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Aggregation of Cancer in First-degree Relatives of Patients with Glioma

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Abstract

Background—Previous studies have been inconclusive in estimating the risk of different cancer sites among close relatives of glioma patients; however, malignant melanoma has been consistently described.

Methods—We obtained family history information from 1,476 glioma patients under age 75 who registered at M.D. Anderson Cancer Center between June 1992 and June 2006. The number of observed cancers (N=1,001) among 8,746 first-degree relatives (FDRs) were compared to the

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number expected from age-, sex-, and calendar-year specific rates from the Surveillance, Epidemiology, and End Results Program using standardized incidence ratios (SIRs).

Results—The overall SIR for any cancer was 1.21 (95% CI; 1.14 – 1.29). Among FDRs under 45 years, the overall SIR was 5.08 and for relatives >45 the overall SIR was 0.95. The SIRs were significantly elevated for brain tumors (2.14), melanoma (2.02), and sarcoma (3.83). We observed an excess of pancreatic cancer which was significantly higher only among mothers.

Conclusion—We observed an overall 21% increase in cancer among the FDRs of glioma patients, including excess cases of brain tumors and melanoma which could point to similar genetic contributions to these two malignancies. A large international linkage study is underway to examine potential genomic regions important for familial glioma.

Keywords

aggregation; cancer; glioma; first-degree relatives

INTRODUCTION

Brain cancer is lethal to 12,820 persons in the U.S. and impacts the remainder of the 18,820 Americans diagnosed with malignant brain tumors each year.(1) Previous studies have contributed little in etiologic understanding, so families of patients, in addition to the grief over the death or disability of relatives, bear anxiety about their own risk of the disease. Researchers report that brain tumors are involved in heritable syndromes such as Li-Fraumeni, neurofibromatosis (types 1 and 2), tuberous sclerosis, nevoid basal cell carcinoma syndrome, familial polyposis, and von Hippel-Lindau, but to what extent is unclear.(2) In a definitive, population-based study of malignant glioma, Li et al. (3) could find only that slightly more than half (58%) of *p53* mutation-positive patients were likely to have a first-degree relative affected with cancer.

Early studies of familial aggregation of brain tumors have been mostly inconclusive; however, recent larger studies suggest an increased risk of primary brain tumors among first degree relatives of glioma cases.(4-10) For individuals with a family history of brain tumors, the risk of developing any cancer has been reported between 1.0 - 1.8, and 1.0 – 9.0 for brain tumors.(4-8;10) Such ranges may be the result of differences in study methodologies, sample sizes, types of relatives included in the study, or in ascertainment and validation of the cancer. Although findings of familial cancer aggregation suggest a genetic etiology, such aggregation may result from shared familial exposure to environmental agents, which may challenge genetic explanations of familial cancer aggregation.

We tested the genetic explanation of family aggregation by determining whether a large group of first degree relatives (FDRs) of glioma patients showed increased incidence for cancer overall, brain tumors, and several other sites.

MATERIALS AND METHODS

Participants included 1,477 primary glioma probands, self-reported Caucasian race, U.S. or Canadian citizens, and registered at The University of Texas M. D. Anderson Cancer Center between June, 1992 and June, 2006. Each proband and/or next of kin was administered an extensive family-health questionnaire to solicit information on the presence of cancer in the proband's FDRs. When possible, we obtained medical records or death certificates for relatives who reported a possible malignancy to confirm the report. Dates of birth, death, and cancer diagnosis were verified for those diagnosed and treated at a U.S. or Canadian

hospital. Cancers were coded according to the International Classification of Diseases for Oncology [ICD-O-3] (11).

