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Case Report

A Single-Institution Retrospective Series of SARS-CoV-2 Infection in Adult Glioma Patients

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Keywords
COVID-19 · Pandemic · SARS-CoV-2 · Glioma · Glioblastoma · Brain tumor

Abstract
A subset of cancer patients is particularly vulnerable to SARS-CoV-2 infection; however, real-world outcomes-based data on primary central nervous system tumor patients is sparse. This retrospective series describes a cohort of adult glioma patients seen at Stanford Cancer Center between January 1, 2020, and June 30, 2022 who contracted SARS-CoV-2, which, to our knowledge, currently represents the largest single-institution comprehensive analysis of this patient population. We performed a retrospective search of patients seen in the Stanford Neuro-Oncology clinic, identifying 29 cases of COVID-19 amongst glioma patients and extracted clinical data via individual chart review. At the time of COVID-19 diagnosis, 15 patients had been vaccinated against SARS-CoV-2, 8 patients were taking dexamethasone, and 8 were undergoing cancer-specific treatment. Obesity, prior tobacco use, and diabetes were the most common comorbidities. Cough, sore throat, and congestion were the most common symptoms. Five patients were admitted to the hospital and two received COVID-19-specific treatment. None died from COVID-related causes or complications. Our data suggest that glioma patients seen at Stanford Cancer Center do not experience an exceptionally high COVID-19 infectivity, hospitalization, or mortality rate, especially when compared to other vulnerable populations such as lung cancer patients. High vaccination rates, adherence to COVID-19 guidelines, and low prevalence of comorbidities may have contributed to these results.

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Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing the coronavirus disease 2019 (COVID-19) pandemic has had a major impact worldwide, resulting in 553 million confirmed cases and a reported 6.3 million deaths as of July 10, 2022 [1]. Several factors such as non-Hispanic non-white race, advanced age, and cardiovascular comorbidities are associated with increased risk of infection, more severe illness course, and worse clinical outcomes including COVID-related death [2, 3]. Initial reports suggest that patients with cancer are also at increased risk of both COVID-19 infection and worse outcomes compared to the general population [4–6]. The COVID-19 and Cancer Consortium (CCC19) was established as a tool to collect and analyze observational data [7]. Reports published from the CCC19 cohort demonstrate that cancer populations share similar risk factors as the general population including race, age, tobacco use, and comorbidities but also revealed that those with specific types of cancer are disproportionally impacted by COVID-19, in particular hematologic and pulmonary malignancies [4–6, 8–10].

Primary central nervous system malignancies account for less than 2% of all cancers in the USA [11]. Several studies have discussed the general effects of the pandemic itself on glioma management [12, 13]. However, given its rarity, there is limited data regarding the impact of COVID-19 on both clinical course and treatment in this vulnerable population. We thus aim to describe the clinical characteristics and outcomes of adult glioma patients with SARS-CoV-2 infection in a single institution.

Methods

This project was approved by the Stanford Institutional Review Board (IRB). We performed a retrospective search using the Cohort Discovery Tool from the Stanford Research Repository. Search parameters were set to identify patients who were (1) seen in the Stanford Neuro-Oncology clinic between January 1, 2020, and June 30, 2022, (2) were at least 18 years old, (3) had a diagnosis of "glioma," "glioblastoma," "astrocytoma," or "oligodendroglioma," (4) had a diagnosis of COVID-19 as determined by a documented positive nucleic acid amplification test (NAAT) and/or antigen test. Individual chart analysis was performed to confirm the authenticity of search parameters and verify diagnoses based on the 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System. An identical search was performed but without a COVID-19 diagnosis in order to identify the total number of patients seen in the Neuro-Oncology clinic in that timeframe. As COVID-19 sequencing data were not routinely obtained, we were unable to identify which specific strain was responsible for illness in each patient and instead, we identified the most common strain in the general US population at the time of diagnosis as a crude extrapolation. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531836).

