Received: 25 July 2023 | Accepted: 26 July 2023

DOI: 10.1002/jha2.764

eJHaem

British Society for Haematology

CORRESPONDENCE

Single-center study of outcomes of patients with hairy cell leukemia who contracted SARS-CoV-2

Kaitlin Annunzio[1] | Michael Ozga[1] | Ying Huang[2] | Mirela Anghelina[3] | Seema A. Bhat[2] | James S. Blachly[2] | Michael R. Grever[2] | Gerard Lozanski[4] | Jasmine Neal[5] | Polina Shindiapina[2] | Kerry A. Rogers[2]

[1]Hematology and Medical Oncology Fellowship Program, The Ohio State University, Columbus, Ohio, USA

[2]Division of Hematology, The Ohio State University, Columbus, Ohio, USA

[3]Department of Biomedical Informatics, The Ohio State University, Columbus, Ohio, USA

[4]Department of Pathology, The Ohio State University, Columbus, Ohio, USA

[5]Center for Clinical and Translational Science, The Ohio State University, Columbus, Ohio, USA

Correspondence
Kaitlin Annunzio, Hematology and Medical Oncology Fellowship Program, The Ohio State University, 1200 Lincoln Tower, 1800 Cannon Drive, Columbus, OH 43210, USA.
Email: Kaitlin.annunzio@osumc.edu

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to impact patients globally, especially patients with hematologic malignancies [1–3]. Several studies have demonstrated that patients with hematological malignancies and COVID-19 are at greater risk for mortality [4–6]. Patients with hairy cell leukemia (HCL) in particular are inherently at risk for profound neutropenia and monocytopenia and treatment-associated severe T-cell dysfunction [7, 8]. In conjunction with the myelosuppressive treatment options available for HCL (i.e., nucleoside analogs, cladribine, and pentostatin), patients with active HCL are susceptible to poor outcomes associated with severe infections [9], including COVID-19. The incorporation of targeted agents into active HCL therapy, including BRAF inhibitors (e.g., vemurafenib), Bruton tyrosine kinase inhibitors (e.g., ibrutinib), and anti-CD20 monoclonal antibodies (e.g., rituximab and obinutuzumab), adds another variable of uncertainty as to the immune dysregulation in HCL patients affected with COVID-19. The implications and efficacy of mRNA vaccinations, COVID-19-targeted monoclonal antibody treatments, and antiviral treatments (e.g., remdesivir) are also unknown in patients with HCL. We thus report the experience of 14 HCL patients who contracted SARS-CoV-2 between September 1, 2020, and January 24, 2022, to provide better guidance to treating hematologists. This is a single institution retrospective cohort study that included adult patients with a diagnosis of HCL who tested positive for SARS-CoV-2 during 2020–2022. The study was conducted after approval by the Institution Review Board. Descriptive statistics were used to summarize and present data for this cohort.

Of the 14 patients reviewed, the median age at HCL diagnosis was 47 years (Table 1). All but one patient was diagnosed with classical HCL, with only one patient having the variant. The majority of patients were male ($n = 10$, 71.4%). Eleven (78.6%) patients had received HCL-directed treatment prior to COVID-19 infection, with a median of two lines of prior treatment (range 1–4). In patients not on active HCL treatment the median time since last treatment was 52.6 months (range 5.5–103.4 months). Two patients were on HCL therapy when diagnosed with COVID-19. Of these, one patient treated with both rituximab and ibrutinib discontinued rituximab and remained on ibrutinib. The other continued ibrutinib throughout the COVID-19 infection course. All treated patients had prior purine analog therapy.

The most common method of diagnosis of SARS-CoV-2 infection was polymerase chain reaction testing ($n = 8$, 66.7%), followed by antigen ($n = 2$, 16.7%) and rapid antigen ($n = 2$, 16.7%) testing. The median time from onset of symptoms to resolution was 13 days (range 5–32 days), with one patient asymptomatic and three in which duration of symptoms was unknown. The most common symptoms were cough ($n = 11$, 78.6%), nasal congestion ($n = 10$, 71.46%), and fatigue ($n = 7$, 50%). Two patients were hospitalized due to COVID-19, with

Kaitlin Annunzio and Michael Ozga contributed equally to this work.

TABLE 1 Baseline characteristics of hairy cell leukemia (HCL) patients.

