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Research Article

Clinical Progression and Outcomes of Glioma Patients Infected with COVID-19

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Abstract

Background: Patients with cancer were susceptible to COVID-19 have been reported in previous study. The clinical progression and outcomes of patients with glioma infected COVID-19 have not been reported until now.

Methods: We included all patients with glioma infected with COVID-19 who were admitted to Wuhan Tongji Hospital in China in this retrospective study. We also enrolled glioma patients without COVID-19 at the same time as controls. We collected and analyzed clinical data from medical records and evaluated outcomes for patients with glioma infected with COVID-19. Cox proportional hazard model was used to evaluate whether the infection with COVID-19 was independent risk of progression for glioma.

Results: From Jan 19 to April 1, 2020, ten patients with glioma infected with COVID-19 and forty glioma patients without COVID-19 were included in this study. The incidence of COVID-19 in glioma patients with was 0.52% (10 of 1926 COVID-19 total hospitalizations). Of ten patients, four had low-grade glioma, three had grade III glioma, two had glioblastoma (GBM),, and one had medulloblastoma, with a mean age of 58±18.3 years (range 13-71 years). Clinical symptoms were fever (nine [90.0%] patients), cough (six [60%] patient), anhelation (five [50%] patients), diarrhea (one [10.0%] patient) and muscle pain (one [10.0%] patient). One patient with GBM progressed to ARDS and died of severe respiratory failure, one patient with GBM was transferred to the ICU because of progression to ARDS, and the remaining eight patients were discharged. The Cox regress analysis showed that progression-free survival of glioma patients without COVID-19 was significantly longer than glioma patients with COVID-19. (hazard ratio [HR] 0.083, 95% confidence interval (CI) 0.007-0.960, P = 0.046).

Conclusions: Our findings suggested that progression-free survival of glioma patients without COVID-19 was significantly longer than glioma patients with COVID-19. Patients with glioma infected with COVID-19 were more higher risk to deteriorate in progression than those patients without COVID-19 during follow-up period.

Keywords: COVID-19; Glioma; Outcomes; Progression; Survival analysis

Introduction

In December, 2019, a pneumonia resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [1,2], named coronavirus disease 2019 (COVID-19) [2], emerged in Wuhan, China. Coronaviruses are enveloped, nonsegmented, positive-sense RNA viruses belonging to the family Coronaviridae and the order Nidovirales and are broadly distributed in humans and other mammals [2,3]. Two serious coronavirus disease outbreaks have occurred in the past two decades [3,4]: Severe Acute Respiratory Syndrome (SARS) in 2003 and Middle East Respiratory Syndrome (MERS) in 2012 [4]. Most coronaviruses cause diseases

in their particular host species [1,3,4]. Previous studies confirmed that COVID-19 is highly infectious, and patients can be infected through human-to-human transmission [1,5-7]. COVID-19 is a significant health threat to the public and can infect all people, especially those with a history of chronic diseases [6,7]. Previous studies reported 30 patients with a history of cancer infected with COVID-19 [8,9]. The number of cases with COVID-19 has increased rapidly, but no data concerning brain tumors patients infected with COVID-19 are available [10-12]. In addition, there is no previous treatment experience of patients with glioma and SARS-CoV-2 infection. We aimed to describe the epidemiological feature, clinical symptoms, laboratory markers, and radiological characteristics, disease progression and outcomes of patients with brain tumors confirmed to have infected with SARS-CoV-2.

Methods

Study Design and Participants

We included all glioma patients with with confirmed COVID-19 (SARS-CoV-2 infection) who were admitted to Wuhan Tongji Hospital, , from Jan 19 to April 1, 2020 in this retrospective study. We also enrolled glioma without COVID-19 (matched up with age, gender and glioma grade, shown in Table 1) in the same period to assess the potential impact of COVID-19 on glioma. The diagnosis of glioma was made by head Magnetic Resonance Imaging (MRI) and pathological examination after operations [13,14]. Patients with glioma underwent a head-enhanced MRI examination each 3-6 months or according to whether the clinical symptoms were aggravated [13,14]. The diagnosis of COVID-19 was based on guidelines issued by the World Health Organization (WHO) [15].

