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CLINICAL STUDY - PATIENT STUDY

Incidence of first primary central nervous system tumors in California, 2001–2005

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Abstract We examined the incidence of first primary central nervous system tumors (PCNST) in California from 2001–2005. This study period represents the first five years of data collection of benign PCNST by the California Cancer Registry. California's age-adjusted incidence rates (AAIR) for malignant and benign PCNST (5.5 and 8.5 per 100,000, respectively). Malignant PCNST were highest among non-Hispanic white males (7.8 per 100,000). Benign PCNST were highest among African American females (10.5 per 100,000). Hispanics, those with the lowest socioeconomic status, and those who lived in rural California were found to be significantly younger at diagnosis. Glioblastoma was the most frequent malignant histology, while meningioma had the highest incidence among benign histologies (2.6 and 4.5 per 100,000, respectively). This study is the first in the US to compare malignant to benign PCNST using a population-based data source. It illustrates the importance of PCNST surveillance in California and in diverse communities.

Keywords Brain and other central nervous system neoplasms · Epidemiology · Cancer incidence · Ethnic groups · Health disparities

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Introduction

Central nervous system (CNS) cancers are neoplasms of the neuroepithelial tissue and membranous coverings of the brain and spinal cord, tumors of the pituitary gland, and cancers arising from the cranial nerves and CNS hematopoietic cells. Compared to other forms of cancer, PCNST are rare. In California, these cancers generally represent only 1.5% of incident cancer cases and 2.6% of cancer deaths [1]. Despite these statistics, PCNST are an important source of cancer morbidity and mortality and generate intense interest from clinicians, researchers, the public health community, and the general public.

Many population-based epidemiologic studies of PCNST are methodologically inconsistent and potentially unreliable. CNS cancers are a heterogeneous group of diseases, comprising many histopathological forms and encompassing numerous gross anatomic sites. Their histopathological progression may be benign, malignant, or of uncertain tumor behavior. Although CNS tumor classification was standardized by the World Health Organization (WHO) in 1993, there remains variation in the organization of histologic codes for presentation and in the creation of histology sub-groups [2]. Coding trends by neuropathologists change with time, resulting in erroneous incidence fluctuations [3]. Furthermore, many epidemiologic studies

are retrospective, have small sample sizes, or lack broad ethnic, cultural, and socioeconomic demographics.

With the enactment of federal Public Law 107-260 in 2004, the Benign Brain Tumor Cancer Registries Amendment Act, all state and metropolitan cancer registries are required to collect data on benign PCNST and those of uncertain tumor behavior [4]. Prior to 2004, many state and metropolitan cancer registries voluntarily collected these data, including the California Cancer Registry (CCR), which has been collecting data on benign and uncertain tumor behavior CNS tumors since 2001. In this study, we examined the incidence of first primary PCNST collected by the CCR from 2001–2005. For benign PCNST, this study period represents the first five years of data collection in California and the first population-based study of benign PCNST in the country. With a population of 36.5 million, California contains over 12% of the U.S. population, with broad ethnic, cultural, and socioeconomic representation [5]. Delineating the epidemiology of PCNST in California will create a backdrop for future basic, translational, clinical, and public health research and can be used as a baseline for monitoring incidence trends over time.

Materials and methods

Case identification

Cases used in these analyses were identified using the California Cancer Registry (CCR), a population-based registry composed of eight regional registries collecting cancer incidence and mortality data for the entire population of California. In 1985, California state law mandated the reporting of all newly diagnosed cancers in California, and statewide implementation began January 1, 1988. This state law was amended to require the collection of benign and uncertain behavior brain and other nervous system tumors beginning January 1, 2001. Cases are reported to the Chronic Disease Surveillance and Research Branch of the California Department of Public Health from all hospitals and any other facilities providing care or therapy to cancer patients residing in California (approximately 2,500 facilities) [6]. Cases diagnosed outside of California, at autopsy, or from death certificates were excluded.

For this study, first primary cases of malignant, benign and uncertain tumor behavior brain and other nervous system tumors diagnosed between January 1, 2001 and December 31, 2005 and reported to the CCR as of October 2007 were used [7]. Only cases diagnosed or treated at the reporting facility were included in these analyses. Diagnoses of 98% of the 24,944 cases were confirmed by histology (79.0%) and radiography (19.3%); the remaining 1.7% was confirmed by a variety of methods, including but not limited to cytology and clinical determination. Less than 0.5% of cases included in these analyses were confirmed by an unknown method. In this manuscript, the term "uncertain behavior" is used and synonymous with "borderline behavior". These terms are defined similarly but their use is specific to certain classification systems. Uncertain behavior is used in the International Classification of Diseases (ICD) systems [7], while borderline behavior is the term used by the Centers for Disease Control and Prevention's (CDC), National Programs for Central Cancer Registries (NPCR) [8], Surveillance, Epidemiology and End Results (SEER) [9] program of the National Cancer Institute, and thus the CCR. Additionally, primitive neuroectodermal tumors are abbreviated throughout the text and tables as PNET.