To determine excess cancers in the FDRs, we computed standardized incidence ratios (SIRs) as the ratio of the observed number of cancer cases among FDRs to the expected number using the Cohort Analysis for Genetic Epidemiology (CAGE) computer program.(12) The expected number of cancers was determined using sex, age and calendar-year specific rates from the Surveillance, Epidemiology, and End Results (SEER) Program, including population-based registry data since 1975. For reported cancer diagnoses prior to 1975, the first year of record for SEER, we used the rates for 1975 to estimate number of expected cancers. We excluded cervical carcinoma *in situ* and non-melanoma skin cancers, which are also excluded in SEER. Person-years were calculated from the date of birth to the first date of the following events: cancer diagnosis, interview, or death. Person-years were calculated to the first primary cancer because CAGE utilizes first primary cancers from SEER to compute the expected number of cancers. The SIRs for cancer among relatives were compared by proband's gender, age of glioma diagnosis, and histologic grade of glioma, and the age and sex of the FDR. The 95% confidence intervals for the SIRs were determined assuming a Poisson distribution for the observed number of cancers among FDRs.

The project was approved by the Institutional Review Board of M. D. Anderson Cancer Center. Each proband was administered a questionnaire by trained interviewers.

RESULTS

A total of 1,476 Caucasian probands (Table 1) and their FDRs were included in this analysis. This group is highly representative of the 1,907 Caucasian glioma patients seen at M. D. Anderson during that time period. All enrolled probands participated in the study; however, one proband and his FDRs were excluded because of a Li-Fraumeni-like pattern of cancers within the pedigree. Among the probands, 24% were proxy-reported. The median age of the probands at presentation was 45 years, respectively; 6% were less than 20 years old at diagnosis. Among the probands, the male to female ratio was 1.4:1, and 47% were diagnosed with a high-grade glioma.

From a total of 8,858 FDRs, 8,746 (99%) were included in this analysis, contributing 391,784 person-years of follow-up (Table 2). The 112 FDRs were excluded due to missing information needed for the analysis (year of birth, sex, or age at cancer diagnosis). Among the FDRs, 17 (0.2%) were missing sex, and 163 (2%) were missing year of birth for which we imputed using the pedigree and birth order data. A previous validation study from our group showed that self-reported cancers were 85% accurate(13); in the current analysis, 84% of validated reported cancers were in agreement with the self-report. During follow-up, 1001 cancers were observed and 825 were expected (SIR = 1.21, 95% CI: 1.14 – 1.29) among the FDRs. Overall SIRs were significantly higher among parents and siblings and non-significantly elevated for the offspring of the probands.

The data partitioned by proband's age at diagnosis showed the highest SIR in relatives of probands diagnosed with glioma under age 35; although, the SIR was elevated regardless of the proband's diagnosis age (Table 2). SIRs for all cancers were similar in relatives, regardless of tumor histology of the proband; although, FDRs of probands with anaplastic tumors had the highest SIR (Table 2). FDRs were five times as likely to develop cancer at an earlier age (<45) than expected (SIR 5.08, 95% CI: 4.49-5.74).

Table 3 shows cancer site-specific SIRs among FDRs for 15 cancers, stratified by the proband's gender and age of the FDR at diagnosis. The FDRs of both male and female probands had elevated SIR for brain tumors and sarcoma. Melanoma was more common

among relatives of male probands, and pancreatic cancer showed a borderline-significant increased SIR among relatives of male probands. Colorectal cancer incidence was elevated among relatives of female probands; however the SIR was of borderline significance. None of the other cancers showed a significant risk increase. While the increase in colorectal cancer among FDRs was not large for any one group of FDRs, the SIR was 9.78 for relatives who developed colorectal cancer at a young age (<45). This increase among young FDRs was also seen for pancreas, prostate, and stomach cancer, although these findings were based on small numbers of observed cases.

Examination of the SIRs by type of relative revealed that excess cases of brain cancer concentrated in fathers, brothers, and sisters, while the aggregation of sarcoma was among mothers and daughters (data not presented). Mothers, fathers, and sisters exhibited significant increases in melanoma, and mothers showed a significant increase pancreas cancer. Brothers had a greater occurrence of leukemia, and daughters showed no other increases at the other sites.