Case Series

A total of 29 cases of COVID-19 (28 individual patients, one who contracted COVID-19 twice) were discovered out of the 440 adult glioma patients seen at the Stanford Neuro-Oncology clinic over this 2.5-year period with an average age of 48 years and 51.7% male (Table 1). In order of decreasing frequency was astrocytoma (62.1%), oligodendroglioma (24.1%), mesiotemporal angiocentric glioma (6.9%), ependymoma (3.4%), and subependymal

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Table 1. Patient characteristics

Characteristics	Total COVID-19 cases (n = 29[a])
Age at COVID-19 diagnosis, mean (range)	48.0 (23–73)
Gender, *n* (%)	
Male	15 (51.7)
Female	14 (48.3)
Type of primary cancer, *n* (%)	
Astrocytoma	18 (62.1)
Oligodendroglioma	7 (24.1)
Mesiotemporal angiocentric glioma	2 (6.9)
Ependymoma	1 (3.4)
Subependymal giant cell astrocytoma	1 (3.4)
Grade, *n* (%)	
1	5 (17.2)
2	10 (34.5)
3	2 (6.9)
4	12 (41.4)
Karnofsky Performance Scale, *n* (%)	
80–100	15 (51.7)
50–70	9 (31.0)
<50	0 (0)
Treatment history	
Resection	28 (96.6)
Radiation therapy	20 (69.0)
Temozolomide	20 (69.0)
Bevacizumab (Avastin)	10 (34.5)
Tumor treating fields (Optune)	2 (6.9)
Comorbidities	
Obesity	8 (27.6)
Prior tobacco use	6 (20.7)
Diabetes	4 (13.8)
CAD	1 (3.4)
Neurofibromatosis type 1	1 (3.4)
Tuberous sclerosis	1 (3.4)
Alcohol use disorder	1 (3.4)
Lupus/sjogrens	1 (3.4)

[a]1 patient contracted COVID-19 twice.

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giant cell astrocytoma (3.4%), encompassing all four grades. Karnofsky Performance Scale (KPS) at the time of COVID-19 diagnosis was most commonly 80–100 (51.7%), indicating patients with relative independence, followed by 50–70 (31.0%), indicating patients unable to work or requiring varying levels of assistance. None had significant disability with KPS <50. In terms of treatment history, 96.6% had undergone resection, 69% had radiation therapy, 69% had temozolomide, 34.5% had bevacizumab, and 6.9% had Tumor Treating Fields (i.e., Optune). Obesity and prior tobacco use were the most common comorbidities, at 27.6% and 20.7%, respectively.

The median delay between original glioma diagnosis and COVID-19 diagnosis was 59 months. At the time of COVID-19 diagnosis (Table 2), 8 (27.6%) patients were taking dexamethasone and 8 (27.6%) were undergoing cancer-specific treatment at the time of diagnosis (2 were on clinical trials, 2 were receiving temozolomide, 2 on bevacizumab, 1 getting radiation therapy, and 1 undergoing resection). Fifteen (51.7%) patients had received at least one vaccine against SARS-CoV-2. At the time of diagnosis, the most common variants were omicron (51.7%) followed by the original strain (37.9%), alpha (6.9%), and epsilon (3.4%); none occurred during the delta variant peak.

Outcomes from COVID-19 are summarized in Table 3. The most common reported symptoms were cough/sore throat/congestion (48.3%), fever (20.7%), shortness of breath/chest pain (20.7%), myalgia/fatigue (20.7%), loss of taste/smell (10.3%), headache (6.9%), and seizures (6.9%); 20.7% were asymptomatic. The diagnosis of COVID-19 delayed cancer-related care in 5 patients (17.2%). Most patients (82.8%) did not require hospital admission. Of the 5 patients who were admitted, only 2 patients qualified for and received COVID-19-directed treatment (remdesivir in both cases, dexamethasone in one case) rather than supportive management alone. At the time of COVID-19 diagnosis, among these 5 admitted patients, one had received 3 COVID-19 vaccines whereas 4 were not yet vaccinated, 2 were taking dexamethasone whereas 3 were not, and none were receiving cancer-directed treatment. The majority of patients (55%) had a KPS that remained the same or improved after contracting COVID-19 whereas KPS worsened in 20.7%. By July 13, 2022 (the date of analysis), 5 patients (17.2%) had died from reasons unrelated to COVID-19 or its complications.

Discussion

To our knowledge, the present case series represents the largest single-institution study of glioma patients who have contracted SARS-CoV-2. At the time of analysis (July 13, 2022), a total of 88,932,987 cases of COVID-19 had been reported in the USA according to the Centers for Disease Control (CDC) for a total COVID-19 incidence rate of 26.8% [14]. In contrast, a COVID-19 incidence rate of 6.4% was seen in our glioma population. Compared to a national mortality rate of 1.1%, no patients in our population died from COVID-19-related causes [14]. The authors of a recent COVID-19 case series in primary brain tumor patients from a Dutch national database reported that 63% of patients had a severe course of COVID-19 and 13% had a fatal outcome related to COVID-19 or its complications [15]. That study, however, was enriched for inpatient cases, thus not likely representing real-world incidence. Our data can also be compared to the CCC-19 dataset where authors reported a 30-day case fatality rate of 11% among patients with all types of cancer [16].

