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Original article

A pooled multisite analysis of the effects of atopic medical conditions in glioma risk in different ethnic groups

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ABSTRACT

Purpose: The incidences of atopic conditions (allergies, asthma, or eczema) and glioma vary by ethnicity. Atopic conditions are inversely associated with gliomas. We conducted a pooled multisite study investigating the associations of atopic conditions with glioma in different race/ethnicity groups.
Methods: Using glioma cases and healthy controls, unconditional logistic regression was conducted to assess the associations of atopic conditions with glioma separately in white, black, Asian, and Hispanic subpopulations. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.
Results: Glioblastoma multiforme cases were less likely than controls to report a history of atopic conditions in whites (OR = 0.46, [95% CI, 0.38–0.54]) and Asians (OR = 0.27, [95% CI, 0.10–0.73]). The same trend was seen when looking at glioma cases of all histologies. An inverse association was not seen in blacks for glioblastoma multiforme or all histologies combined.
Conclusions: The inverse association between glioma and atopic conditions may vary by ethnicity due to a difference in the biology of atopic conditions in different ethnicities but may be due to chance because of the limitations of small nonwhite sample sizes.

Introduction

The broad category of glioma represents 30% of all primary brain tumors. Glioblastoma multiforme (GBM), a highly aggressive form of glioma, accounts for 54% of gliomas. Less than 5% of GBM patients are still alive at 5 years after diagnosis [1]. The etiology of glioma is not well established. The only environmental factor consistently associated with increased glioma risk is exposure to ionizing radiation [2,3]. Thus, identifying other risk factors for this cancer is crucial.

An inverse association of glioma risk with atopic medical conditions has been consistently reported in the literature, with odds ratios (ORs)/relative risks ranging from 0.5 to 0.7 [4-8]. A meta-analysis using several of these studies gave a combined relative risk of 0.61 (95% confidence interval [CI], 0.55–0.67) for allergy, 0.68 (95% CI, 0.58–0.80) for asthma, and 0.69 (95% CI, 0.58–0.82) for eczema [7]. Previous studies using the data presented here have also confirmed that allergies, asthma, and other related medical conditions appear to be inversely associated with glioma risk [7-9].

The association between atopic conditions and glioma may be complex, as studies assessing the association of atopic conditions in conjunction with other possible risk factors show mixed results. A recent study showed that antihistamine use was significantly associated with glioma risk among individuals reporting a history of allergies/asthma but not in those without this history. In this same study, in individuals without allergies/asthma, a history of chickenpox was strongly protective against glioma risk, whereas among individuals with allergies/asthma, the OR was in the opposite direction, although statistically insignificant [10]. Additionally, associations may not be consistent among histologic types. A pooled case-control study found that risk of oligodendrogliomas was not reduced because of allergies alone [11]. Finally, timing of atopic conditions may also have an impact on glioma risk. A recent brain tumor study found that inverse associations with asthma and

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hay fever strengthened with increasing age of allergy onset and weakened with longer time since onset [12].

Glioma incidence rates vary by ethnicity, with whites holding the highest rates [13,14]. Studies have investigated whether there is a genetic component to the differences between ethnicities in glioma biology with conflicting results [14-16]. The prevalence of atopic conditions also varies between ethnicities, although the causes of these differences are unclear [17]. There are studies suggesting there are associations between gene polymorphisms and the presence of atopic conditions [18-20]. Thus, the associations between atopic conditions and different ethnicities may be biologically based. However, these associations may also be due to environment rather than being inherently due to ethnicity [21,22]. Whether or not the association between atopic conditions and glioma varies by ethnicity was recently evaluated. This study found no differences in rate ratios between blacks and whites. It should be noted that this study included brain tumors other than glioma, although the majority were stated to be gliomas. Additionally, this study excluded females [23].

To evaluate the associations between atopic conditions and glioma in whites, blacks, Hispanics, and Asians in a study sample with adequate statistical power, we created pooled data obtained from three separate institutions and populations.

Materials and methods

Data were obtained from three separate case-control studies of glioma risk factors conducted by the University of Illinois at Chicago (UIC)/Duke, the University of Texas MD Anderson Cancer Center (MDACC), and the University of California, San Francisco (UCSF). Institutional Review Board approvals were obtained from all institutions.