DISCUSSION

This analysis of cancer in FDRs of glioma patients is among the largest performed to date, apart from one study describing the Swedish population(7;8). As cancer incidence varies among Caucasians in different parts of the world, it is important to conduct well-designed cohort studies in different populations. We sought to determine whether a patient's family faced increased risk of cancer and showed that this was true for certain cancer sites and was often gender and age specific. Given that rates of glioma incidence are highest for whites and the registry data from SEER are more complete for whites, we focused on this group for the current analysis. We anticipate further analyses for our African-American (n=58) and Hispanic (n=114) probands utilizing the race/ethnic-specific rates available from SEER.

We found an overall 16-32% increase in expected cases for all malignancies in the FDRs of glioma cases. We also found an increase in the number of brain tumors among FDRs of glioma patients (SIR=2.14, 95% CI: 1.57-2.86). Malmer et al. (7;8) observed a similar SIR (2.12, 95% CI: 1.18, 3.49) among FDRs of probands with astrocytoma in Sweden. They later showed that the risk of low-grade gliomas (LGG) was highest among FDRs whose family member also had a LGG, and similarly those family members with high-grade gliomas (HGG) were at highest risk if the proband also had a HGG.(14) They reported a high risk for glioma among siblings, which we also found (SIR=2.75). Paunu et al.(15) showed a 4-fold increased incidence of CNS tumors among families that included 2 or more glioma cases. In addition, they showed that the incidence of CNS tumors was higher for relatives of late-onset glioma cases. We also observed the highest SIR for brain tumors in the FDRs of glioma probands who were diagnosed after age 35. By comparing the medical histories of FDRs of 462 glioma patients with those of 443 controls, Wrensch et al. (10) found similar family histories of cancer overall but an increased odds ratio for brain tumors (2.3, 95% CI: 1.0 – 5.8) in the proband's relatives. They concluded that a family history of brain tumors might be a risk factor for glioma. In addition, Hill et al. (6) showed that glioma patients had an increased odds of having an FDR with Hodgkin's lymphoma, stomach, colon, or prostate cancer compared to controls.

The highest SIRs among FDRs were observed for sarcoma. This is similar to the results for bone cancer by Hill et al.(6) In our study, the majority (55%) of the sarcomas were in the bone, this could account for the slightly lower SIR in our study than Hill's. We also observed a significant nearly two-fold excess of pancreatic cancer in the male proband's mothers. Although this might be a chance finding, the presence of a cancer predisposing mutation influenced by imprinting could result in an increase in pancreatic cancer in women.

Our observed increased risk of melanoma is supported by linkage of melanoma to regions of chromosome 9 (16;17), for which deletions have also been described in gliomas (18;19). The melanoma-neural system tumor syndrome in which affected families have increased risk of melanoma and astrocytomas was recently linked to loss of both *p16* and *p14* genes that are present on chromosome 9.(20) Therefore, deletion of a common tumor suppressor gene may explain the association of glioma and melanoma found in our study, with *p16* as an obvious candidate gene for further investigation in these families. Our results are comparable with studies by Malmer et al. (7) and Paunu (15) which included whole nuclear families and showed an association with melanoma.

The deficit of bladder, lung, and uterine cancers in FDRs in our study is similar to what was reported by Hill et al.(6) We found a slight increase in colorectal cancer in our cohort compared to decreases of colon and breast cancer reported by Malmer et al. (7) in a recent study from Sweden. Wrench et al. showed an increased risk of brain tumors among cases with a family history of breast cancer(10), and Hemminki et al. showed an aggregation of ependymomas, but not astrocytomas, in cases with a family history of breast cancer(5). An advantage of our study is that it comprised whole nuclear families, whereas the cohorts from the Swedish multi-generation registry excluded siblings born before 1932 and persons who died before 1961. Patients die young from diseases like glioma, which might have biased the results in those studies towards the null.(5;8)

This large study confirms that family members of glioma patients experience cancer, including brain tumors, at rates in excess of the general population, indicating that there must be genetic factors contributing to the increased risk. These data provided support to initiate the Gliogene study - an international consortium to study familial glioma. The study includes 15 research groups in North America, Europe, and Israel to characterize genes in glioma families using a genome-wide single-nucleotide polymorphism approach and conduct linkage analysis in order to identify new genomic regions or loci that could harbor genes important for gliomagenesis.