Hospitalization rate in our population was 17.2% which is higher than the national average admission rate of 5.6% although this may reflect that cancer patients are more likely than other patients to seek medical care and be admitted out of caution [14]; moreover, only 6.9% of patients qualified for and received COVID-19-specific treatment during admission. Of note, our hospitalization rate was much lower than that published in the CCC-19 database (55%) [16]. Although KPS declined in 20.7% of patients after contracting COVID-19, this

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Table 2. COVID-19 characteristics

Characteristics	Total COVID-19 cases (n = 29[a])
On dexamethasone at time of COVID-19 diagnosis, *n* (%)	
Yes	8 (27.6)
No	21 (72.4)
Cancer-specific treatment at time of COVID-19 diagnosis, *n* (%)	
Temozolomide	2 (6.9)
Bevacizumab	2 (6.9)
Clinical trial	2 (6.9)
Resection	1 (3.4)
Radiation therapy	1 (3.4)
Vaccination brand prior to COVID-19, *n* (%)	
Pfizer	10 (34.5)
Moderna	7 (24.1)
Janssen	1 (3.4)
Number of vaccinations prior to COVID-19, *n* (%)	
0	14 (48.3)
1	1 (3.4)
2	3 (10.3)
3+	11 (37.9)
Presumed COVID-19 variant[b]	
Original	11 (37.9)
Epsilon	1 (3.4)
Alpha	2 (6.9)
Delta	0 (0)
Omicron	15 (51.7)

[a]1 patient had COVID-19 twice (28 total patients).
[b]Based on dominant variant in the USA at time of diagnosis.

functional decline is not unexpected in the natural history of glioma. On individual review of charts, this decline was felt to be due to disease progression as opposed to symptomatic sequelae from COVID-19 infection.

In summary, compared to the national average, our population of glioma patients had lower incidence rates of COVID-19, did not appear to be prone to a severe illness course, nor demonstrated an increased mortality rate. These findings suggest that glioma patients are not at increased risk of contracting or experiencing worse outcomes from COVID-19 infection. Several factors may have contributed to these results. First, anecdotally speaking, our neuro-oncology patient population tends to have high vaccination rates against SARS-CoV-2. It would reason that non-vaccination would be enriched in the current population of those who contracted COVID-19 (in this case, 48.3% of patients had not yet received a vaccine). However, it is important to note that by the end of analysis; all but 1 patient had eventually become vaccinated. This fact might also explain the relatively low rate of COVID-19 reinfection (1 patient, 3.4%).

Our study has several limitations. First, this was a retrospective analysis, which confers its own limitations. The limited sample size precludes ability to make meaningful statistical comparisons; however, we reiterate that this study currently represents the

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Table 3. COVID-19 outcomes

Outcomes	Total COVID-19 cases (n = 29[a])
Symptoms, *n* (%)	
Fever	6 (20.7)
Cough/sore throat/congestion	14 (48.3)
Shortness of breath/chest pain	6 (20.7)
Headache	2 (6.9)
Seizures	2 (6.9)
Myalgia/fatigue	6 (20.7)
Loss of taste or smell	3 (10.3)
None (asymptomatic)	6 (20.7)
COVID-19-specific admission/treatment, *n* (%)	
Not admitted	24 (82.8)
Admitted but did not receive specific treatment	3 (10.3)
Admitted and received COVID-specific treatment	2 (6.9)
Cancer treatment delays due to COVID-19, *n* (%)	
Did not delay treatment	24 (82.8)
Delayed treatment	5 (17.2)
Change in KPS pre- and post-COVID-19, *n* (%)	
Improved by 10	3 (10.3)
No change	13 (44.8)
Worsened by 10	3 (10.3)
Worsened by 20	2 (6.9)
Worsened by 30	1 (3.4)
Clinical outcome, *n* (%)	
Alive	24 (82.8)
Died from non-COVID-related causes	5 (17.2)
Died from COVID-related causes	0 (0)

[a]1 patient had COVID-19 twice (28 total patients).

largest single-institution study of its kind. Single-institution studies are not necessarily generalizable, although they have the benefit of providing in-depth retrospective analysis of cases in a real-world population and are less likely than national databases to be skewed toward inpatient populations. In this case, single-institution analysis also allows for a relatively standardized set of practices for both glioma and COVID-19 management.