Baseline characteristics (*N* = 14)	
Age at HCL diagnosis, median (range)	47 (23–67)
Sex, *n* (%)	
Female	4 (28.6)
Male	10 (71.4)
COVID-19 diagnosis and vaccination status	
Vaccinated, *n* (%)	
No	3 (21.4)
Yes	11 (78.6)
First vaccination before positive COVID-19 testing	5 (35.7)
First vaccination after positive COVID-19 testing	6 (42.9)
Vaccination dose and type, *n* (%) (*n* = 11)	
One dose: Moderna	1 (9.1)
Two doses (same product):	5 (45.5)
Moderna	2
Pfizer	2
Janssen	1
Three doses:	5 (45.5)
Moderna	2
Pfizer	3 (1 previously received Janssen)
HCL treatment history	
Has HCL been treated, *n* (%)	
No	3 (21.4)
Yes	11 (78.6)
Number of lines of prior treatment (*n* = 11)	
Median (range)	2 (1–4)
On Tx at COVID-19 dx?, *n* (%)	
No	9 (81.8)
Yes	2 (18.2)
NA	2
Last IgG level prior to COVID-19 Dx	
Median (range)	988 (728–1216)
NA	8
Last CD4 count	
Median (range)	349 (259–460)
NA	9
Last CD8 count	
Median (range)	157 (112–380)
NA	9
Management of COVID-19	
Treatment, *n* (%)	
Monoclonal antibody[a]	7 (50)
Remdesivir	1 (7.1)
Other[b]	2 (28.6)

Abbreviations: IgG, immunoglobulin G; NA, not available.
[a]Monoclonal antibody received: casirivimab, imdevimab (*n* = 1), sotrovimab (*n* = 2), and bamlanivimab (*n* = 2).
[b]Other treatments: antibiotics (*n* = 1) and Paxlovid (*n* = 1).

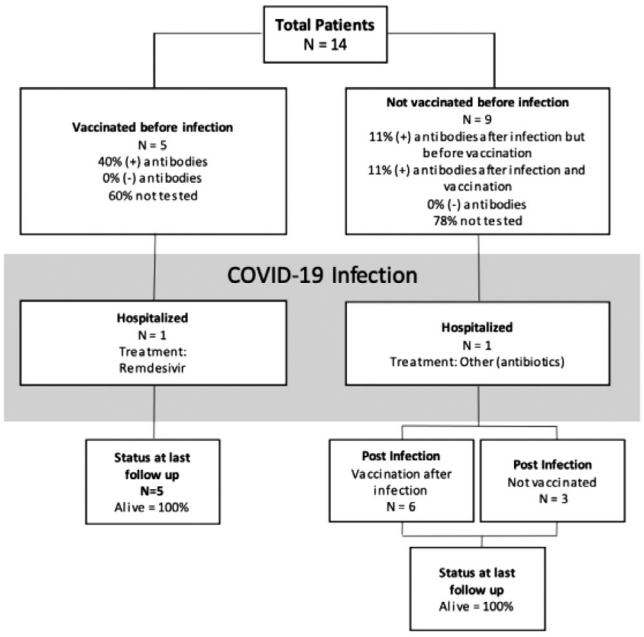

FIGURE 1 Flow diagram of hairy cell leukemia (HCL) patients COVID-19 course.

median length of stay of 4 days (range 3–5 days). Of the two hospitalized patients, one had SARS-CoV-2 antibodies detected several months prior to hospitalization, presumed to be from previous vaccination. The other patient was not vaccinated prior to infection. No patients required intensive care unit level of care, and none died due to complications of COVID-19 infection. Ten (71.4%) patients received treatment, seven (50%) of whom received monoclonal antibodies, and the remaining three received remdesivir (*n* = 1), Paxlovid (*n* = 1), and antibiotics (*n* = 1). No patients were diagnosed with arterial or venous thrombosis during or after active COVID-19 infection, and two patients were put on prophylactic anticoagulation.

Regarding vaccination status, only five out of the 14 patients received at least one dose of a vaccine before testing positive for COVID-19. Of these, two received Pfizer and three received Moderna. Six patients received vaccinations after COVID-19 diagnosis. In total, six patients received Moderna (one received one dose, three received two doses, and two received three doses), four received Pfizer (three received two doses and one received three doses), and one received Janssen (two doses). Only four patients underwent spike antibody testing, with two patients having detectable antibodies after the first vaccine but prior to COVID-19 infection, one after COVID-19 diagnosis and before first vaccine, and the last having positive antibodies after both infection and first vaccine (Figure 1).

This is a case series describing the treatment and outcomes of HCL patients who contracted COVID-19. It is notable that most patients had relatively mild COVID-19 symptoms, with only two admitted due to infection and no deaths. The majority of patients were able to receive COVID-19-specific treatments such as monoclonal antibodies and Paxlovid, which may have contributed to their recovery. It is interesting that cases were mild even though 64% of patients were unvaccinated at the time they tested positive.