Only cases with anatomical sites, histology codes and tumor behavior defined as reportable in Cancer Reporting in California: Abstracting and Coding Procedures for Hospitals, Volume 1, Section II.1.9.1 and Appendix V were included in these analyses. Anatomical sites included were the meninges (C70.0–C70.9); brain (C71.0–C71.9); cerebrum (C71.0); brain lobes (C71.1–C71.4); ventricle, NOS (C71.5); cerebellum, NOS (C71.6); brain stem (C71.7); spinal cord (C72.0); cauda equina (C72.1); cranial nerves (C72.2); pituitary gland (C75.1); craniopharyngeal duct (C75.2); and pineal gland (C75.3) [10]. For other selected analyses, overlapping lesions of brain (C71.8); brain, NOS (C71.9); and/or nervous system, NOS (C72.9) were included. Although the use of some anatomical sites and histology codes differed, the 2007–2008 report of the Central Brain Tumor Registry of the United States (CBTRUS), 2000–2004, was used as a guide for the organization of histology codes in Table 2 [11]. In this study, pilocytic astrocytoma (ICD-O-3, 9421) is classified as having benign tumor behavior as is directed in ICD-O-3 [7]. This is contrary to the classification stipulated in Cancer Reporting in California: Abstracting and Coding Procedures for Hospitals, Volume 1, Section II.1.9.1 and Appendix V, in which it is classified as malignant, in accordance with SEER reporting requirements [10].

The collection of benign and borderline brain and other nervous system tumors became a statewide effort beginning in 2001; however, the nationwide effort did not begin until 2004. Inconsistencies in data collection may have occurred as a result of coding rule changes for cases diagnosed in 2004 and 2005. To utilize all eligible cases, we identified inconsistencies by cross tabulations of cases by histology, tumor behavior, and anatomical site; these were reviewed by the authors, a regional registry quality control coordinator, and a neurosurgeon to determine the accuracy of coding and the appropriate categorization for presentation. Based on their assessment, approximately 400 cases were reassigned histology, tumor behavior, and/or anatomical

site codes, and approximately 100 cases were deleted from the research database entirely for this study. Specifically, all craniopharyngiomas were recoded to uncertain behavior of the craniopharyngeal duct. All cases coded as benign adenomas (ICD-O-3 8140) of the pituitary gland were recoded to pituitary adenomas (ICD-O-3 8272). Some cases ($n = 65$), were recoded based on visual review of the individual case abstract for various reasons. Cases with ICD-O-3 codes 9450, 9391-9393, 9380, 9370-9372, were recoded to malignant behavior. Myxopapillary ependymomas were recoded to uncertain behavior. The cases coded as hemangioblastic meningioma were recoded to hemangioblastoma.

Variables

The age, sex, race/ethnicity, and residential address of the patients that were used in these analyses were collected by the CCR from each patient's medical record. Race/ethnicity was derived from patient self-identification, assumptions based on personal appearance, or inferences based on the race/ethnicity of the parents, birthplace, surname, or maiden name. Race/ethnicity was classified into four mutually exclusive categories of non-Hispanic white, non-Hispanic black, Hispanic, and Asian/Pacific Islander. Hispanic ethnicity identification was enhanced by the use of computerized comparisons to the 1980 U.S. census list of Hispanic surnames. Patients identified as Hispanic on the medical record, or patients identified as white, black, or of unknown race with a Hispanic surname were classified as Hispanic. Use of this method can misclassify some persons as Hispanic when they are not [12].

Residential census tracts of cases, including those who used post office boxes as residential addresses and the denominator population were classified by the 2000 Rural Urban Commuting Areas (RUCA) codes. The RUCAs were developed by the University of Washington's Rural Health Research Center and the Economic Research Service [13]. The RUCAs are a census tract-based taxonomy that utilizes the standard Census Bureau Urbanized Area and Urban Cluster definitions in combination with other work that commuted data to characterize the nation's census tracts regarding their urban and rural status and functional relationships [14]. For these analyses, urban and rural census tracks in California were dichotomized based on Categorization C as recommended in "Using RUCA Data," published by the Rural Health Research Center [14].

Socioeconomic status (SES) was assigned based on the patient's census block group (2000 U.S. census) derived from their address at time of initial diagnosis as reported in the medical record. This SES variable is an index that utilizes education, employment characteristics, median household income, proportion of the population living 200% below the Federal Poverty Level, median rent, and median housing value of census tract of residence for case and denominator population. A principal components analysis was used to identify quintiles of SES ranging from one, the lowest, to five, the highest [15].

Statistical analysis

Counts and proportions were calculated using SAS 9.0 (SAS Institute, Cary, NC). Age-adjusted incidence rates (AAIR) were adjusted by the direct method and standardized to the 2000 U.S. population [16]. Age-specific incidence rates (ASIR) were calculated specific to each 5 year age group. Denominators were based on the 2000 U.S. census. All rates were calculated using SEER*Stat 6.3.6 (National Cancer Institute, Silver Spring, MD). Statistical comparisons of incidence rates were assessed using their respective confidence intervals [16]. If two comparative AAIR or ASIR confidence intervals do not overlap, the difference in the rates is considered statistically significantly.