	Patient1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Age range, years	50-59	70-79	60-69	50-59	60-69	50-59	60-69	Oct-18
Intracranial tumor	Low-grade glioma	GBM	Meningioma	PIML	Chordoma	Low-grade glioma	Low-grade glioma	Medulloblastoma
Contact history	Family	Community	Unknown	Community	Unknown	Community	Unknown	Unknown
History of chronic basic diseases	No	Hypertension	Diabetes	No	Hypertension	No	No	No
Manifestations of COVID-19								
Fever (days)	Yes (4)	Yes (8)	No (6)	Yes (5)	Yes (4)	Yes (4)	Yes (4)	Yes (3)
Cough	No	Yes (8)	Yes (5)	Yes (4)	No	Yes (4)	Yes (4)	No
Shortness of breath	Yes (2)	Yes (4)	Yes (4)	No	Yes (2)	No	No	No
Diarrhoea	No	No	No	No	No	Yes (1)	No	No
Muscle pain	No	Yes (5)	No	No	No	No	No	No

Incubation period, days	8	3	5	4	3	7	4	3

Low-grade glioma: indicating Ior II grade glioma (WHO); GBM: glioblastoma; PIML: intracranial primary malignant lymphoma.

Table 1: Clinical characteristics of eight intracranial tumor patients with COVID-19.

Procedures

We reviewed and collected clinical electronic medical records for all patients. The admission data of these patients, including epidemiological feature, clinical symptoms, laboratory markers, and radiological characteristics were also collected [1,6,7]. Acute Respiratory Distress Syndrome (ARDS) was defined as acute-onset hypoxemia (the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen [Pao2: Fio2]<300) [16]. Any missing or uncertain records were collected and clarified through direct communication with the families or attending physician [6,7]. Laboratory confirmation of SARS-CoV-2 infection was performed at Wuhan Tongji Hospital. All laboratory procedures for clinical samples had been previously reported [1,2,16]. Briefly, throat-swab specimens from the upper respiratory tract were obtained from all patients at admission and put into viral transport medium [1,2,7,11,15]. SARS-CoV-2 was confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) within three hours [1,2,7,11,15]. RT-PCR assays were performed in accordance with the protocol established by the WHO [2,5,15]. Real-time RT-PCR detection reagents were provided by Wuhan Tongji Hospital. Other respiratory viruses, including influenza A virus, influenza B virus, respiratory syncytial virus, parainfluenza virus, and adenovirus, were also tested by real-time RT-PCR [3,4]. Sputum or endotracheal aspirates were obtained upon admission for the identification of possible causative bacteria or fungi [1,2,5].

Plasma was separated using EDTA bottles. Laboratory examinations were performed at admission, including a complete blood count, serum biochemistry, coagulation profile, infection-related biomarkers, myocardial enzymes, myoglobin, and troponin [6,11,15,16]. All laboratory examinations were performed according to the manufacturer's instructions.

Outcomes

We evaluated and compared disease progression and outcomes of glioma patients with and without COVID-19. Treatment outcomes for COVID-19 were defined as improved, cured, or failed. Improved outcome referred to the end of fever and improvement in pneumonia (via CT scan) and improvement in upper respiratory manifestations. Failed outcome referred to disease progression to critical illness or death. Clinical outcome was evaluated in accordance with the Chinese management guideline for COVID-19 (version 7.0) [16]. Progressive deterioration of glioma was defined as glioma-related death, recurrence, and tumor volume increase. Statistical analysis. Statistical data was analyzed using SPSS (version 26.0). Descriptive tests are expressed as means (standard deviation, SD), medians (interquartile range, IQR), or numbers (%). Categorical variables are expressed as counts (%) and analyzed with the chi-square test or Fisher exact test. Continuous measurements are directly expressed as ranges and compared with the Student t-test. Differences were considered to be significant with a p value < 0.05. Multivariable Cox proportional hazard model was used to evaluate the independent risk of progression for glioma.