As the SARS-CoV-2 virus continues to mutate, patients with hematological malignancies remain at risk for infection. This limited series demonstrates that HCL patients are able to recover from SARS-CoV-2 infection even when unvaccinated. However, patients are still at risk for infections, especially as new variants emerge, and should remain vigilant. As this only describes a group of 14 patients, larger studies are needed to confirm these results. It is also not known what variant was involved in each of these patients, as patients infected with delta variant would be expected to have worse outcomes than those infected with omicron. Providers should continue to encourage vaccination of HCL patients against COVID-19 as well as advocate for continued safety measures, especially for those receiving immunosuppressive treatment. It is notable that no patients in our series were receiving treatment with purine analogs at the time of SARS-CoV-2 infection. The majority of patients in our cohort received COVID-19-directed treatment, which likely improved outcomes. Therefore, physicians should consider early treatment of COVID-19 with the best available therapies in HCL patients.

AUTHOR CONTRIBUTIONS

Kaitlin Annunzio and Michael Ozga performed the data collection. Ying Huang analyzed the data. Mirela Anghelina and Jasmine Neal provided patient support. Seema Bhat, James Blachly, Michael Grever, and Kerry Rogers cared for the patients included in this correspondence. Gerard Lozanski contributed essential reagents or tools. Polina Shindiapina designed the research study. All authors participated in the writing of this correspondence.

ACKNOWLEDGMENTS

N/A.

CONFLICT OF INTEREST STATEMENT

James Blachly: AbbVie, AstraZeneca, Astellas, MingSight, patent on a leukemia diagnostic device, patent pending on a leukemia classification scheme. Ying Huang: Statistical consulting for AstraZeneca. Kerry Rogers: Research funding Genentech, AbbVie, and Novartis.Consulting AbbVie, Genentech, AstraZeneca, Janssen, Pharmacyclics, LOXO@lilly, and Beigene. Other authors declare they have no conflicts of interest.

FUNDING INFORMATION

The authors received no specific funding for this work.

DATA AVAILABILITY STATEMENT

For original data, please contact Kaitlin.annunzio@osumc.edu.

ETHICS STATEMENT

This study was reviewed and approved by the Institutional Review Board.

PATIENT CONSENT STATEMENT

Waiver of consent obtained as this was a non-interventional study. Research involved no more than minimal risk to the patients.

CLINICAL TRIAL REGISTRATION

The authors have confirmed clinical trial registration is not needed for this submission.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

No material from other sources was used in this correspondence.

ORCID

Kaitlin Annunzio https://orcid.org/0009-0001-4365-2178

REFERENCES

1. Grever M, Andritsos L, Banerji V, Barrientos JC, Bhat S, Blachly JS, et al. Hairy cell leukemia and COVID-19 adaptation of treatment guidelines. Leukemia. 2021;35:1864–72. https://doi.org/10.1038/s41375-021-01257-7
2. He W, Chen L, Chen L, Yuan G, Fang Y, Chen W, et al. COVID-19 in persons with haematological cancers. Leukemia. 2020;34:1637–45.
3. Martín-Moro F, Marquet J, Piris M, Michael BM, Sáez AJ, Corona M, et al. Survival study of hospitalised patients with concurrent COVID-19 and haematological malignancies. Br J Haematol. 2020;190:e16–20.
4. Fattizzo B, Giannotta JA, Sciumè M, Cattaneo D, Bucelli C, Fracchiolla NS, et al. Reply to "COVID-19 in persons with haematological cancers": a focus on myeloid neoplasms and risk factors for mortality. Leukemia. 2020;34:1957–60. https://doi.org/10.1038/s41375-020-0877-y
5. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19 death using Open SAFELY. Nature. 2020;584:430–6. https://doi.org/10.1038/s41586-020-2521-4
6. Wise-Draper TM, Desai A, Elkrief A, Rini BI, Flora DB, Bowles DW, et al. LBA71 systemic cancer treatment-related outcomes in patients with SARS-CoV-2 infection: a CCC19 registry analysis. ESMO. 2020. Available from: https://www.annalsofoncology.org/article/S0923-7534(20)42394-4/fulltext
7. Kraut E. Infectious complications in hairy cell leukemia. Leuk Lymphoma. 2011;52(Suppl 2):50–2. https://doi.org/10.3109/10428194.2011.570819
8. Van De Corput L, Falkenburg JH, Kluin-Nelemans JC. T-cell dysfunction in hairy cell leukemia: an updated review. Leuk Lymphoma. 1998;30(1–2):31–9. https://doi.org/10.3109/10428199809050927
9. Damaj G, Kuhnowski F, Marolleau JP, Bauters F, Leleu X, Yakoub-Agha I, et al. Risk factors for severe infection in patients with hairy cell leukemia: a long-term study of 73 patients. Eur J Haematol. 2009;83:246–50. https://doi.org/10.1111/j.1600-0609.2009.01259.x

How to cite this article: Annunzio K, Ozga M, Huang Y, Anghelina M, Bhat SA, Blachly JS, et al. Single-center study of outcomes of patients with hairy cell leukemia who contracted SARS-CoV-2. eJHaem. 2023;4:1200–1202. https://doi.org/10.1002/jha2.764