Results

We identified 24,923 cases of first PCNST in the CCR from 2001 to 2005. A total of 9,236 (37.1%) cases were malignant, 14,057 (56.4%) cases were benign, and 1,630 (6.5%) cases were of uncertain tumor behavior. As shown in Table 1, our study population was 59.5% adult, 20–64 years old; 54.5% female; 60.8% non-Hispanic white; 46.5% of high SES; and 93.5% urban residents at time of diagnosis. The proportion of cases by age groups, SES, and location of residence at diagnosis was similar across tumor behavior, although tumors of uncertain tumor behavior appeared to occur more in the 0–19 year old age group than malignant and benign. There were statistically significant differences in the median age at diagnosis of patients with PCNST by tumor behavior ($P < 0.05$). For malignant PCNST, males, ethnic minorities, those of low SES, and those who lived in urban areas were significantly younger at diagnosis than females, those of high SES, non-Hispanic whites, and those who lived in rural areas. For benign PCNST, Hispanics and Asian/Pacific Islanders, those of low SES, and those who lived in urban areas were significantly younger at diagnosis ($P < 0.05$). The proportional incidence of PCNST, regardless of tumor behavior, was highest among those at the highest SES.

The overall sex-specific AAIR for malignant PCNST was highest among males, at 6.6 per 100,000 (C.I., 6.4, 6.8). For benign PCNST, the AAIR was highest for females, at 10.0 per 100,000 (C.I., 9.8, 10.2). The sex-specific AAIR

Table 1 Number of cases and percent of first primary central nervous system tumors, population demographic characteristics and median age at diagnosis by behavior, California, 2001–2005

Demographic characteristics	Malignant			Benign			Uncertain			Total	
	n	%	Median age	*n*	%	Median age	*n*	%	Median age	*n*	%
Age group, years											
0–19	1,114	12.1		698	5.0		284	17.4		2,096	8.4
20–64	5,202	56.3		8,676	61.7		941	57.7		14,819	59.5
65+	2,920	31.6		4,683	33.3		405	24.8		8,008	32.1
Sex											
Male	5,232	56.6	53*	5,277	37.5	55	830	50.9	44*	11,339	45.5
Female	4,004	43.4	57	8,780	62.5	56	800	49.1	50	13,584	54.5
Race/ethnicity											
Non-Hispanic White	5,965	64.6	58	8,266	58.8	58	919	56.4	53	15,150	60.8
Non-Hispanic Black	378	4.1	51*	902	6.4	57	116	7.1	47*	1,396	5.6
Hispanic	2,122	23.0	43*	3,092	22.0	47*	424	26.0	34*	5,638	22.6
Asian-Pacific Islander	726	7.9	51*	1,605	11.4	57*	157	9.6	48*	2,488	10.0
Other/unknown	45	0.5	40*	192	1.4	52*	14	0.9	49	251	1.0
Socioeconomic status											
Low	3,020	32.7	51*	4,573	32.5	54*	585	35.9	42*	8,180	32.8
Medium	1,907	20.6	56	2,909	20.7	56	352	21.6	50	5,169	20.7
High	4,309	46.7	56	6,575	46.8	56	693	42.5	49	11,579	46.5
Level of urbanization											
Rural	631	6.8	58	859	6.1	58	127	7.8	54	1,617	6.5
Urban	8,605	93.2	54*	13,198	93.9	55*	1,503	92.2	47	23,306	93.5
Total	9,236			14,057			1,630			24,923	

* *P*-value < 0.05; female; Non-Hispanic white; SES high and rural were used as the referent catagories

for PCNST of uncertain tumor behavior were nearly equal for males and females at 1.0 and 0.9 per 100,000.

Age-specific incidence of malignant tumors was lowest, for both males and females, in their early 20s. The ASIR for males was higher than the ASIR for females, with the gap increasing between ages 40 and 79. Incidence of malignant tumors peaked for both males and females in their late 70s and decreased thereafter. In contrast to malignant tumors, benign tumors were lowest in childhood and adolescence and increased with increasing age. ASIRs for benign tumors were consistently higher among females for all age groups except ages 10–14 (Fig. 1).

In Fig. 2, incidence of malignant tumors was highest for non-Hispanic white males, followed by Hispanic males (7.8 and 5.7 per 100,000, respectively), and lowest for Asian/Pacific Islander and non-Hispanic black females (3.0 and 3.1 per 100,000, respectively). Incidence of benign tumors was highest for all females, with rates for non-Hispanic black, non-Hispanic white, and Hispanic females being very close (10.5, 10.2 and 9.8 per 100,000, respectively).

In Table 2 we see that malignant PCNST were primarily glioblastoma (45.3%), followed distantly by lymphoma (7.5%) and anaplastic astrocytoma (7.0%). The vast majority of benign tumors consisted of meningiomas (51.6%), pituitary tumors (24.1%), and nerve sheath tumors (18.0%). Tumors of uncertain behavior were distributed similarly to benign tumors, with the largest proportion being meningiomas (26.0%), followed by craniopharyngiomas (16.6%), which are tumors of the sellar region like those of the pituitary gland. These two groups were followed by hemangioblastoma (13.3%), which are considered tumors of the meninges.

