

- 16 (57%) patients were managed as inpatient
- Among symptomatic patients (n=24), the most common symptoms at presentation were fever (71%), cough (54%), shortness of breath (33%), fatigue (29%), chills (29%), (17%), headache (17%), nausea/vomiting (17%), anosmia (17%), diarrhea (8%), abdominal pain (4%), sore throat (4%) and nasal congestion (4%).

Results 2

Table 1. Characteristics of study subjects (n=28)

Characteristic	n (%)
Age, median (IQR), years	57 (50-67)
Male sex	16 (57)
Type of transplant	
Autologous	12 (42.8)
Allogeneic	15 (53.6)
CAR-T	1 (3.6)
Days from transplant to infection, median (IQR), days	656 (333 – 1,274)
Underlying diagnosis	
Leukemia	6 (21.4)
Lymphoma	8 (28.6)
MDS/MPN	4 (14.3)
Multiple Myeloma/Plasma cell Disorder	9 (32.1)
Conditioning regimen^	
Myeloablative	14 (50)
Reduced intensity	12 (43)
ATG	5 (18)
Stem cell source	
Peripheral blood	25 (89)
Bone marrow	1 (4)
Type of donor^	
HLA-Mismatched Unrelated	2 (13)
HLA-Matched Unrelated	4 (27)
HLA-Haploidentical	2 (13)
HLA-Identical Sibling	6 (40)
Immunosuppression at time of COVID-19	11 (39)
Tacrolimus	3 (11)
Tacrolimus plus prednisone	2 (7)
Tacrolimus plus dasatinib	1 (4)
Corticosteroids (prednisone >20mg/daily)	3 (11)
Ruxolitinib plus prednisone	1 (4)
Mycophenolate mofetil plus sirolimus	1 (4)
Charlson Comorbidity Score, median (IQR)	2 (2– 3)

- Comorbidities: 39% of patients had hypertension, 11% had diabetes mellitus **and** 21% had obesity

Radiological findings

- 14/17 patients had an abnormal CXR (82%) and 7/9 (78%) had organizing pneumonia on chest CT.

Laboratory findings

- Lymphopenia 60% median 0.79 cells/ μ L
- Elevated CRP 100% with a median 10.5mg/L
- LDH was elevated in 85% of cases median 270 U/L
- 83% of patients had increased ferritin, median 1,736 μ g/L
- IL-6 elevated in 83% of cases, median 147 pg/mL (70.8 – 247 pg/mL)
- Among assessable patients (n=18), 14 (77.8%) had documented virological clearance defined as one negative PCR (without subsequent tests) or two consecutive negative PCRs;
- Median time to clearance was 34 days (range, 21-56).
- Median shedding time (among patients with at least two consecutive positive tests (n= 14) was 25 days (range, 7-64).

Treatment

- Five (45%) immunosuppression reduced or discontinued.
- Steroids 67% median duration 7 days
- Remdesivir 60% median duration 5 days
- Azithromycin 40%
- Hydroxychloroquine 27%
- Convalescent plasma 27%
- IVIG 13%
- Tocilizumab 14%
- Empiric antibiotics 43%

Outcomes

COVID-19 severity		
Mild	Mild symptoms and no infiltrate on chest imaging	43%
Moderate	Pneumonia on imaging	28.5%
Severe	ARDS, mechanical ventilation or shock	28.5%

Results 3

- A quarter of the patients required mechanical ventilation
- Superimposed infections, occurred following COVID-19 diagnosis in seven (25%) cases.
- Out of 28, 12 (43%), 7 (25%) and 9 (32%) patients had mild, moderate and severe disease, respectively.
- Overall mortality was 25%, nearly identical for autologous and allogeneic HCT; and exclusively seen in hospitalized patients, older than 50 years of age with severe COVID-19. None of the patients with mild (n=12) or moderate (n=7) COVID-19 died whereas 7/9 patients (78%) with severe COVID-19 died (P=0.00003). Patients diagnosed with COVID-19 within 12 months of HCT exhibited higher mortality (57% vs 14%; P=0.04).
- All-cause 30-day mortality (n=4) was 14%. A higher proportion of patients who died within 30 days of COVID-19 diagnosis (3/4) were receiving \geq 2 immunosuppressants, compared to patients who survived beyond 30 days after COVID-19 diagnosis (2/24; 75% vs. 8%; P=0.01).

Conclusions

- Our study reveals that COVID-19 HCT patients at had higher mortality than age-matched general US population, but similar to other HCT cohorts (21-33%)²⁻⁴
- Mortality in HCT patients with COVID-19 is largely dependent on age, disease severity, timing from HCT and intensity of immunosuppression.
- Lack of fever on presentation can occur, therefore a high index of clinical suspicion is needed
- Prolonged SARS-CoV2 shedding is common
- Antibiotics, although commonly prescribed, are only justified only in a minority of patients.

References

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