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Reduced Allergy and Immunoglobulin E among Adults with Intra-cranial Meningioma Compared to Controls

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Abstract

Meningioma, the most frequent tumor in the central nervous system, has few recognized risk factors. We explored the role of allergies in a population-based case-control consortium study of meningioma in five geographic areas. We also studied serum levels of a marker of atopic allergy (IgE) in a subset of study participants, a first for a study on meningioma. Participants (N = 1,065) with surgically resected, pathologically confirmed meningioma and controls (N = 634) selected via random-digit dialing were recruited and interviewed. Cases were less likely than controls to report history of physician-diagnosed allergy [odds ratio (OR) = 0.64; 95% confidence interval (95% CI): 0.51 – 0.80]. Also, cases (N = 295) had lower total serum IgE than controls [N = 192; OR = 0.85, 95% CI: 0.75–0.98 for each unit of Ln(IgE)]. Similar to glioma and cancers at several other sites, meningioma appears to have an inverse relationship with history of allergies and a biomarker of atopic allergy. Since some common opposing predisposition or developmental processes for allergy and meningioma may exist, further research into immune processes that can affect the incidence and natural history of meningioma is warranted.

Keywords

Meningioma; epidemiology; risk factors; neurosurgery; brain tumor; genetics; immune factors

Introduction

Meningiomas are the most frequently diagnosed primary brain and central nervous system tumor accounting for 34% of brain tumors in the US (2002–2006) [1]. Risk factors for meningioma remain relatively unexplored with ionizing radiation exposure to the head being the only established environmental risk factor [2, 3]. Gliomas, the second most common subgroup of brain tumors, have been consistently inversely associated with history of allergy

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and allergy-associated IgE [reviewed in [4]], indicating that allergy or related immune factors may be protective for glioma. Allergy history has also shown inverse associations with risk of cancers of the colon, larynx, esophagus, oral cavity, pancreas, stomach, uterine, cervix, and non-Hodgkin lymphoma [5, 6], suggesting that anti-cancer immune mechanisms related to allergy may be a prevalent phenomenon. However, allergy history has demonstrated a positive association with risk of bladder cancer, lung, prostate, lymphoma, and myeloma, although results have not been completely consistent across all studies [5].

The relationship between meningioma and allergies is to date preliminary but consistent: one case-control study, from the United Kingdom branch of the INTERPHONE study and including 475 cases and 1,716 controls, demonstrated significantly reduced risk with allergies [OR = 0.76; 95% CI: 0.61–0.96 [7]], while several others demonstrated a reduced but non-significant risk with odds ratios ranging from 0.87 to 0.98 [8–11]. For this report, we evaluated whether self-reported allergy history and total serum IgE, a biomarker of atopic allergy, were associated with meningioma case status in a multicenter case-control study. Compared to previous studies, this study has a larger size, population-based recruitment method specifically for meningioma, and a biomarker of atopic allergy.

Materials and Methods

Study subjects

Eligible cases included all persons aged 20 to 79 with newly diagnosed, pathologically confirmed, intra-cranial meningioma among residents of the states of Connecticut, Massachusetts, and North Carolina as well as the Alameda, San Francisco, Contra Costa, Marin, San Mateo, and Santa Clara counties of California, and the Brazoria, Fort Bend, Harris, Montgomery, Chambers, Galveston, Liberty, and Waller Counties of Texas, from May 1, 2006 to December 12, 2009. Cases were identified through the Rapid Case Ascertainment (RCA) systems at most sites (Connecticut, Massachusetts, North Carolina, and California), and through review of hospital pathology departments and statistical-based tumor registries at sites without a formal RCA mechanism (Texas). Controls were selected by random-digit-dialing methods by an outside consulting firm (Kreider Research) and were frequency-matched to cases by five-year age interval (except for the youngest group which was 20–40 years), sex, and state of residence. Cases or controls with a previous history of meningioma and/or a brain lesion of unknown diagnosis were excluded. The study, consent forms and data collection instruments were approved by the Institutional Review Boards at the Yale University School of Medicine, Brigham and Women's Hospital, the University of California at San Francisco, the M.D. Anderson Cancer Center, and the Duke University School of Medicine.