As shown in Table 3, the highest incident histologies were glioblastoma (2.6 per 100,000) for malignant and meningioma (4.5 per 100,000) for benign PCNST. The AAIR for glioblastomas was 1.7 times greater in males compared to females, while the rate of meningiomas was 2.3 times greater in females compared to males. Non-Hispanic white males had the highest AAIR of glioblastoma (3.9 per 100,000), which was significantly higher than all other race/ethnic groups by sex. Non-Hispanic

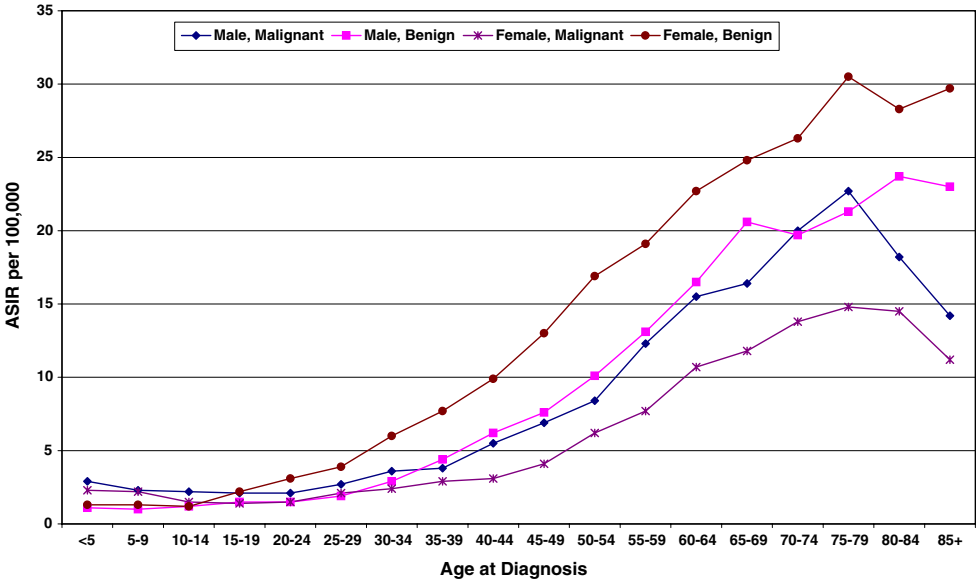

Fig. 1 Age-specific incidence rates (ASIR) of first primary benign and malignant brain and other nervous system tumors by sex, California, 2001–2005

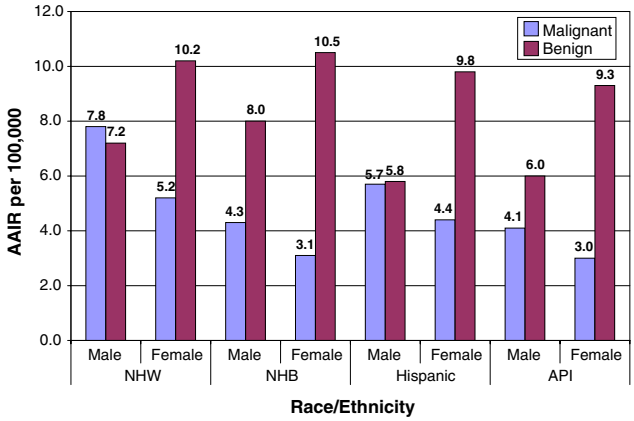

Fig. 2 Age-adjusted incidence rates (AAIR) of first primary central nervous system tumors by race/ethnicity, behavior and sex, California, 2001–2005

white males had significantly higher AAIRs than other race/ethnic groups; a higher incidence of anaplastic astrocytoma, except for Hispanic males; and a higher incidence of nerve sheath tumors, except for Asian/Pacific Islander males. The AAIRs for astrocytoma, NOS, and pilocytic astrocytoma were significantly higher for non-Hispanic white males compared to Asian/Pacific Islander males. Among females, non-Hispanic white females had the highest rate of glioblastoma (2.4 per 100,000), regardless of race/ethnicity. Non-Hispanic white females had a significantly higher AAIR compared to other race/ethnic groups for nerve sheath tumors, except for Asian/Pacific Islander females.

Non-Hispanic black males had significantly higher AAIR for pituitary tumors (3.8 per 100,000) compared to all other race/ethnic groups by sex and a significantly higher AAIR for meningiomas compared to Hispanic males. Non-Hispanic black females had a significantly higher AAIR for pituitary tumors compared to males and females in other race/ethnic groups, except non-Hispanic black males and Hispanic males and females.

Table 4 shows that malignant tumors occurred most often among adults, 20–64 years old. The exception was PNET/medulloblastoma (71.9%) which occurred mostly among children, adolescents and teens, 0–19 years old. Adults aged 65 years and older had higher proportions of glioblastomas (44.3%) and lymphomas (40.6%). Malignant tumors occurred chiefly among males with the exception of glioma and pilocytic astrocytoma, which occurred slightly more often among females. Hispanics had higher proportions of PNET/medulloblastoma (47.4%) and ependymoma/anaplastic ependymoma (33.5%). A higher proportion of lymphoma (13.5%) was seen among Asian/Pacific Islanders compared to other histologies. Most cases lived in areas of high SES, except for PNET/medulloblastoma, where 41.9% of the cases were of the lowest SES group.

