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Genomic and Molecular Characterization of Brain Tumors in Asian and Non-Asian Patients of Los Angeles: A Single Institution Analysis

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Background   Worldwide, approximately 2% of new cancers are of the brain. Five-year survival rates among brain cancer patients have been reported as a little over a third. Differences in clinical outcomes between brain tumor patients of different races remain poorly understood.

Methods   A retrospective chart review was performed on brain tumor resection patients ≥18 years old. Demographics, treatment variables, and survival outcomes were collected. Primary outcomes were length of stay, recurrence rate, progression-free survival (PFS), and overall survival (OS).

Results   A total of 452 patients were included in analysis. Females and males had nearly a 1:1 ratio (n=242 and n=220, respectively). Mean age was 54.8 years (SD: 14.5 range: 18−90). Females composed 69% (n=48) of Asian patients; males constituted 31% (n=22). Mean age of the Asian patients was 55.9 years (SD: 14.6 range: 26−89). Asian-only cohort tumor pathologies included glioblastoma (GBM) (n=14), high-grade glioma (n=7), low-grade glioma (n=4), meningioma (n=38), and metastases (n=7). Of the 185 meningioma patients, non-Asian patients comprised 79% of the group (n=146). Of the 65 GBM patients in total, non-Asian patients made up 89% of the GBM cohort (n=58). There were no statistically significant differences between these groups of both cohorts in recurrence (p=0.1580 and p=0.6294, respectively), PFS (p=0.9662 and p=0.4048, respectively), or OS (p=0.3711 and p=0.8183, respectively).

Conclusion   Studies evaluating the survival between patients of different racial backgrounds against several tumor varieties are rare. Patients of certain racial backgrounds may need additional consideration when being attended to despite the same mutational composition as their counterparts. Repeated studies using national databases may yield more conclusive results.

Key Words   Biomarkers; Race; Glioblastoma; Meningioma; Brain neoplasms.

INTRODUCTION

Worldwide, less than 2% of new cancer diagnoses are of the brain and central nervous system [1,2]. Five-year survival rates among brain cancer patients have been reported as a little over a third, a mortality rate twenty-five times that of its incidence [2]. Comparatively, breast cancer's 5-year survival rates have been reported as over 80% despite having a higher incidence rate than brain cancer [2,3].

Brain tumor epidemiology in specific races has been documented, and studies into the mechanisms of mutation by race and pathology are well-established [1,4-31]. However, differences in clinical outcomes between brain tumor patients of different races are still being elucidated [25,32,33]. A prior study showed a higher probability of worse outcomes in Asian/Pacif-

ic Islanders than in their white counterparts [25]. While these reports evaluated outcomes in a single tumor pathology, studies evaluating the survival between patients of different racial backgrounds against several tumor types are rare.

To optimize treatment for patients with brain tumors, racial differences in progression-free survival (PFS) and overall survival (OS) should be considered. Patients of certain racial backgrounds may need additional consideration despite identical mutational composition as their counterparts because of different underlying genotypic variations [33]. Compared to the white population, the Asian cohort had a higher incidence of isocitrate dehydrogenase (IDH), suggesting additional consideration for glioblastoma (GBM) treatment in Asian patients [33]. The majority of existing studies focus on Asian populations, who compose 5.6% (n=17,320,856) of the total United States population [5,25,34-36]. At our institution, Asians comprise over 10% of the brain tumor population, nearly double the national percentage [37]. To further explore differences within this population group, we assessed differences in genetic markers and survival outcomes in patients of either Asian or non-Asian descent diagnosed with brain tumors.

MATERIALS AND METHODS

Inclusion criteria

A retrospective chart review was performed. Patients who had undergone brain tumor resection from March 2013 (year in which the electronic chart system was established at our institution) through January 2017 were included. Patients with "unknown" race were excluded. This study was approved by our center's Medical Institutional Review Board.

Data collection

Patient demographics (age, sex, race, and ethnicity), treatment variables, and survival outcomes were collected. The entire population was stratified by race, with the subgroups as "white," "black," "Hispanic or Latino," and "Asian." Patients in the Asian category were separately grouped by ethnicity. Categorization was chosen based on examples from the most recent United States Census Bureau data [36,37]. Treatment variables included operation duration, extent of resection (gathered from operative report), chemotherapy, and radiation modality and dosage. Primary outcomes were length of stay, discharge disposition, recurrence rate, PFS, and OS.