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REFERENCES

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2006. CA Cancer J Clin 2006;56:106–130. [PubMed: 16514137]
2. Bondy M, Wiencke J, Wrensch M, Kyritsis AP. Genetics of primary brain tumors: a review. J Neurooncol 1994;18:69–81. [PubMed: 8057137]
3. Li Y, Millikan RC, Carozza S, et al. p53 mutations in malignant gliomas. Cancer Epidemiol Biomarkers Prev 1998;7:303–308. [PubMed: 9568785]
4. Goldgar DE, Easton DF, Cannon-Albright LA, Skolnick MH. Systematic population-based assessment of cancer risk in first-degree relatives of cancer probands. J Natl Cancer Inst 1994;86:1600–1608. [PubMed: 7932824]
5. Hemminki K, Li X, Collins VP. Parental cancer as a risk factor for brain tumors (Sweden). Cancer Causes Control 2001;12:195–199. [PubMed: 11405324]
6. Hill DA, Inskip PD, Shapiro WR, et al. Cancer in first-degree relatives and risk of glioma in adults. Cancer Epidemiol Biomarkers Prev 2003;12:1443–1448. [PubMed: 14693735]

7. Malmer B, Gronberg H, Bergenheim AT, Lenner P, Henriksson R. Familial aggregation of astrocytoma in northern Sweden: an epidemiological cohort study. Int J Cancer 1999;81:366–370. [PubMed: 10209950]
8. Malmer B, Henriksson R, Gronberg H. Familial brain tumours-genetics or environment? A nationwide cohort study of cancer risk in spouses and first-degree relatives of brain tumour patients. Int J Cancer 2003;106:260–263. [PubMed: 12800203]
9. O'Neill BP, Blondal H, Yang P, et al. Risk of cancer among relatives of patients with glioma. Cancer Epidemiol Biomarkers Prev 2002;11:921–924. [PubMed: 12223439]
10. Wrensch M, Lee M, Miike R, et al. Familial and personal medical history of cancer and nervous system conditions among adults with glioma and controls. Am J Epidemiol 1997;145:581–593. [PubMed: 9098174]
11. World Health Organization: ICD-O-3 International Classification of Diseases for Oncology. World Health Organization; Geneva: 2000.
12. Lustabader, ED.; McLaughlin, PR. CAGE: cohort analysis for genetic epidemiology. Fox Chase Cancer Center; Philadelphia, PA: 1995.
13. Airewele G, Adatto P, Cunningham J, et al. Family history of cancer in patients with glioma: a validation study of accuracy. J Natl Cancer Inst 1998;90:543–544. [PubMed: 9539252]
14. Malmer B, Henriksson R, Gronberg H. Different aetiology of familial low-grade and high-grade glioma? A nationwide cohort study of familial glioma. Neuroepidemiology 2002;21:279–286. [PubMed: 12411730]
15. Paunu N, Pukkala E, Laippala P, et al. Cancer incidence in families with multiple glioma patients. Int J Cancer 2002;97:819–822. [PubMed: 11857361]
16. Cannon-Albright LA, Goldgar DE, Meyer LJ, et al. Assignment of a locus for familial melanoma, MLM, to chromosome 9p13-p22. Science 1992;258:1148–1152. [PubMed: 1439824]
17. Cannon-Albright LA, Kamb A, Skolnick M. A review of inherited predisposition to melanoma. Semin Oncol 1996;23:667–672. [PubMed: 8970585]
18. Bello MJ, de Campos JM, Vaquero J, et al. Molecular and cytogenetic analysis of chromosome 9 deletions in 75 malignant gliomas. Genes Chromosomes Cancer 1994;9:33–41. [PubMed: 7507698]
19. James CD, He J, Carlbom E, et al. Chromosome 9 deletion mapping reveals interferon alpha and interferon beta-1 gene deletions in human glial tumors. Cancer Res 1991;51:1684–1688. [PubMed: 1998958]
20. Randerson-Moor JA, Harland M, Williams S, et al. A germline deletion of p14(ARF) but not CDKN2A in a melanoma-neural system tumour syndrome family. Hum Mol Genet 2001;10:55–62. [PubMed: 11136714]