Conclusions

In conclusion, our data suggest that glioma patients seen at Stanford Cancer Center do not experience an exceptionally high COVID-19 infectivity, hospitalization, or mortality rate, especially when compared to other contemporaneous populations. COVID-19 represents an

under-studied field within the neuro-oncological community. With COVID-19 variants continuing to impact the world, we hope that our results provide insight as to how this disease affects glioma patients and will drive future research in this important topic.

Statement of Ethics

This is an observational study. The Stanford Institutional Review Board (IRB) approved the collection of retrospective data and completion of this study (ID: 65117). Written informed consent was waived for this type of chart review by Stanford Committee Panel #IRB-61.

Conflict of Interest Statement

All authors have no conflicts of interest to declare.

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Author Contributions

T.L., A.R., and SN conceived of this report. T.L. and A.R. performed chart review and compiled data. All authors significantly contributed to, read, and approved of the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Coronavirus disease (COVID-2019) weekly epidemiological update and weekly operational update. [cited 2022]; Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19—13-july-2022.
2 Li J, Li R, Zhang C, Guo Z, Wu X, An H. Epidemiology of COVID-19: a systematic review and meta-analysis of clinical characteristics, risk factors, and outcomes. Antibiot. 2021;10(12):1449–58.
3 Muñoz-Price, LS, Nattinger AB, Rivera F, Hanson R, Gmehlin CG, Perez A, et al. Racial disparities in incidence and outcomes among patients with COVID-19. JAMA Netw Open, 2020. 3(9):e2021892.
4 Elkrief A, Hennessy C, Kuderer NM, Rubinstein SM, Wulff-Burchfield E, Rosovsky RP, et al. Geriatric risk factors for serious COVID-19 outcomes among older adults with cancer: a cohort study from the COVID-19 and Cancer Consortium. Lancet Healthy Longev. 2022;3(3):e143–52.
5 Grivas P, Khaki AR, Wise-Draper TM, French B, Hennessy C, Hsu CY, et al. Association of clinical factors and recent anticancer therapy with COVID-19 severity among patients with cancer: a report from the COVID-19 and Cancer Consortium. Ann Oncol. 2021;32(6):787–800.
6 Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet. 2020;395(10241):1907–18.
7 Rubinstein SM, Steinharter JA, Warner J, Rini BI, Peters S, Choueiri TK. The COVID-19 and cancer consortium: a collaborative effort to understand the effects of COVID-19 on patients with cancer. Cancer Cell. 2020;37(6):738–41.
8 Fu J, Reid SA, French B, Hennessy C, Hwang C, Gatson NT, et al. Racial disparities in COVID-19 outcomes among black and white patients with cancer. JAMA Netw Open. 2022;5(3):e224304.
9 Lei H, Yang Y, Zhou W, Zhang M, Shen Y, Tao D, et al. Higher mortality in lung cancer patients with COVID-19? a systematic review and meta-analysis. Lung Cancer. 2021;157:60–5.

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DOI: 10.1159/000531836

10 Rubinstein SM, Bhutani D, Lynch RC, Hsu CY, Shyr Y, Advani S, et al. Patients recently treated for B-lymphoid malignancies show increased risk of severe COVID-19. Blood Cancer Discov. 2022;3(3):181–93.
11 Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, Kruchko C, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2012–2016. Neuro Oncol. 2019; 21(Suppl 5):v1–100.
12 Mohile NA, Blakeley JO, Gatson NTN, Hottinger AF, Lassman AB, Ney DE, et al. Urgent considerations for the neuro-oncologic treatment of patients with gliomas during the COVID-19 pandemic. Neuro Oncol. 2020;22(7): 912–7.
13 Pessina F, Navarria P, Bellu L, Clerici E, Politi LS, Tropeano MP, et al. Treatment of patients with glioma during the COVID-19 pandemic: what we learned and what we take home for the future. Neurosurg Focus. 2020; 49(6):E10.
14 Covid-19; 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/index.html.
15 de Joode K, Taal W, Snijders TJ, Hanse M, Koekkoek JAF, Oomen-de Hoop E, et al. Patients with primary brain tumors and COVID-19: a report from the Dutch Oncology COVID-19 Consortium. Neuro Oncol. 2022;24(2): 326–8.
16 Shah DP, Shah PK, Warner JL, Batist G. An update on the overall epidemiology, clinical characteristics, and outcomes from the COVID-19 and Cancer Consortium (CCC19). American Society of Clinical Oncology; 2022.