Mutational statuses and diagnoses were gathered from pathology reports. For patients diagnosed with GBM specifically, statuses were gathered for IDH, phosphate and tensin homologue (PTEN), tumor protein p53 (p53), chromosome 1p and chromosome 19q (1p/19q), epidermal growth factor receptor (EGFR), type III epidermal growth factor receptor (EGFRvIII),

overall antigen Ki-67 (Ki67) percentages, and methylation mutational statuses. World Health Organization (WHO) grade, glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA), and S100 mutational statuses were accumulated for meningioma patients. Patients were then organized by tumor histological subtype.

Statistical analysis

Wilcoxon signed-rank and Pearson's tests were performed. Correlation analyses were performed to identify relationships between race and all variables of interest for GBM and meningioma patients. Statistical analyses were performed using SAS, version 9.3 (SAS Institute, Cary, NC, USA). A p-value less than 0.05 was considered statistically significant.

RESULTS

General population

A total of 452 patients were included in the study. Demographics of both cohorts are summarized in Table 1. Whites comprised 71% of the cohort (n=323), Asian 16% (n=70), Hispanic or Latino 9% (n=40), black 4% (n=18), and unspecified 0.2% (n=1). Pathologies stratified by race are summarized in Table 2. The Asian-only population consisted of: Filipino 17% (n=12), Chinese 14% (n=10), Korean 10% (n=7), Vietnamese 4% (n=3), Pacific Islander 3% (n=2), Japanese 3% (n=2), Burmese 1% (n=1), and unspecified 47% (n=33). Tumor pathologies in the Asian-only cohorts included are summarized in Table 3.

Glioblastoma

We identified 65 GBM patients in total across all races. Of patients diagnosed with GBM, non-Asian patients comprised 89% of the cohort (n=58) with the remaining 11% (n=7) being Asian patients. There were no statistically significant differences between the groups in PTEN loss (p=0.705), p53 (p=0.086), 1p/19q loss (p=0.282), EGFR amplification (p=0.709), EGFRvIII (p=0.118), overall Ki67 (p=0.695), O6-methylguanine methyltransferase (*MGMT*) gene promoter methylation status (p=0.090), or other gathered variables (Table 4).

Table 1. Demographics of all populations

	General	Glioblastoma	Meningioma
Age (years, SD, range)	54.8, 14.5, 18−90	54.1, 13.1, 28−69	57.5, 14.7, 18−90
Sex, % (n)			
Female	52.4 (242)	38.8 (64)	71.9 (133)
Male	47.6 (220)	61.2 (101)	28.1 (52)

SD, standard deviation

Table 2. Summary of pathologies by race

Pathology	Race			
	White or Caucasian	Black or African American	Hispanic or Latino	Asian
GBM/gliosarcoma	30.5 (141)	0.2 (1)	3.1 (14)	3.1 (14)
Low-grade glioma	5.8 (27)	0 (0)	0 (0)	0.9 (4)
High-grade glioma	8.2 (38)	0.2 (1)	0 (0)	1.5 (7)
Meningioma	22.9 (106)	3.1 (14)	5.6 (26)	8.4 (38)
Metastases	2.4 (11)	0.4 (2)	0 (0)	1.5 (7)

All values given in percentage and (n). GBM, glioblastoma

Table 3. Summary of pathologies by Asian ethnicity

Pathology	Race							
	Pacific Islander	Burmese	Korean	Filipino	Vietnamese	Chinese	Japanese	Unspecified
GBM/gliosarcoma	0 (0)	0 (0)	2.86 (2)	2.86 (2)	1.43 (1)	2.86 (2)	0 (0)	10.00 (7)
Low-grade glioma	1.43 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4.29 (3)
High-grade glioma	1.43 (1)	0 (0)	0 (0)	1.43 (1)	0 (0)	0 (0)	0 (0)	7.14 (5)
Meningioma	0 (0)	1.43 (1)	7.14 (5)	11.83 (8)	1.43 (1)	10.00 (7)	2.86 (2)	20.00 (14)
Metastases	0 (0)	0 (0)	0 (0)	1.43 (1)	1.43 (1)	1.43 (1)	0 (0)	5.71 (4)

All values given in percentage and (n). GBM, glioblastoma

Meningioma

A total of 185 meningioma patients were included. Non-Asian patients comprised 79% of the group (n=146) while Asian patients composed the last 21% of meningioma patients (n=39). There were no statistically significant differences between these groups in WHO grade (p=0.643), histological subtype (p=0.783), GFAP (p=0.197), EMA (p=0.057), S100 (p=0.549), Ki67 (p=0.592), or other collected variables (Table 4).

DISCUSSION

Differences in races, specifically Asians in contrast to other groups, in respect to brain tumor epidemiology has already been well studied [1,4-31]. Due to the considerable Asian patient population at our institution, we endeavored to compare races within the cohort. We performed a retrospective chart analysis of patients, who underwent brain tumor resection at our institution. Race and all collected variables were tested in both GBM and meningioma patients. Survival outcomes were measured in those two cohorts against our collected variables.