Table 1

Demographic and Clinical Characteristics of Glioma Probands (N=1,476)

	Number	Percentage
Age at Diagnosis		
0 – 19	94	6%
20 – 29	148	10%
30 – 39	280	19%
40 – 49	387	26%
50 – 59	337	23%
60 – 69	191	13%
70 – 76	30	2%
Mean age of probands at diagnosis (SE) = 43.7 years (0.39)		
Median age of probands at diagnosis = 45 years		
Gender		
Male	864	59%
Female	612	41%
Male:Female ratio = 1.4:1		
Number of FDR with cancer per family		
0 FDRs with cancer	667	45%
1 FDRs with cancer	563	38%
2 FDRs with cancer	194	13%
3+ FDRs with cancer	52	3.5%
Number of FDR with brain tumor (BT) per family		
0 FDRs with BT	1429	97%
1 FDRs with BT	46	3%
2 FDRs with BT	1	0.07%
Histology *		
High Grade	691	47%
Anaplastic	461	31%
Low Grade	288	20%
Other	35	2%

Anaplastic: Anaplastic forms of Astrocytoma, Ependymoma, Glioma, Mixed (Oligoastrocytoma), Oligodendroglioma

Low-grade: A strocytoma, Pilocytic Astrocytoma, Subependymal Giant Cell Astrocytoma, Ependymoma, Ganglioma, JPA, Mixed Glioma, Myxopapillary Ependymoma, Oligodendroglioma, Optic Nerve Glioma, Pleomorphic Xanthoastrocytoma, Subependymoma

Other: Astroblastoma, DNET, PNET, Glioma NOS, Unclassified Astrocytoma

*High-grade: Glioblastoma, Gliosarcoma, Ependym oblastoma

Table 2

Standardized incidence ratios (SIRs) by proband characteristics (age, tumor histology), relative age at diagnosis, and relationship for all cancers in first-degree relatives

	Number	P-Y	Obs	Exp	SIR	95% CI
Proband Age						
Proband less than 35 years	1664	59031	108	74.80	1.44	1.18-1.74
Proband between 35 and 50 years	3327	139382	356	269.31	1.32	1.19-1.47
Proband greater than 50 years	3755	193371	537	481.37	1.12	1.02-1.21
Proband's histology						
High Grade	4377	209204	564	480.39	1.17	1.08-1.28
Anaplastic	2646	112745	277	216.83	1.28	1.13-1.44
Low grade	1555	64060	148	118.99	1.24	1.05-1.46
Relative's Age						
Relative less than 45 years	4514	123334	262	51.55	5.08	4.49-5.74
Relative >= 45 years	4232	268450	739	773.93	0.89	0.89-1.03
Relationship						
Fathers	1418	90451	352	297.98	1.18	1.06-1.31
Mothers	1436	93487	341	295.22	1.16	1.04-1.28
Siblings	3345	148941	277	210.17	1.32	1.17-1.48
Offspring	2547	58905	31	22.12	1.40	0.95-1.99
TOTAL	8746	391784	1001	825.48	1.21	1.14-1.29

Cancer Epidemiol Biomarkers Prev. Author manuscript; available in PMC 2010 November 30.

Table 3

Cancer specific standardized incidence ratios (SIRs) for first-degree relatives by gender of proband