Results

From Jan 19 to April 1, 2020, ten glioma patients infected with COVID-19 were admitted to our hospital. The incidence of COVID-19 among patients with glioma was 0.52% (10 of 1926) of total hospitalizations. The patients' clinical characteristics are presented in Table 2. All patients had no history of exposure to the Huanan Seafood Wholesale Market. The route of transmission was by close contact with family members (one [10%] patient), the community (five [50%] patients) or unknown (four [40%] patients). Of ten patients, four had low-grade glioma, three had grade III glioma, two had glioblastoma (GBM) and one had medulloblastoma , with a mean age of 58±14.6 years (range 13-71 years). No hospitalized patients with glioma were infected with COVID-19. The mean incubation period was 4.9 ±1.9 days (range 3-8 days). No patient tested positive for influenza A, influenza B, or other respiratory viruses. The patients' laboratory tests at admission are shown in Table 3. The typical findings of chest CT were patchy lesions or multifocal peripheral ground-glass changes. Forty glioma patients without COVID-19 (matched up with age, gender and glioma grade) were included as controls. The management of glioma was according to Standards for diagnosis and treatment of

glioma [13,14] and performed by a neurosurgeon. These patients were treated with temozolomide, chemotherapy and targeted therapy according to glioma. To maximize the benefit and minimize the risk of transmission during hospitalization [8], patients undergoing radiotherapy temporarily discontinued treatment after consultation with neurosurgeons and oncologists in the epidemic era, but chemotherapy continued according to the original plan. Except it may delay radiotherapy during the short period of the outbreak, the overall treatment process of glioma had be continued.

Laboratory tests (normal range)	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Blood routine								
Leucocytes (3.5-9.5 × 10^9/ L)	2.9	11.5	9.7	3.38	2.35	5.9	2.86	6.3
Lymphocytes (1.1-3.2 × 10^9/ L)	1.0	0.58	1.08	0.80	1.15	0.88	0.64	2.2
Platelets (125.0 -350.0 × 10^9/ L)	130	60	244	65	85	210	105	175
HGB (130.0-175.0 × 10^9/ L)	138.0	68.0	142.0	109.0	122.0	135.0	103.0	125.0
D-dimer (0.0-0.5μg / L)	1.5	3.1	0.5	1.6	1.7	0.7	0.8	0.6
Blood biochemistry								
ALT (0.0-41.0 U/L)	35	48	31	37	57	29	44	21
AST (0.0-40.0 U/L)	46	31	17	45	43	20	27	23
TB (0.0-26.0 μmol/L)	12.1	24.6	18.0	8.4	26.1	6.6	13.0	8.2
BUN (3.1-8.0 mmol/L)	5.4	7.2	7.9	3.8	8.1	4.9	5.6	4.1
Scr (59.0-104.0 μmol/L)	81	112	98	77	100	89	105	67
CK (0.0-190·0 U/L)	76.0	112.0	200.0	66.0	190.0	61	162.0	27
LDH (135.0-225.0 U/L)	170	484	245	310	215	283	199	152
Troponin (0.0-34.2 pg/ml)	17.0	36.2	33.0	21.0	32.0	38.4	31.0	9.2
Glucose (4.11-6.05 mmol/L)	5.11	5.99	8.9	5.6	4.11	5.89	7.16	4.28
Infection-related biomarkers								
ESR(0.0-15.0 mm/h)	17	54	28	16	21	7	14	15
IL2R (223-710 U/L)	708	1670	461	820	790	608	706	901
IL6 (0.0–7.0 pg/mL)	1.70	71.24	42.88	10.9	17.2	8.8	21.6	3.2
IL10 (0.0-9.1 pg/mL)	5.0	31.1	18.0	19.0	7.7	9.5	9.0	9.9
PCT (0.02-0.05 ng/mL)	0.06	1.20	0.09	0.04	0.08	0.03	0.07	0.05
CRP (0.0-1.0 mg/L)	0.5	91.1	1.0	10.7	2.2	7.0	0.6	0.8
TNF-α (0.0-8.1 pg/mL)	8.8	17.2	4.2	13.6	12.2	8.0	11.4	7.1
Blood culture for bacteria	Negative	Klebsiella	Negative	Negative	Negative	Negative	Negative	Negative

HGB: Hemoglobin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TB: Total bilirubin; BUN: Blood urea nitrogen; Scr: Serum creatinine; CK: Creatine kinase; LDH: lactate dehydrogenase; ESR: Erythrocyte sedimentation rate; IL2R: Interleukin-2 receptor; IL6: Interleukin-6; IL10: Interleukin-10; PCT: Procalcitonin; CRP: C-reactive protein; TNF-α: Tumor necrosis factor-α.

