Cytopenias Associated with COVID-19 in Patients with Hematologic Malignancy

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Background

- In patients with active or prior hematologic malignancy, new or worsening cytopenias are often indicators of relapse or disease progression. In these patients, unexplained cytopenias can trigger extensive work-ups, invasive procedures, and considerable anxiety. Identifying alternate causes of cytopenias is important in these patients.
- COVID-19 infection has been associated with abnormalities of many organ systems, including lymphopenia. However, the impact of COVID-19 on other hematological parameters has not been well-described.

Objective

- Given the unique significance of cytopenias in patients with hematologic malignancy, we retrospectively analyzed clinical characteristics, hematologic parameters, and outcomes of patients with hematologic malignancy and COVID-19 at the University of Minnesota.

Results - Characteristics

- We identified 165 adult patients with history of hematologic malignancy diagnosed with COVID-19 between March 2020 to February 2021.
- The most common underlying malignancies were non-Hodgkin lymphoma (48%), plasma cell neoplasm (16%), and acute leukemia (16%). 33% had prior hematopoietic stem cell transplant. 67% were in remission at time of COVID-19 diagnosis. COVID-19 illness was mild in 65%, moderate in 24%, and severe in 10%. **(Table 1)**
- Overall survival (OS) by Kaplan-Meier method for the entire cohort at 30, 60, and 120 days after COVID-19 diagnosis was 95% (95% CI 90-97%), 93% (CI 88-96%), and 85% (CI 78-90%) respectively.

Table 1: Patient and Cancer Characteristics

Characteristic	Number (Percent)
Median age at dx (years)	62 (range 19-91)
Sex	
Female	76 (45%)
Male	91 (55%)
Race	
White	144 (87%)
Black	8 (5%)
Asian	7 (4%)
Hispanic/Latino	5 (3%)
Comorbidities	
Cardiovascular disease	105 (64%)
Lung disease	43 (26%)
Diabetes	32 (19%)
HSCT Recipient	54 (33%)
Autologous	29 (18%)
Allogeneic	21 (13%)
COVID Severity	
Mild (outpatient management)	107 (65%)
Moderate (requiring O2/hospital)	39 (24%)
Severe (requiring ICU/intubation)	16 (10%)

Characteristic	Number (Percent)
Underlying malignancy	
Acute leukemia	26 (16%)
Bone marrow failure/MDS	9 (5%)
Hodgkin lymphoma	9 (5%)
Myeloproliferative neoplasm	14 (8%)
Non-Hodgkin lymphoma	80 (48%)
Plasma cell neoplasm	27 (16%)
Cancer status at COVID dx	
Remission	109 (67%)
Active	21 (13%)
Inactive	14 (9%)
Stable	19 (12%)
Type of treatment in last 8 weeks	
Cytotoxic-containing regimen	17 (11%)
Immunotherapy + targeted agent	5 (3%)
Immunotherapy alone	9 (6%)
Targeted agent alone	27 (17%)
Experimental cell therapy	2 (1%)
No treatment/observation	101 (63%)
Median time from last tx to COVID	157 days
Median follow-up duration	120 days

Figure 1: Blood Counts

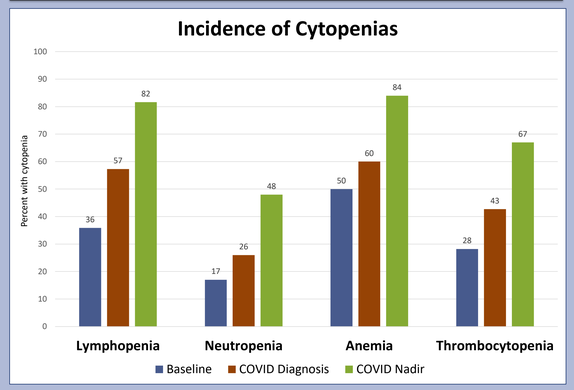

Figure 1: Incidence of cytopenias at baseline, COVID diagnosis, and nadir during COVID course (n=103). New or worsening lymphopenia and thrombocytopenia were the most common abnormalities observed.

Figure 2: Survival

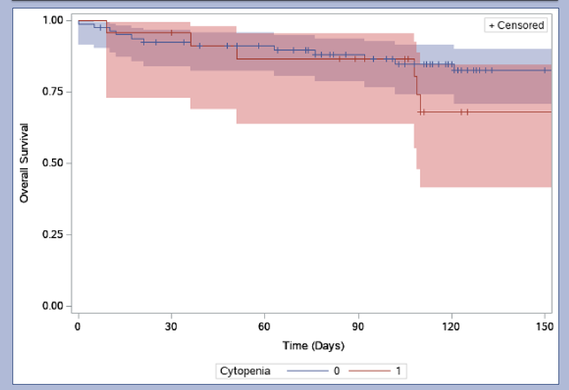

Figure 2: Overall survival by Kaplan-Meier method (with 95% confidence interval) by cytopenia status. There was no difference in OS between those with-versus-without COVID-19 associated cytopenias (p=0.16).

Results - Cytopenias

- 103 patients had complete blood count data available at both baseline and time of COVID-19 diagnosis. 65 patients (63%) developed new or worsening cytopenia in at least one cell line **(Figure 1).** Of these, 1/3 (23 patients) had no likely alternate explanation for their cytopenia other than COVID-19.
- 7 of these 23 patients (30%) had bone marrow biopsies with no evidence of disease progression.
- Among COVID-19-associated cytopenia cases, 91% had lymphopenia (median absolute lymphocyte count nadir 0.4 10^9/L), 61% had thrombocytopenia (median platelet nadir 58 10^9/L), and 39% had neutropenia (median absolute neutrophil count nadir 1.1 10^9/L). *Median time to count recovery was 15-20 days for each cell line.*
- OS was not significantly different between patients with-versus-without COVID-19-associated cytopenias (log-rank p=0.16) **(Figure 2).** This also held true on multivariate Cox proportional hazards regression after adjusting for demographics, comorbidities, COVID severity, underlying cancer, cancer status, and time from last therapy (p=0.11).

Conclusions

- OS in our cohort of patients with hematologic malignancy and COVID-19 was favorable with 60-day survival of 93% (95% CI 88-96%).
- 23% developed cytopenias felt to be attributable only to COVID-19. Lymphopenia was most common as in patients without hematologic malignancy, but a high incidence of thrombocytopenia and neutropenia was also observed.
- Cytopenias were largely self-limited with most counts recovering in 2-3 weeks. These data suggest that new/worsening cytopenias in the setting of COVID-19 can often be attributed to infection and may not require further work-up.