Patients with benign tumors were more similar demographically across histology groups than those with malignant tumors. Unlike malignant tumors, benign tumors occurred chiefly among females (62.5%). Benign PCNST occurred most often among adults, 20–64 years old (61.7%); non-Hispanic whites (58.8%) followed by Hispanics (22.0%); those in the higher SES groups (46.8%) followed by those in the lowest (32.5%); and urban residents (93.9%) at time of diagnosis. Meningiomas were highest among females (73.5%). Pilocytic astrocytoma (76.0%) occurred mostly among children, adolescents and teens, 0–19 years old. Among Hispanics and non-Hispanic blacks, tumors of the pituitary gland occurred more often than other anatomic sites (33% and 9.5%, respectively).

Table 2 Number of cases and percent of first primary central nervous system tumors by behavior and histology, California, 2001–2005

Histology	ICD-O3 histology codes	Malignant		Benign		Uncertain		Total	
		n	%	*n*	%	*n*	%	*n*	%
Tumors of the neuroepithelial tissue									
Pilocytic astrocytoma	9421	0	0.0	488	3.5	0	0.0	488	2.0
Diffuse astrocytoma (protoplasmic, fibrillary)	9410, 9420	87	0.9	0	0.0	0	0.0	87	0.3
Anaplastic astrocytoma	9401, 9411	644	7.0	0	0.0	0	0.0	644	2.6
Unique astrocytoma variants	9383, 9384, 9424	36	0.4	0	0.0	82	5.0	118	0.5
Astrocytoma, NOS	9400, 9412	587	6.4	0	0.0	3	0.2	590	2.4
Glioblastoma	9440, 9441, 9442	4,180	45.3	0	0.0	0	0.0	4,180	16.8
Oligodendroglioma	9450	448	4.9	0	0.0	0	0.0	448	1.8
Anaplastic oligodendroglioma	9451, 9460	207	2.2	0	0.0	0	0.0	207	0.8
Ependymoma/Anaplastic ependymoma	9391, 9392, 9393	418	4.5	0	0.0	0	0.0	418	1.7
Ependymoma variant, Myxopapillary	9394	0	0.0	0	0.0	146	9.0	146	0.6
Mixed glioma	9382	313	3.4	0	0.0	0	0.0	313	1.3
Glioma malignant, NOS	9380	497	5.4	0	0.0	0	0.0	497	2.0
Choroid plexus	9390	20	0.2	68	0.5	5	0.3	93	0.4
Neuroepithelial	9381, 9423, 9430, 9444	25	0.3	0	0.0	<5	0.2	27	0.1
Neuronal/glial, neuronal and mixed	8680, 9413, 9490, 9492, 9493, 9500, 9501, 9505, 9506, 9508	59	0.6	91	0.6	200	12.3	350	1.4
Pineal parenchymal	9360, 9361, 9362	34	0.4	0	0.0	26	1.6	60	0.2
PNET/medulloblastoma	9470, 9471, 9472,9473, 9474	399	4.3	0	0.0	0	0.0	399	1.6
Tumors of cranial & spinal nerves									
Nerve sheath tumors	9540, 9550, 9560, 9561, 9570	17	0.2	2,537	18.0	23	1.4	2,577	10.3
Tumors of meninges									
Meningioma	9530, 9531, 9532, 9533, 9534, 9537, 9538, 9539	138	1.5	7,257	51.6	424	26.0	7,819	31.4
Other mesenchymal	8324, 8728, 8801, 8806, 8810, 8815, 8850, 8861, 8890, 8900, 8920, 9150, 9260	25	0.3	21	0.1	49	3.0	95	0.4
Hemangioblastoma	9131, 9161, 9535	0	0.0	17	0.1	217	13.3	234	0.9
Lymphomas									
	9590, 9591, 9650, 9670, 9671, 9675, 9680, 9684, 9687, 9690, 9691, 9695, 9698, 9699, 9702, 9705, 9714, 9719, 9727, 9728, 9729, 9731, 9733, 9734, 9740, 9741, 9750, 9755, 9930	694	7.5	0	0.0	0	0.0	694	2.8

Table 2 continued

Histology	ICD-O3 histology codes	Malignant		Benign		Uncertain		Total	
		n	%	*n*	%	*n*	%	*n*	%
Germ cell tumors	9060, 9064, 9065, 9070, 9071, 9080, 9081, 9084, 9085	157	1.7	25	0.2	0	0.0	182	0.7
Tumors of sellar region									
Pituitary tumors	8270, 8271, 8272, 8280, 8290, 8300,9580	15	0.2	3,384	24.1	0	0.0	3,399	13.6
Craniopharyngioma	9350, 9351, 9352	0	0.0	0	0.0	271	16.6	271	1.1
Local extensions from regional tumors									
Chordoma	9370, 9371, 9372	23	0.2	0	0.0	0	0.0	23	0.1
Unclassifed tumors									
Hemangioma	9120, 9121, 9122, 9130, 9133	0	0.0	93	0.7	3	0.2	96	0.4
Neoplasm, unspecified	8000, 8005, 8010	208	2.3	76	0.5	179	11.0	463	1.9
All other	8720, 8728, 9580, 9751	5	0.1	0	0.0	0	0.0	5	0.0
Total	–	9,236	–	14,057	–	1,630	–	24,923	–

PNET primitive neuroectodermal tumors

Discussion

Thirty-seven percent of California's PCNST were found to be malignant and 56% benign. The AAIR of malignant PCNST in California was 5.8 cases per 100,000 persons, and benign PCNST was 8.5 cases per 100,000 persons.