Table 2: Laboratory values of eight intracranial tumor patients with COVID-19.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Nucleic acid test of SARS-CoV-2	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Intracranial tumor management								
Surgery time (months)	24	3	10	6	10	31	6	12
Postoperative treatment	Temozolomide	RT+TT	N/A	RT+CT+TT	RT	TT	Temozolomide	RT
Antiviral								
Interferon alpha (days)	Yes (7)	Yes (10)	No	Yes (7)	Yes (10)	Yes (5)	Yes (6)	Yes (10)
Lopinavir and ritonavir (days)	Yes (10)	Yes (10)	Yes (10)	Yes (10)	No	Yes (10)	Yes (10)	No
Chloroquine phosphate (days)	No	No	Yes (7)	No	Yes (7)	No	No	No
Riba Welin (days)	Yes (3)	No	No	No	No	No	No	Yes (7)
Arbidol (days)	No	No	No	Yes (3)	No	Yes (5)	Yes (4)	No
Antibiotics								
Quinolones (days)	Yes (7)	Yes (7)	Yes (7)	Yes (7)	Yes (7)	Yes (7)	No	No
Cephalosporins (days)	No	No	No	Yes (10)	Yes (4)	No	Yes (7)	Yes (7)
Carbapenems (days)	No	Yes (14)	No	No	No	No	No	No
Linezolid (days)	No	Yes (7)	No	No	No	No	No	No
Methylprednisolone	No	Yes	Yes	Yes	No	No	No	No
Other therapy	TCML	Mannitol+TCML	TCML	Mannitol+TCML	TCML	TCML	TCML	TCML
Length of hospital stay (days)	23	32	26	19	28	21	21	28
Outcome	Discharge	Death	Discharge	ICU	Discharge	Discharge	Discharge	Discharge

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; RT: radiotherapy; CT: chemotherapy; TT: targeted therapy N/A: no treatment for intracranial tumor; TCML:Traditional Chinese medicine as Lianhuaqingwen capsules. Interferon alpha inhalation (50 μg twice daily), lopinavir and ritonavir (500 mg twice daily, orally), Riba Welin (500 mg twice daily, intravenously), arbidol (200 mg twice daily, orally), chloroquine phosphate (500 mg twice daily, orally).

Table 3: Clinical treatments and outcomes of eight intracranial tumor patients with COVID-19.

Patients treatments were based on the Chinese management guideline for COVID-19 (version 7.0)[16]. All patients received supportive therapy, including nutrition support and supplemental oxygen. Effective oxygen therapy was given by nasal catheter, mask oxygen and transnasal high-flow oxygen. All patients received antiviral treatment with interferon alpha inhalation (50 μg twice daily) [6,11,16], lopinavir and ritonavir (500 mg twice daily, orally) [16], Riba Welin (500 mg twice daily, intravenously), arbidol (200 mg twice daily, orally) or chloroquine phosphate (500 mg twice daily, orally) [11,16]. In the same time period, each patient was administered one or two antiviral drugs. Traditional Chinese medicine such as Lianhuaqingwen capsules was also administered to every patient [16]. All patients were given antibiotic treatment (oral or intravenous): five (50%) patients were treated with a single antibiotic, and three (30%) patients were given combination therapy [6,11,16].

Outcomes and Survival Analysis

The average hospital stay was 24.3±5.3 days (range 16-33 days) for COVID-19. One (10.0%) patient continued to progress to ARDS and died of severe respiratory failure. Two (20.0%) patients with transferred to the ICU because of progression to ARDS. The remaining seven patients were discharged from the hospital according to discharge criteria [6,11,15,16]. Patients who were discharged from the hospital had to be quarantined for 14 days and were subjected to medical observation for 14 days. Clinical outcomes were followed up to July 15, 2021 and the longest follow-up time was 68 weeks. After adjusting for important risk factors and potential confounders, including age, gender, glioma grade, time to surgery/treatments. The Cox regress analysis showed that

progression-free survival of glioma patients without COVID-19 was significantly longer than glioma patients with COVID-19. (Hazard Ratio [HR] 0.083, 95% Confidence Interval (CI) 0.007-0.960, P = 0.046).