We contacted physicians of eligible cases in accordance with each site's Institutional Review Board's requirements to obtain approval to approach each case. Cases approved for contact by their physicians and controls identified by Kreider were sent a letter of introduction. Approximately 1–2 weeks after mailing the letters a trained interviewer contacted the potential study participant by telephone to administer the interview, or schedule it for a future date. Oral consent for study participation was obtained at the time of the telephone interview. Concurrently, written consents for specimen collection and medical release forms were also reviewed over the phone and participants were asked to sign, date, and mail forms to the study central office at Yale University prior to further contact for blood or saliva. The same interviewers conducted interviews for both cases and controls, and interviews averaged 43 minutes. The questionnaire included detailed questions about family history of cancer, reproductive factors including pregnancy and menstrual history, exogenous hormone history, demographics, medical history including history of allergy, and exposure to ionizing radiation, smoking, and alcohol consumption. Allergy was recorded as

positive only if the study subject answered yes to "*Did a doctor or other medical practitioner ever tell you that you had allergy?*" Interviewers were instructed to probe the study participant further to ensure that a "yes" answer for allergy was confirmed by prescription medication and/or physician diagnosis. Additional questionnaire information used for the current analysis included basic demographic information, and history of smoking, asthma, and eczema. A licensed phlebotomist obtained blood and/or saliva specimens for laboratory analysis at a home visit, which occurred subsequent to the interview.

We identified 1,990 eligible cases and 1,652 eligible controls for this analysis. Ninety-three percent of eligible cases had a consenting physician. Among cases with a consenting physician, 60% participated in the interview portion of the study, while 54% of eligible controls participated in the interview. Allergy history was therefore available for 1065 cases and 634 controls. Ninety percent of interviewed cases and 74% of interviewed controls agreed to provide a blood or saliva specimen. Blood samples for IgE testing were available for 295 cases and 192 controls.

IgE testing

Total IgE was assessed using Phadia Diagnostics ImmunoCAP assay (Portage, MI) as previously described [12]. Briefly, 40 uL of serum were incubated on the mix of allergens or anti-IgE antibodies bound to solid-phase ImmunoCAP. Incubations with enzyme-labeled antibodies against the heavy chain (constant) for total IgE were followed by incubations of developer and stop solutions, and measurements were made on a UniCAP 100. IgE was analyzed as a continuous variable, and also as a categorical variable using clinically-accepted cutoffs: IgE levels of 100 kilounits/liter (kU/L) are clinically "elevated," IgE levels of 25 to 100 (kU/L) are "borderline," and IgE levels of <25 (kU/L) are "normal."

Statistical Analysis

For the current analysis, we constructed two datasets. First, we analyzed the subset of cases and controls with available blood for IgE testing. Second, we used our full set of available cases and controls with questionnaire data to ensure that the subset with serologic testing was equivalent to the larger series, and also to gain better power for questionnaire-derived variables. Descriptive statistics including T-tests and chi-square tests were used to examine the association between the risk of meningioma and independent covariates. Unconditional logistic regression was used to provide maximum likelihood estimates of odds ratios (ORs) (adjusted and unadjusted) with 95% confidence intervals (CIs) using the statistical package PC-SAS [13]. For all analyses, as indicated in the tables, odds ratios were adjusted for age (continuous), smoking (2 levels, <100, and ≥100 cigarettes or more in a lifetime), gender, and race (white/non-white). We also adjusted odds ratios by a measure of socioeconomic status (SES). Approximately 16% of our study population did not provide income information. Education level (4 levels) and income (5 levels) were correlated (Spearman's r = 0.33, P < 0.0001), and we chose to adjust on education level only (4 levels). Concordance and kappa measures were also calculated in SAS.