Consistent with findings of other studies, the incidence of malignant tumors increased with increasing age except for the youngest (0–14 years) and oldest (>65 years) members of our study population [11, 17, 18]. A similar, but more monotonic age-related pattern was found for benign tumors. The highest incidence for both malignant and benign PCNST was among adults, 20–64 years old. Median age at diagnosis ranged widely by sex, race/ethnicity, SES, and the level of urbanization of patient residence. Significant differences were found in median age at diagnosis by sex for malignant but not for benign PCNST. Non-Hispanic whites were the oldest (57 years old) while Hispanics were the youngest (41 years old). Those in the lowest SES level and those who lived in rural California were significantly younger at the time of diagnosis. Disparities in median age at diagnosis could indicate etiologic differences in PCNST or disparities in healthcare utilization, access and diagnostics among these groups.

The incidence of malignant PCNST was highest among non-Hispanic white males, followed by Hispanic males [17, 19, 20]. Benign PCNST in California occurred more often among females. The AAIRs were similar across all race/ethnic groups, lead slightly by non-Hispanic black females (10.5 per 100,000). In our race/ethnicity analyses, we found significantly higher AAIRs for glioblastoma, pilocytic astrocytoma, anaplastic astrocytoma, oligodendroglioma, and nerve sheath tumors among non-Hispanic white males and females. In comparison, non-Hispanic black males and females had significantly higher rates of meningiomas and pituitary tumors [21–28]. We found higher incidence rates of nerve sheath tumors among Asian/Pacific Islanders. Unlike other studies, we found that the AAIR of pituitary tumors among Asian/Pacific Islanders was nearly the same rate as reported for non-Hispanic whites [29–32].

Overall PCNST proportional incidence, regardless of tumor behavior, was highest for the highest SES group, followed by the lowest SES group [28, 33]. Inskip et al. (2003) found similar results for gliomas and meningiomas, in which the incidence was highest among those with more education, greater income, and private insurance. The incidence among those with public insurance was also somewhat higher, possibly betraying a reporting bias linked to population healthcare coverage [33, 34]. Differential tumor detection and reporting between those with and without health insurance may account for some of the observed differences.

Table 3 Age-Adjusted Incidence Rates (AAIR)* of selected first primary malignant and benign central nervous system tumors by histology and sex, California, 2001–2005