Discussion

SARS-CoV-2 is an emerging contagious pathogen causing a high prevalence of COVID-19 among infected individuals [6,7]. Higher severity of the illness and death appear to be associated with old age and underlying diseases [6-9], such as diabetes, cardiopulmonary disease, cerebrovascular disease and immunosuppressive diseases. In previous studies, nearly half of patients with COVID-19 had underlying chronic diseases [6,7], such as diabetes, hypertension, cardiovascular disease, cerebrovascular disease and malignant tumors [8,9]. There is also concern that cancer patients and survivors are more likely to get SARS-CoV-2 infection and are more likely to die from complications of COVID-19 [8-10]. However, the clinical progression and long outcomes of COVID-19 in glioma patients with had not been reported. This was the first study on the clinical progression and outcomes of patients with glioma infected with COVID-19. The incidence of COVID-19 among patients with glioma was 0.52% (10 of 1926) of total hospitalizations, with an increased incidence compared with that of the general Chinese population (0.52% vs 0.29%) [8]. The clinical characteristics of COVID-19 in patients with glioma were similar to those of general population with COVID-19. More importantly, our findings suggest that progression-free survival of glioma patients without COVID-19 was significantly longer than glioma patients with COVID-19.

In terms of clinical manifestations [6,7], the common symptoms of these patients at the onset of COVID-19 were fever, dry cough, shortness of breath, muscle pain and bilateral ground-glass opacities on chest CT scans [6,7,11], which greatly resembled clinical manifestations of COVID-19 in patients without glioma [6,7,11,12]. Laboratory tests indicated that leukocytes were normal; absolute lymphocyte counts were decreased; and IL2R, IL6, IL10, CRP, PCT, ESR and D-dimer TNF-α levels were increased in most of the eight patients, probably leading to a "cytokine storm" and T-helper-1 (Th1) cell responses [16]. Moreover, the death and the patient transferred to the ICU had elevated concentrations of IL2R, IL6, CRP and D-dimer for relatively long periods of time, which may be associated with disease severity. Five (50%) and four (40%) of the ten patients had decreased blood platelets and leukocyte counts, respectively, that were higher than the decreased rates in previous reports [6,7,17]. The findings may indicate signs of bone marrow toxicity due to radiotherapy and chemotherapy, which may result in a shorter progression-free survival for glioma patients infected with COVID-19. High grade malignant glioma can grow rapidly in short periods of time [13,14], and deferral of therapy brings about a high risk of neoplasm recurrence [13]. Therefore, chemotherapy and radiotherapy should be continued while taking strict precautions to minimize exposures and potential contacts. When a patient progresses to ARDS, intracranial pressure may increase. Therefore, preventive use of dehydrating drugs (mannitol), which prevent potential increases in intracranial pressure, might be a better choice for safety considerations [14]. Because COVID-19 is an emerging infectious disease [1,2], the optimal treatment for affected individuals has not yet been established [15,16]. Therefore, meticulous supportive care should be recommended for patients with glioma infected with COVID-19.. In this study, all patients were treated with antiviral drugs. As SARS-CoV-2 is an emerging novel coronavirus [1,2,5], an effective antiviral drug has not yet been developed [18-20]. Looking for effective and safe treatments should be quickly initiated. Active development of a SARS-CoV-2 vaccine may control the COVID-19 pandemic. Because patients with high grade glioma usually develop secondary bacterial infections and have a more rapid clinical deterioration, antibiotics and interferon alpha are used routinely in glioma to reduce complications and mortality. However, the time of use was strictly controlled in this study. No safety concerns were identified regarding the use of traditional Chinese medicine in this study. Previous studies suggested that corticosteroids should not be routinely given systemically [21]. Three of the ten patients were treated with corticosteroids in anticipation to reduce the systemic inflammatory response of a "cytokine storm."

This study suggested that progression-free survival of glioma patients without COVID-19 was significantly longer than glioma patients with COVID-19. The previous study demonstrated patients infected with COVID-19 more likely to trigger cytokine immune response and form a cytokine storm [6,19]. At the same time, a cytokine storm starts with extensive activation of cytokine-secreting cells with innate and adaptive immune mechanisms both of which contribute to a poor prognosis [22]. Some patients were treated with corticosteroids to reduce the immune response [6,22]. However, corticosteroids also limit immune responses and thereby might counteract anti-glioma therapy. Moreover, the entry of SARS-CoV-2 into human cells triggers both an innate and adaptive immune response to eliminate viral infection and break the balance of host immune response [23]. The number of lymphocyte, especially T cells significantly decreased, lymphopenia can cause immunoregulatory defects [24]. Nevertheless, anti-glioma treatment depended on a fine host immune balance [13,14]. Disruption of immune balance increased the chance of glioma progression and deterioration [14]. This study has several limitations. First, interpretation of our findings might be limited by the sample size. However, we validated the results by evaluating and comparing matched glioma patients without COVID-19 to minimize the adverse effects of a sample size. Additional larger sample, multi-