Results

Study Population

Cases and controls were well-matched on age and ethnicity, and those from the subset with blood collection were not significantly different from the larger dataset with regard to age, gender, smoking, or any of the variables of interest for this analysis, *i.e.*, prevalence of allergy, asthma, eczema, or smoking (Table 1). We had 1.6 times as many cases as controls because of the delayed recruitment of controls in our study relative to cases necessary to maintain our matching scheme. Cases were less likely than controls to report history of

health provider-diagnosed allergy (23% of cases versus 33% of the controls, P < 0.0001, Table 1). Allergies were also related to demographic variables including income and education (Table 1).

Case and Control Comparison for Allergies and IgE

Age, gender, smoking, race, and education-adjusted odds ratios for allergies for cases compared to controls was 0.64 (95% CI: 0.51–0.80, P<0.0001, Table 2). Cases also were less likely than controls to report histories of asthma (adjusted OR = 0.65; 95% CI: 0.50–0.86, P = 0.003), but not eczema (Table 2). Odds ratios for these same variables were consistent among the subset of subjects from which blood was obtained (OR = 0.64, 0.51, and 0.66 for allergies, asthma, and chicken pox, see Table 2); both allergy and asthma were significant (P = 0.03 and 0.01, respectively).

IgE levels and Demographics

IgE values were natural log (Ln) transformed to approximate a normal distribution (as in reference [12]). Mean IgE levels were different between cases and controls (P = 0.02, Table 3). In adjusted analyses, IgE was lower among cases compared to controls when assessed as a continuous variable [OR = 0.85 for each unit Ln(IgE); 95% CI: 0.75–0.98], and in clinically-relevant categories (Table 2); however, statistical significance was not reached for the latter. When split into quartiles, the lowest quartile of IgE (0 to 9.01 kU/L) had a gender, race, smoking, age, and education adjusted OR = 0.64 (95 % CI: 0.37–1.13, P = 0.01) when compared to the highest quartile (>66.65 kU/L) as a reference (data not presented in Tables). Mean levels of Ln(IgE) were 17% lower in female cases than male cases (P = 0.003) but only 10% lower in female controls compared to male controls (P = 0.13). When stratified by gender, the odds of reporting allergies was lower in meningioma cases in both females and males (OR = 0.62 and 0.69, respectively, in the full dataset). However, IgE was only significantly lower in female cases compared to female controls (for females, adjusted OR = 0.80 for each unit Ln(IgE), 95% CI: 0.67–0.95, P = 0.01; for males, adjusted OR = 0.98 for each unit Ln(IgE), 95% CI: 0.78–1.22, P = 0.86, data not presented in Tables).

History of clinician-diagnosed allergy and IgE levels displayed limited concordance with each other, with Kappa values of less than 0.1 in both cases and controls (Table 4). Because of this, we evaluated whether reported allergies and IgE levels were reflecting different phenomena. We stratified the data by using study subjects that did not report allergy and with normal IgE as a control, we calculated odds ratios for those without allergies but with borderline/high IgE, and for the normal and borderline/high IgE groups *with* allergies (Table 5). The odds of being a case was about two-fold lower for those with allergies, and IgE levels did little to further reduce the magnitude of the odds ratio (i.e., comparing the OR of 0.53 to 0.54, Table 5).

Discussion

Our data indicate that allergies, or associated immune phenomena, are less frequent among individuals who are diagnosed with meningioma, compared to controls. Serum IgE levels, a biological marker of atopic allergy, are also lower, providing support to the questionnaire-derived data. The association for IgE appeared to be stronger for females than males. Self-reported physician-diagnosed allergies and IgE were poorly concordant with each other, suggesting that they may be indirectly related to each other via an immunomodulatory mechanism that protects from meningioma and promotes allergy.

Several mechanisms have been proposed to explain the link between allergy and cancer, one or more of which may apply to meningioma. The characterization of such a mechanism may

help to identify those persons most susceptible for the disease, promote the development of early detection methods, and/or assist in the development of anti-meningioma therapies based on immune rejection of the tumor. One mechanism is commonly called “immune surveillance” which posits that active immune systems that are highly allergic may also be more competent in recognizing and responding against nascent tumors which are recognized as foreign [14]. Other theories posit a more specific mechanism related to allergy, such as the promotion of an active immune rejection of the tumor based on activation of macrophages, mast cells, and eosinophils, which are characteristics of allergy [15]. Some cancers and in particular intracranial gliomas, are highly adept at suppressing specific cell-mediated anti-tumor immune mechanisms via the expression of immunosuppressive cytokines, and decoy and death receptors [16–18]. Our current data do not illuminate on particular mechanisms for the role of allergies in meningioma but illustrate this as a potentially fruitful future research area.