	Total				Male Proband				Female Proband				FDR <45 yrs old				FDR ≥45 yrs old			
	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI
All Malignancies	**1001**	**825.48**	**1.21**	**1.14-1.29**	**610**	**492.71**	**1.24**	**1.14-1.34**	**391**	**332.77**	**1.17**	**1.06-1.30**	**262**	**51.55**	**5.08**	**4.49-5.74**	739	773.93	0.95	0.89-1.03
Bladder	**29**	**46.16**	**0.63**	**0.42-0.90**	**17**	**27.96**	**0.61**	**0.35-0.97**	12	18.20	0.66	0.34-1.15	**3**	**0.56**	**5.37**	**1.08-15.70**	**26**	**45.6**	**0.57**	**0.37-0.84**
Sarcoma	**9**	**2.35**	**3.83**	**1.75-7.26**	**5**	**1.39**	**3.61**	**1.16-8.41**	**4**	**0.97**	**4.14**	**1.11-10.60**	**5**	**0.75**	**6.69**	**2.16-15.61**	4	1.61	2.49	0.67-6.38
Brain	**46**	**21.45**	**2.14**	**1.57-2.86**	**27**	**12.73**	**2.12**	**1.40-3.09**	**19**	**8.71**	**2.18**	**1.31-3.41**	**21**	**3.58**	**5.87**	**3.63-8.97**	25	17.87	1.40	0.91-2.07
Breast (Female)	160	150.31	1.06	0.91-1.24	98	88.94	1.10	0.89-1.34	62	61.4	1.01	0.77-1.29	**38**	**6.40**	**5.93**	**4.20-8.15**	122	143.91	0.85	0.70-1.01
Colorectal	104	85.89	1.21	0.99-1.47	58	51.94	1.12	0.85-1.44	46	33.96	1.35	0.99-1.81	**9**	**0.92**	**9.78**	**4.46-18.56**	95	84.97	1.12	0.90-1.37
Hodgkin's	15	12.03	1.25	0.70-2.06	11	7.07	1.56	0.78-2.78	4	4.96	0.81	0.22-2.07	**9**	**3.48**	**2.58**	**1.18-4.91**	6	8.54	0.70	0.26-1.53
Leukemia	38	32.74	1.16	0.82-1.59	26	19.6	1.33	0.87-1.94	12	13.14	0.91	0.47-1.60	**20**	**4.00**	**5.01**	**3.06-7.73**	**18**	**28.74**	**0.63**	**0.37-0.99**
Lung	**109**	**145.41**	**0.75**	**0.62-0.90**	**65**	**87.64**	**0.74**	**0.57-0.95**	44	57.76	0.76	0.55-1.02	**4**	**1.03**	**3.90**	**1.05-9.98**	**105**	**144.38**	**0.73**	**0.59-0.88**
Melanoma	**72**	**35.69**	**2.02**	**1.58-2.54**	**55**	**21.08**	**2.61**	**1.97-3.40**	17	14.61	1.16	0.68-1.86	**30**	**5.11**	**5.88**	**3.69-8.39**	42	30.59	1.37	0.99-1.86
NHL	30	37.84	0.79	0.53-1.13	21	22.58	0.93	0.58-1.42	9	15.25	0.59	0.27-1.12	**10**	**3.25**	**3.07**	**1.47-5.65**	**20**	**34.58**	**0.58**	**0.35-0.89**
Pancreas	32	23.34	1.37	0.94-1.94	21	14.14	1.49	0.92-2.27	11	9.2	1.20	0.60-2.14	**2**	**0.14**	**14.20**	**1.59-51.27**	30	23.20	1.29	0.87-1.85
Prostate	86	96.40	0.89	0.71-1.10	55	58.39	0.94	0.71-1.23	31	38.01	0.82	0.55-1.16	**2**	**0.05**	**44.15**	**4.96-159.39**	84	96.35	0.87	0.70-1.08
Stomach	17	18.58	0.91	0.53-1.46	6	11.31	0.53	0.19-1.16	11	7.27	1.51	0.75-2.71	**5**	**0.19**	**26.22**	**8.45-61.19**	12	18.39	0.65	0.34-1.14
Thyroid	12	16.4	0.73	0.38-1.28	6	9.64	0.62	0.23-1.35	6	6.77	0.89	0.32-1.93	7	2.96	2.36	0.95-4.87	**5**	**13.44**	**0.37**	**0.12-0.87**
Uterine	**27**	**40.76**	**0.66**	**0.44-0.96**	16	24.44	0.65	0.37-1.06	11	16.32	0.67	0.34-1.21	**14**	**0.61**	**23.14**	**12.64-38.83**	**13**	**40.15**	**0.32**	**0.17-0.55**

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