Behavior	Histology	Sex	Total		NH White		NH Black		Hispanic		API	
			AAIR	95% CI	AAIR	95% CI	AAIR	95% CI	AAIR	95% CI	AAIR	95% CI
Malignant	Astrocytoma, anaplastic	Total	0.4	0.3, 0.4	0.5	0.4, 0.5	0.1	0.1, 0.2	0.3	0.3, 0.4	0.2	0.2, 0.3
		Male	0.4	0.4, 0.5	0.6	0.5, 0.6	0.1	0.0, 0.2	0.4	0.3, 0.5	0.3	0.2, 0.4
		Female	0.3	0.3, 0.4	0.4	0.3, 0.5	0.2	0.1, 0.3	0.3	0.2, 0.4	0.2	0.1, 0.3
	Astrocytoma, NOS	Total	0.3	0.3, 0.4	0.4	0.4, 0.5	0.2	0.2, 0.4	0.3	0.3, 0.4	0.2	0.1, 0.2
		Male	0.4	0.3, 0.4	0.5	0.4, 0.5	0.4	0.2, 0.6	0.4	0.3, 0.5	0.2	0.1, 0.3
		Female	0.3	0.3, 0.3	0.3	0.3, 0.4	0.1	0.1, 0.3	0.3	0.2, 0.4	0.2	0.1, 0.3
	Glioblastoma	Total	2.6	2.5, 2.7	3.1	3.0, 3.2	1.5	1.3, 1.8	2.3	2.1, 2.5	1.2	1.1, 1.4
		Male	3.3	3.1, 3.4	3.9	3.7, 4.1	2.0	1.6, 2.5	2.8	2.5, 3.1	1.6	1.3, 1.9
		Female	2.0	1.9, 2.1	2.4	2.3, 2.5	1.1	0.9, 1.5	1.9	1.7, 2.2	0.9	0.7, 1.1
	Oligodendroglioma	Total	0.3	0.2, 0.3	0.3	0.3, 0.4	0.1	0.0, 0.2	0.2	0.2, 0.2	0.2	0.1, 0.2
		Male	0.3	0.3, 0.3	0.4	0.3, 0.5	0.1	0.0, 0.3	0.2	0.1, 0.3	0.2	0.1, 0.3
		Female	0.2	0.2, 0.2	0.3	0.2, 0.3	0.1	0.0, 0.2	0.2	0.1, 0.3	0.1	0.1, 0.2
	Anaplastic oligodendroglioma	Total	0.1	0.1, 0.1	0.2	0.1, 0.2	0.0	0.0, 0.1	0.1	0.1, 0.1	0.1	0.1, 0.1
		Male	0.1	0.1, 0.1	0.1	0.1, 0.2	0.1	0.0, 0.2	0.1	0.1, 0.2	0.1	0.1, 0.2
		Female	0.1	0.1, 0.1	0.2	0.1, 0.2	0.0	0.0, 0.1	0.1	0.0, 0.1	0.1	0.0, 0.1
	Ependymomas, anaplastic	Total	0.2	0.2, 0.3	0.3	0.2, 0.3	0.2	0.1, 0.3	0.2	0.2, 0.3	0.2	0.1, 0.2
		Male	0.2	0.2, 0.3	0.3	0.2, 0.3	0.2	0.1, 0.4	0.2	0.2, 0.3	0.1	0.1, 0.2
		Female	0.2	0.2, 0.3	0.3	0.2, 0.3	0.2	0.1, 0.3	0.2	0.2, 0.3	0.2	0.1, 0.3
	Mixed glioma	Total	0.2	0.2, 0.2	0.2	0.2, 0.3	0.1	0.0, 0.2	0.1	0.1, 0.2	0.2	0.1, 0.2
		Male	0.2	0.2, 0.2	0.3	0.2, 0.3	0.1	0.0, 0.2	0.1	0.1, 0.2	0.2	0.1, 0.3
		Female	0.2	0.1, 0.2	0.2	0.1, 0.2	0.1	0.0, 0.3	0.1	0.1, 0.2	0.2	0.1, 0.2
	Glioma malignant, NOS	Total	0.3	0.3, 0.3	0.3	0.3, 0.4	0.3	0.2, 0.4	0.3	0.2, 0.3	0.2	0.2, 0.3
		Male	0.3	0.3, 0.4	0.4	0.3, 0.4	0.3	0.1, 0.5	0.3	0.2, 0.4	0.3	0.2, 0.4
		Female	0.3	0.2, 0.3	0.3	0.2, 0.4	0.3	0.2, 0.5	0.3	0.2, 0.4	0.2	0.1, 0.3
	PNET/Meduloblastoma	Total	0.2	0.2, 0.2	0.2	0.2, 0.3	0.1	0.1, 0.2	0.2	0.2, 0.3	0.2	0.1, 0.2
		Male	0.3	0.2, 0.3	0.3	0.2, 0.4	0.1	0.0, 0.2	0.3	0.2, 0.4	0.1	0.1, 0.2
		Female	0.2	0.1, 0.2	0.2	0.1, 0.2	0.1	0.0, 0.2	0.2	0.1, 0.2	0.2	0.1, 0.3
	Lymphomas	Total	0.4	0.4, 0.5	0.4	0.4, 0.5	0.4	0.3, 0.5	0.4	0.3, 0.5	0.5	0.4, 0.6
		Male	0.5	0.5, 0.6	0.5	0.4, 0.6	0.4	0.3, 0.6	0.5	0.4, 0.6	0.6	0.4, 0.7
		Female	0.3	0.3, 0.4	0.3	0.3, 0.4	0.3	0.2, 0.5	0.3	0.2, 0.4	0.4	0.3, 0.5
Benign	Pilocytic astrocytoma	Total	0.3	0.2, 0.3	0.4	0.3, 0.4	0.2	0.2, 0.3	0.2	0.2, 0.2	0.1	0.1, 0.2
		Male	0.3	0.2, 0.3	0.4	0.3, 0.4	0.2	0.1, 0.4	0.2	0.2, 0.3	0.1	0.1, 0.2
		Female	0.3	0.2, 0.3	0.4	0.3, 0.5	0.2	0.1, 0.4	0.2	0.2, 0.3	0.2	0.1, 0.3
	Nerve sheath	Total	1.5	1.4, 1.6	1.8	1.7, 1.8	0.7	0.5, 0.9	1.0	0.9, 1.1	1.5	1.3, 1.7
		Male	1.6	1.5, 1.7	1.9	1.7, 2.0	0.8	0.5, 1.0	0.9	0.8, 1.1	1.6	1.4, 1.9
		Female	1.4	1.4, 1.5	1.7	1.5, 1.8	0.6	0.4, 0.9	1.0	0.9, 1.2	1.4	1.2, 1.6
	Meningioma	Total	4.5	4.4, 4.6	4.7	4.5, 4.8	5.0	4.5, 5.5	4.0	3.7, 4.2	4.2	3.9, 4.5
		Male	2.7	2.5, 2.8	2.9	2.7, 3.1	3.2	2.6, 3.8	2.0	1.7, 2.2	2.3	2.0, 2.7
		Female	6.1	5.9, 6.3	6.3	6.1, 6.5	6.5	5.8, 7.2	5.7	5.3, 6.1	5.8	5.3, 6.2
	Pituitary tumors	Total	2.0	1.9, 2.1	1.7	1.6, 1.8	3.2	2.9, 3.6	2.5	2.3, 2.7	1.8	1.6, 2.0
		Male	2.1	2.0. 2.2	1.8	1.7, 2.0	3.8	3.2, 4.5	2.5	2.3, 2.8	1.8	1.5, 2.1
		Female	2.0	1.9, 2.1	1.6	1.5, 1.7	3.0	2.5, 3.5	2.6	2.4, 2.8	1.8	1.6, 2.1

* Age-adjusted incidence rates are per 100,000 population. Rates are standardized to the 2000 US population

PNET primitive neuroectodermal tumors

Table 4 Number of cases and percent of selected first primary malignant and benign central nervous system tumors by demographics and histology, California, 2001–2005