One question that may arise is the accessibility of meningioma to the immune system. Meninges exist only partially behind the blood brain barrier, as significant permeability exists to contrast agents. Meningioma tumors themselves are highly vascular and completely lack capillaries capable of establishing the blood-brain barrier, and are supplied predominantly by the dural vessels [19–21]. Both nascent meningeal neoplasms and the mature tumors are therefore far more exposed to the normal immune repertoire, in contrast to gliomas and other CNS tumors which must form, in their early stages, within the restricted environment behind the blood brain barrier. Meningioma, with a relatively benign and differentiated phenotype compared to glioblastoma, may evade immune recognition via the fact that tissue phenotype more closely approximates normal arachnoid fibroid tissue, and the encapsulated tumor does not elicit cellular invasion or destruction. Meningiomas do, however, express autoantigens that can be recognized as foreign tissue to the immune system [22, 23]. This observation, combined with our current results (significant deficit of reported allergy and biologically measured IgE among cases), suggest that immune recognition of the tumor combined with appropriate activation may be helpful in treatment and prevention modalities for meningioma, and aspects of immune recognition of meningioma may provide suitable targets for early detection.

IgE levels were found to be related to several demographic/behavior variables in the expected directions – including gender (higher in males), ethnicity (lower in whites), and smoking (higher in smokers). We note that gender differences in IgE levels were more extreme among cases (17% difference, P = 0.003) than controls (10% difference, P = 0.13). The IgE assay is highly quantitative with an intra-class correlation coefficient of 0.99 in our laboratory [24], so this difference is likely to be genuine. Females exhibited a strong case-control difference with IgE (OR = 0.80, P = 0.01), while males were largely null (OR = 0.98). Whether gender-specific immune factors can account for some of the large 2:1 gender bias in meningioma rates [3] cannot be answered with these data, but is an intriguing point for further study. As allergies are more common in female adults than males, with possible influence from hormones [25], it is not likely that allergy plays a role effecting the absolute rate difference between the genders.

Several epidemiology studies have examined meningioma and the role of allergies. The meningiomas were often collected with other central nervous system tumors including glioma. Nearly all of these studies showed *reduced* (though not statistically significant) odds ratios indicating an inverse relationship consistent with the data in the current report [8–11, 26]. Several prior studies had an issue with sufficient power (small sample size) but in one study with a relatively large sample (N = 1,201), only eczema was significantly inversely related to meningioma status (OR = 0.74; 95% CI: 0.60–0.91) but not overall allergy (OR = 0.87, 95% CI: 0.66–1.44) [11]. While eczema was not significantly related to meningioma in our

study, it is interesting to note that eczema is typically mediated by non-atopic (ie., non-IgE mediated) mechanisms. This result in Wigertz et al. [11], agrees closely with another large multinational study (N = 319 meningiomas) that demonstrated an OR of 0.89, 95% CI: 0.65–1.22 [8]. The definition of "allergy" is changeable in various questionnaire instruments: most require allergy diagnosis to be physician defined, resulting in prevalence of around 20–40% [8]. Self-reported, self-diagnosed allergies can demonstrate prevalence up to 85% [27]. Our current analysis required diagnosis by a doctor or health practitioner, and we found that the prevalence of allergies was 33% among controls. One prior study showed an overall significant result with regards to allergy and meningioma (OR = 0.76; 95% CI: 0.61 – 0.96) [7]. Although this study from the United Kingdom combining two catchment regions did not specify "physician-diagnosed" allergy, the allergy prevalence of 38% among controls was similar to ours. Interestingly, Schoemaker *et al.*, captured data on age of allergy onset and found that childhood onset allergies exhibited the most risk reduction with odds ratios of 0.43, 0.50, and 0.46 for asthma, hay fever, and eczema, respectively [7]. The fact that childhood-onset allergies are more likely atopic than adult allergies is not entirely consistent with the results in the current analysis which points to the most risk reduction for non-atopic allergy. Further research is necessary to understand the finer points regarding mechanism.