Study population

UIC/Duke

Hospital-based glioma cases were identified from Duke and North Shore University Health System during the period of August 2003 to April, 2008 with a pathologically confirmed new diagnosis with the following International Classification of Diseases (ICD) codes: (ICD-O-3 sites C70.0-C72.9 and C75.1-C75.3) of GBM (ICD-O-3 histology codes 9440–9442), astrocytoma (9400–9411 and 9420–9421), or oligodendroglioma (9450–9460). Patients who were aged 18 years or older, English speaking, and United States residents were eligible for recruitment. After screening ($n = 1712$), 1039 were determined as eligible to participate. Seven hundred forty-one patients consented to participate (participation rate = 71%). Among those who consented, 429 (41% of eligible) completed the self-report surveys as of August 18, 2008. Clinic-based controls were recruited from patients seen at Duke University (96% from orthopedic clinics and 4% from other clinics) and North Shore University Health System (from neurology clinics). Clinic controls were aged 18 years or older, had to reside in the United States, and could not have had a brain tumor or history of a neurodegenerative disease, and were frequency matched to cases by age (10-year interval), gender, and race/ethnicity. Subjects who consented to participate were asked to complete a web-based or telephone survey that included information on demographics, personal and family medical history, as well as occupational, residential, dietary, and numerous potential environmental exposures.

MD Anderson Cancer Center

Using population-based methods, cases consisted of adults over the age of 18 years with newly diagnosed, pathologically confirmed glioma (ICD-O-3 codes 9380-9481) identified in the MDACC Neuro-Oncology clinic between January 2001 and January 2006 who live in several counties around Houston, Texas. Controls were obtained through a contracting company by random-digit dialing in the same geographic areas as the cases and were frequency matched to cases on age (within 5 years), race/ethnicity, and sex. The participation rate was 77% for cases and 53% for controls. Questionnaires were used to conduct detailed in-person or telephone interviews for cases, their proxies or controls through which data on demographic factors, health characteristics, medications, reproductive factors, and familial attributes [24].

University of California, San Francisco

Study subjects were recruited by population-based methods in the San Francisco Bay Area from 1997 to 2004. Cases included all individuals diagnosed with pathologically confirmed glioma (ICD codes 9380 to 9481) and were identified via rapid case ascertainment methods using the Northern California Cancer Registry. All cases and controls were 20 years of age or older. Population-based controls were selected through random-digit dialing and frequency matched to cases by age, race, and gender. Subjects or their proxies completed a detailed in-person interview including history of allergies. Data were also collected on demographic factors, health characteristics, medications, and reproductive factors [20,25]. The participation rate was 75% for cases and 73% for controls.

Pooled study population

The UIC/Duke data included 697 cases and 614 controls. Four cases and one control from this data set were deleted from the analysis due to missing responses for presence of an atopic condition. The final UIC/Duke data used for the pooled analysis had 693 cases and 613 controls. The UCSF data included 939 cases and 934 controls. Four cases and three controls from this data set were deleted from the analysis due to missing responses for presence of an atopic condition. The final UCSF data used for pooled analysis included 935 cases and 931 controls. The MDACC data included 622 cases and 662 controls. No cases or controls were excluded from the MDACC data. Seventy-two percent of the UCSF case data ($n = 673$) was obtained through self-report, and 91.4% of the MD Anderson case data ($n = 569$) was obtained through self-report.

The UIC/Duke contributions were as follows: cases: 93.1% white ($n = 645$), 2.3% black ($n = 16$), and 4.6% other ($n = 32$), controls: 87.0% white ($n = 533$), 8.0% black ($n = 49$), and 5.1% other ($n = 31$). The MD Anderson contributions were as follows: cases: 86.0% white ($n = 535$), 3.9% black ($n = 24$), 8.0% Hispanic ($n = 50$), 1.1% Asian ($n = 7$), and 1.0% other ($n = 6$), controls: 87.7% white ($n = 579$), black 6.7% ($n = 44$), 3.3% Hispanic ($n = 22$), 1.5% Asian ($n = 10$), and 1.0% other ($n = 7$). The UCSF contributions were as follows: cases: 78.2% white ($n = 731$), 3.6% black ($n = 34$), 8.0% Hispanic ($n = 75$), 7.1% Asian ($n = 66$), and 3.1% other ($n = 29$), controls: 78.5% white ($n = 731$), 4.3% black ($n = 40$), 7.6% Hispanic ($n = 71$), 7.9% Asian ($n = 73$), and 1.7% other ($n = 16$).

Table 1
Description of study populations and prevalence of atopic conditions*

Institution	Definition of atopic conditions	Prevalence of atopic conditions in cases	Prevalence of atopic conditions in controls
UCSF	Personal history of asthma or allergies	710/935 (75.9%)	800/931 (85.9%)
UIC/Duke	History of allergies, asthma and eczema)	101/693 (16.3%)	223/613 (33.8%)
MDACC	Personal history of asthma or allergies	251/622 (36.6%)	308/662 (50.8%)

* UCSF, UIC/Duke, and MDACC and pooled study of all institutions combined.