Though several studies have reported significant proclivities between tumor pathologies and certain races, there were no statistically significant differences between race and tumor pathologies in our population cohort [1,4-31,38-42]. Maile et al. [8] studied 35,663 patients in England and found that the general white population had the highest occurrence of GBM among other races. They also reported Pakistanis had two times the incidence of brain neoplasms compared to that of Bangladeshis (p<0.001) [8]. However Brown et al. [4] found that in a cohort of 2,096 pediatric patients, age-specific inci-

Table 4. Elements investigated in pathology cohorts

	Glioblastoma p-values	Meningioma p-values
Age	0.0703	0.3581
Sex	0.0986	0.7487
Chemotherapy	0.2547	0.9903
Radiation	0.6093	0.5779
Surgery duration	0.5631	0.3395
Extent of resection	0.2671	0.0918
Length of stay	0.3900	0.1118
Discharge disposition	0.2397	0.8238
Follow up duration	0.8293	0.4121
Recurrence	0.6294	0.1580
Progression-free survival	0.4048	0.9662
Overall survival	0.8183	0.3711

dence of tumor pathology was not statistically different between races. In that report, even when stratified by age, there were no significant differences or correlations between race and tumor pathology [4].

In our patients with GBM, there was no significant difference between Asians and non-Asians for any of our variables. PFS and OS between the two groups were not statistically distinct from one another. There are several studies that document the mutational statuses of GBM, with some demonstrating disparities in PFS and OS between races [23,25,26,28,32,33, 35,43-68]. Dai et al. [33] performed a meta-analysis of GBM patients which included studies from Europe, North America, and Asia. In their study of 3,464 patients, IDH mutation associated mortality rate decreased nearly two times more in Euro-

pean populations than it did in Asian populations [33]. Additional multivariate analysis between race, treatment modalities, and mutational variation is one approach that warrants further study to understand PFS and OS. A study by Wu et al. [28] examined *MGMT* methylation in GBM patients of different ethnic groups and found no statistically significant differences between these groups with mutational statuses and OS. Because *MGMT* methylation results in higher sensitivity to chemotherapeutic agents, the lack of differences between methylation scores of various ethnic groups should contribute to similar PFS or OS among races [69-72]. This is consistent with our analysis of races in the GBM population. Emerging racial disparities already published in GBM patients could be used in large meta-analysis studies to continue this line of research.

In addition, we examined correlates between race and other prognostic markers in patients with meningioma. While we found no significant correlations, several studies show a proclivity of meningiomas with certain ethnicities [5,73-75]. Das et al. [5] published an article on 48,001 patients from a Singaporean hospital and found that Chinese patients had the highest rate of meningioma occurrence. According to their study, over 90% of their malignant meningiomas were expressed in Chinese patients [5]. Despite the ethnic propensity for meningioma they found, PFS and OS in patients are comparable between ethnicities [5]. Analyses of mutational statuses and their effects as confounding factors in the survival outcomes of these patients propose a valid area of research that should be explored more in depth. This model of analysis has already been well-applied to GBM research.

Our study was a retrospective review, which incurs several limitations. Data was gathered in a limited setting; therefore, the tested variables are not as homogenous as a prospective study. Patients with unspecified race or unknown mutational statuses, although still included here, could not be further distinguished. Additionally, we reported from a single institution, while several similar studies acquired their cohort from a large, national database [6-8,13,25,32,34,38,61,76]. Therefore, our sample population may be limited in both size and location. Socio-economic status of patients has been acknowledged to affect rates of brain tumor occurrence and may be a confounding variable [13,20-22,28,32,42,76-83]. While our analysis only used univariate statistics, future studies analyzing confounding factors, such as age, in survival rates are the next approaches in identifying racial disparities.

Our single institution study facilitated the acquisition of socio-economic status, which in our future studies could elucidate the role of socio-economic status on OS and PFS. Additional multivariate analysis includes investigating the role of mutational statuses as confounding factors in race and survival outcome correlations. Racial disparities have been documented

in a few studies similar to the one performed by the authors. Continued evaluation of those disparities is necessary to assure standardized treatment across all races.

In conclusion, while there are few studies assessing survival outcomes of different racial cohorts with various tumor pathologies, patients with the same mutational configuration may not have the same treatment response between varying racial backgrounds. Additional studies using larger cohorts, such as the Surveillance, Epidemiology, and End Results database, are necessary for more decisive results.

Conflicts of Interest

The authors have no financial conflicts of interest.

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