Our study is subject to several potential sources of bias or measurement error, which may have affected our results. Because our cases are obtained largely via population-based registries, and there is virtually no early mortality, ascertainment bias of cases is not likely a problem. In addition, the subset of subjects that provided blood was highly similar to the larger set of subjects (both cases and controls, Table 1), bolstering confidence in the IgE results. Since serum levels were obtained after diagnosis and treatment of meningioma, it is possible that "reverse causality" played a role – *i.e.*, that the disease itself or treatment modalities induced suppression of IgE levels. We consider this unlikely for several reasons – first, meningiomas unlike gliomas are not noted for immunosuppressive characteristics. IgE measurements are only taken at one time point and are not likely to adequately represent a life history of atopic allergy. This may be one reason for the poor concordance of self-reported, physician-diagnosed allergy and IgE. Also, treatment modalities for meningioma are not known to affect immune parameters; all of our cases have had surgical intervention, but none were subjected to radiation or cytotoxic chemotherapy. Bias in information can also result from control selection. Controls recruited via random-digit dialing tend to be more highly educated, have higher income, and therefore higher socioeconomic status than cases recruited from the same population. There was some evidence for this phenomenon in the current study regarding income and education status (Table 1), however, statistical adjustments for income did not appreciably change odds ratios for allergy and IgE in relation to meningioma (data not shown). Finally, there is a potential for recall bias. Since it is unlikely for the public to have any prior knowledge of allergies being related to meningioma, differential recall between cases and controls is unlikely. Also we note that many meningioma patients typically recover from surgery with full mental faculties, and lack of recall due to the disease is unlikely. Some lack of recall is possible in both cases and controls, which will likely be non-directional, and therefore bias results toward the null. The results are therefore likely to be robust despite potential sources of bias.

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Table 1

Demographic Characteristics and Immune Parameters for Meningioma Cases and Population Controls: Menigioma Consortium Study, 2006–2010.

	Full dataset: N = 1699					Subjects with available sera: N = 487				
N	**Case (n)**	**%**	**Controls (n)**	**%**	**p-value***	**Case (n)**	**%**	**Controls (n)**	**%**	**p-value***
1699	1065	63	634	37		295	61	192	39	
Age (yrs)										
Mean Age	57.58		56.77		0.16	58.90		57.96		0.36
Median Age	57.74		57.19			59.54		58.61		
Std err	0.353		0.469			0.637		0.818		
Std dev	11.526		11.787			10.933		11.331		
Female	785	74	417	66	0.0005	214	73	122	64	0.04
Male	280	26	217	34		81	27	70	36	
Race										
White	886	83	535	84	0.58	251	85	168	88	0.45
Non-white/Other	177	17	99	16		44	15	24	13	
Blank										
Income										
$24,999 or less	158	25	64	10		46	16	21	11	
$25,000–$49,999	188	28	76	11		52	18	23	12	
$50,000–$74,999	178	17	76	12	<0.001	58	20	23	12	0.06
$75,000–$99,999	127	12	69	11		38	13	18	9	
$100,000 or more	273	26	204	32		72	24	60	31	
Refused	89	8	39	6		21	7	5	3	
Dk**	43	4	6	1		8	3	1	1	
Blank	9	1	100	16		0	0	41	21	
Education										
Less than HS	53	5	20	3		11	4	4	2	
HS graduate/ GED	234	22	86	14		65	22	19	10	
Some college/vocational	312	29	162	26	<0.0001	89	30	47	24	<0.0001
College graduate	264	25	187	29		80	27	58	30	
Post graduate	200	19	178	28		50	17	64	33	