center, cross-regional study should be analyzed to obtain a more comprehensive understanding of glioma patients with g infected with COVID-19. Second, there may be differences in the time the patient took the MRI examination. In addition to checking strictly every 3-6 months, the clinical symptoms are also the basis for the check. Which may well eliminate the error in the assessment of glioma progression.

Conclusions

In conclusion, the clinical characteristics of glioma patients with COVID-19 were similar to those of general population with COVID-19. More importantly, our findings suggested that progression-free survival of glioma patients without COVID-19 was significantly longer than glioma patients with COVID-19. Patients with glioma infected with COVID-19 were more higher risk to deteriorate in progression than glioma patients without COVID-19 during follow-up period. Patients with glioma should take strict precautions to avoid exposure and prevent SARS-CoV-2 infection in the epidemic area.

Reference

1. Zhu N, Zhang D, Wang W, Li X, Yang B, et al. (2020) A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 382: 727-733.
2. Lu R, Zhao X, Li J, Niu P, Yang B, et al. (2020) Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 395: 565-574.
3. Su S, Wong G, Shi W, Liu J, Lai ACK, et al. (2016) Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. Trends Microbiol 24: 490-502.
4. de Wit E, van Doremalen N, Falzarano D, Munster VJ (2016) SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol 14: 523-534.
5. Chan JF, Yuan S, Kok KH, To KKW, Chu H, et al. (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 395: 514-523.
6. Wang D, Hu B, Hu C, Zhu F, Liu X, et al. (2020) Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA 323: 1061-1069.
7. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395: 507-513.
8. Liang W, Guan W, Chen R, Wang W, Li J, et al. (2020) Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 21: 335-337.
9. Yu J, Ouyang W, Chua MLK, Xie C (2020) SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China. JAMA Oncol 6: 1108-1110.
10. Mohile NA, Blakeley JO, Gatson NTN, Hottinger AF, Lassman AB, et al. (2020) Urgent Considerations for the Neuro-oncologic Treatment of Patients with Gliomas During the COVID-19 Pandemic. Neuro Oncol 22: 912-917.
11. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395: 497-506.
12. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, et al. (2020) China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 382: 1708-1720.
13. Sonoda Y (2020) Clinical impact of revisions to the WHO classification of diffuse gliomas and associated future problems. Int J Clin Oncol 25: 1004-9.
14. Yang P, Wang Y, Peng X, You G, Zhang W, et al. (2013) Management and survival rates in patients with glioma in China (2004-2010): a retrospective study from a single-institution. J Neurooncol 113: 259-266.
15. World Health Organization. Coronavirus disease (COVID19) outbreak 2020.
16. National Health Commission of the People's Republic of China. Chinese management guideline for COVID-19 (version 7.0) 2020.
17. Chung M, Bernheim A, Mei X, Zhang N, Huang M, et al. (2020) CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology 295: 202-207.
18. Liu WJ, Zhao M, Liu K, Xu K, Wong G, et al. (2017) T cell immunity of SARSCoV: implications for vaccine development against MERSCoV. Antiviral Res 137: 82-92.
19. Yang X, Yu Y, Xu J, Shu H, Xia J, et al. (2020) Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 8: 475-481.
20. Sheahan TP, Sims AC, Leist SR, Schäfer A, Won J, et al. (2020) Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat Commun 11: 222.
21. Russell CD, Millar JE, Baillie JK (2020) Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet 395: 473-475.
22. Azkur AK, Akdis M, Azkur D, Sokolowska M, van de Veen W, et al. (2020) Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. Allergy 75: 1564-1581.
23. Trombetta AC, Farias GB, Gomes AMC, Godinho-Santos A, Rosmaninho P, et al. (2021) Severe COVID-19 Recovery Is Associated with Timely Acquisition of a Myeloid Cell Immune-Regulatory Phenotype. Front Immunol 12: 691725.
24. Qin C, Zhou L, Hu Z, Zhang S, Yang S, et al. (2020) Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis 71: 762-768.