	Full dataset: N = 1699					Subjects with available sera: N = 487				
N	**Case (n)**	**%**	**Controls (n)**	**%**	**p-value***	**Case (n)**	**%**	**Controls (n)**	**%**	**p-value***
Refused	2	0	0	0		0	0	0	0	
Don't Know/ Blank	0	0	1	0		0	0	0	0	
Smoking										
Yes ***	503	47	316	50	0.37	142	48	92	48	0.93
No	554	52	318	50		152	52	100	52	
Dk	0	0	0	0		0	0	0	0	
Blank	8	1	0	0		1	0	0	0	
Allergy										
Yes	247	23	209	33	<0.0001	69	23	61	32	0.04
No	809	76	425	67		226	77	131	68	
Dk	0	0	0	0						
Blank	9	1	0	0						
Asthma										
Yes	138	13	114	18	0.01	33	11	35	18	0.03
No	919	86	520	82		262	89	157	82	
Dk	0	0	0	0						
Blank	8	1	0	0						
Eczema										
Yes	96	9	62	10	0.62	22	8	15	8	0.88
No	960	90	570	90		272	92	176	92	
Dk	1	0	2	0		1	0	1	0	
Blank	8	1	0	0						

* P values derived from chi-square test, comparing cases to controls.

** Dk = don't know, or declined to answer

*** 100 cigarettes or more in lifetime

Int J Cancer. Author manuscript; available in PMC 2012 October 15.

Table 2

Multivariate case/control Odds Ratios for IgE levels and medical conditions: the Meningioma Consortium, 2006–2010

		Full dataset, N=1699					Subjects tested for IgE, N=487					
		N					N					
Model		**Cases**	**Controls**	**OR**	**(95% CI)**	**P-value**	**Cases**	**Controls**	**OR**	**(95% CI)**	**P-value**	**Trend test ***
	N	1065	634				295	192				
1	Total IgE = ln(IgE)						265	145	0.85	(0.75 – 0.98)	0.02	
2	Normal						159	90	1.00			
	Borderline						93	66	0.77	(0.50 – 1.18)	0.22	0.095
	Elevated						42	36	0.65	(0.37 – 1.14)	0.13	
3	No allergies	803	425	1.00			225	131	1.00			
	Allergies	247	208	0.64	(0.51 – 0.80)	<0.0001	39	61	0.64	(0.42 – 0.97)	0.03	
4	No chicken pox	122	55	1.00			35	16	1.00			
	Chicken pox	872	554	0.70	(0.50 – 0.99)	0.04	241	166	0.66	(0.34 – 1.27)	0.22	
5	No Shingles	935	549	1.00			263	164	1.00			
	Shingles	111	80	0.79	(0.58 – 1.09)	0.15	31	28	0.65	(0.37 – 1.15)	0.14	
6	No Eczema	955	570	1.00			271	176	1.00			
	Eczema	96	61	0.95	(0.67 – 1.34)	0.76	22	15	0.93	(0.46 – 1.89)	0.85	
7	No Asthma	914	519	1.00			261	157	1.00			
	Asthma	138	114	0.65	(0.50 – 0.86)	0.003	33	35	0.51	(0.29 – 0.87)	0.01	

Each model was adjusted for gender, race, smoking, age (continuous), and education

* For "allergies" 17 subjects were deleted from total n=1699 popln for the model due to missing values
For "chicken pox" 97 subjects were deleted from total n=1699 popln for the model due to missing values
For "shingles" 25 subjects were deleted from the total n=1699 popln for the model due to missing values
For "asthma" 15 subjects were deleted from total n=1699 for the model due to missing values
For "eczema" 18 subjects were deleted from total n=1699 popln for the model due to missing values

Each model was adjusted for gender, race, smoking, age (continuous), and education

* For "LIgE & IgE_level" 1 subject was deleted from n=487 for the model due to missing values
For "allergies" 1 subject were deleted from n=487 for the model due to missing values
For "chicken pox" 29 subjects were deleted from n=487 for the model due to missing values
For "shingles" 1 subject was deleted from n=487 for the model due to missing values
For "asthma" 1 subject was deleted from n=487 for the model due to missing values

For "eczema" 3 subjects were deleted from n=487 for the model due to missing values

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Table 3

Relationship of IGE levels to Demographic and Immune Parameter Variables: The Meningioma Consortium, 2006–2010.

	N	Mean	Median	Std Err	*p-value
Case status					
Case	295	2.97	2.90	0.09	0.02
Control	192	3.29	3.26	0.11	
Female	336	2.94	2.87	0.08	0.0006
Male	151	3.44	3.43	0.13	
Race					
White	419	2.95	2.87	0.07	<0.0001
Non-white/Other	68	3.97	4.08	0.19	
Agegroups					
20–34	11	2.64	3.02	0.49	0.34
35–39	17	2.93	2.73	0.25	
40–44	34	3.25	3.10	0.23	
45–49	46	3.01	2.97	0.18	
50–54	76	2.90	2.95	0.18	
55–59	70	3.41	3.18	0.19	
60–64	86	3.22	3.34	0.19	
65–69	73	2.80	2.71	0.16	
70–74	40	3.05	3.30	0.23	
75–79	33	3.46	3.41	0.27	
80 +	1	3.13	3.13	–	
Age-category					
< 40	28	2.81	2.84	0.24	0.58
40–60	226	3.13	3.02	0.10	
60 +	233	3.09	3.14	0.10	
Income					
$24,999 or less	67	3.16	3.50	0.18	0.27
$25,000–$49,999	75	3.11	2.79	0.20	
$50,000–$74,999	81	3.15	3.28	0.17	

	N	Mean	Median	Std Err	*p-value
$75,000–$99,999	56	3.06	3.05	0.18	
$100,000 or more	132	2.95	2.93	0.12	
Refused	21				
Dk (unknown)	8				
Education					
Less than H.S	15	3.97	3.89	0.56	
H.S grad/ GED	84	2.96	2.76	0.15	
Vocational/some college	136	3.13	3.14	0.13	0.20
College grad	138	3.03	3.06	0.13	
Post graduate	114	3.12	3.00	0.14	
Allergy					
Yes	130	3.28	3.30	0.08	0.10
No	357	3.03	2.88	0.15	
Asthma					
Yes	68	3.77	3.71	0.20	<0.0001
No	419	2.99	2.90	0.07	
Eczema					
Yes	37	3.32	3.43	0.26	0.33
No	448	3.07	3.02	0.07	
Smoke (100 cigs or more in lifetime?)					
Yes	234	3.35	3.33	0.10	0.0003
No	252	2.86	2.74	0.09	

*p-values derived from one-way ANOVA comparing the means of Log IgE for the variables indicated.

Table 4

Concordance between Reported Allergy and IgE levels: The Meningioma Consortium, 2006–2010

CASES				
	Reported allergies			
	None	Any	% Concordance	κ *
Total IgE				
Normal	129	31	57	0.09
Bord/Elev	97	38		
Total		295		
CONTROLS				
	Reported allergies			
	None	Any	% Concordance	κ *
Total IgE				
Normal	65	25	53	0.07
Bord/Elev	66	36		
Total		192		

* $\kappa \geq 0.75$, excellent agreement; $\kappa = 0.40$-0.75, intermediate agreement; $\kappa \leq 0.40$, poor agreement.

Table 5

Case control Odds Ratios for IgE and Allergy using No Allergy/Normal IgE as a Reference: The Meningioma Consortium, 2006–2010

		Cases		Controls				
	IgE Level	**N**	**%**	**N**	**%**	**Odds Ratios** *	**95% CI**	**p-value**
Allergy NO	IgE (Normal)	129	44	65	34	1.00		
	IgE (Borderline/Elevated)	97	33	66	34	0.69	(0.49 – 1.09)	0.11
Allergy YES	IgE (Normal)	31	11	25	13	0.54	(0.98 – 1.01)	0.05
	IgE (Borderline/Elevated)	38	13	36	19	0.53	(0.30 – 0.95)	0.03

*adjusted for age, race, gender, smoking, and education