Malignant

Demographic characteristics	Anaplastic astrocytoma		Glioblastoma		Ependymoma/ anaplastic ependymoma		Glioma, NOS		PNET/ medullo-blastoma		Lymphoma		Other		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Age group (years)																
0–19	52	8.1	53	1.3	128	30.6	166	33.4	287	71.9	18	2.6	410	17.1	1,114	12.1
20–64	443	68.8	2,277	54.5	253	60.5	183	36.8	110	27.6	394	56.8	1,542	64.1	5,202	56.3
65+	149	23.1	1,850	44.3	37	8.9	148	29.8	<5	0.5	282	40.6	452	18.8	2,920	31.6
Sex																
Male	363	56.4	2,441	58.4	212	50.7	247	49.7	248	62.2	398	57.3	1,323	55.0	5,232	56.6
Female	281	43.6	1,739	41.6	206	49.3	250	50.3	151	37.8	296	42.7	1,081	45.0	4,004	43.4
Race/ethnicity																
Non-Hispanic White	423	65.7	3,059	73.2	219	52.4	276	55.5	164	41.1	400	57.6	1,424	59.2	5,965	64.6
Non-Hispanic Black	16	2.5	143	3.4	23	5.5	29	5.8	13	3.3	38	5.5	116	4.8	378	4.1
Hispanic	152	23.6	724	17.3	140	33.5	140	28.2	189	47.4	156	22.5	621	25.8	2,122	23.0
Asian-Pacific Islander	50	7.8	242	5.8	34	8.1	47	9.5	31	7.8	94	13.5	228	9.5	726	7.9
Other/unknown	<5	0.5	12	0.3	<5	0.5	5	1.0	<5	0.5	6	0.9	15	0.6	45	0.5
Socioeconomic status																
Low	218	33.9	1,218	29.1	157	37.6	184	37.0	167	41.9	245	35.3	831	34.6	3,020	32.7
Medium	131	20.3	875	20.9	69	16.5	105	21.1	77	19.3	141	20.3	509	21.2	1,907	20.6
High	295	45.8	2,087	49.9	192	45.9	208	41.9	155	38.8	308	44.4	1,064	44.3	4,309	46.7
Level of urbanization																
Rural	52	8.1	305	7.3	26	6.2	34	6.8	19	4.8	47	6.8	148	6.2	631	6.8
Urban	592	91.9	3,875	92.7	392	93.8	463	93.2	380	95.2	647	93.2	2,256	93.8	8,605	93.2
Total	644		4,180		418		497		399		694		2,404		9,236	

Benign

	Pilocytic astrocytoma		Nerve sheath tumors		Meningioma		Pituitary tumors		Other		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Age group (years)												
0–19	371	76.0	48	1.9	30	0.4	143	4.2	106	27.1	698	5.0
20–64	111	22.7	2,037	80.3	3,863	53.2	2,444	72.2	221	56.5	8,676	61.7
65+	6	1.2	452	17.8	3,364	46.4	797	23.6	64	16.4	4,683	33.3
Sex												
Male	240	49.2	1,290	50.8	1,923	26.5	1,634	48.3	190	48.6	5,277	37.5
Female	248	50.8	1,247	49.2	5,334	73.5	1,750	51.7	201	51.4	8,780	62.5
Race/ethnicity												
Non-Hispanic White	250	51.2	1,639	64.6	4,626	63.7	1,528	45.2	223	57.0	8,266	58.8
Non-Hispanic Black	31	6.4	74	2.9	460	6.3	322	9.5	15	3.8	902	6.4
Hispanic	168	34.4	423	16.7	1,273	17.5	1,116	33.0	112	28.6	3,092	22.0
Asian-Pacific Islander	30	6.1	326	12.8	829	11.4	385	11.4	35	9.0	1,605	11.4
Other/unknown	9	1.8	75	3.0	69	1.0	33	1.0	6	1.5	192	1.4
Socioeconomic status												
Low	191	39.1	630	24.8	2,323	32.0	1,299	38.4	130	33.2	4,573	32.5
Medium	94	19.3	488	19.2	1,537	21.2	689	20.4	101	25.8	2,909	20.7
High	203	41.6	1,419	55.9	3,397	46.8	1,396	41.3	160	40.9	6,575	46.8

Table 4 continued

Benign	Pilocytic astrocytoma		Nerve sheath tumors		Meningioma		Pituitary tumors		Other		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Level of urbanization												
Rural	35	7.2	165	6.5	469	6.5	159	4.7	31	7.9	859	6.1
Urban	453	92.8	2,372	93.5	6,788	93.5	3,225	95.3	360	92.1	13,198	93.9
Total	488		2,537		7,257		3,384		391		14,057	

NOS not otherwise specified, *PNET* primitive neuroectodermal tumors

As in other studies, glioblastoma was the dominant histologic category for malignant PCNST (43%) in California [35, 36]. Although the proportion of cases we found in California was exceedingly higher than that found by others [11, 37], California's AAIR (2.6 per 100,000 cases) was lower than those recorded elsewhere, which range from 3.1 to 4.8/100,000 [11, 38, 39]. The AAIR of lymphoma (0.4 per 100,000) was similar in California to that reported elsewhere [11, 38–40], despite changes in their histological classification and their effect over time [41].

The dominant histologic categories for benign PCNST were meningiomas (53.5%), tumors of the pituitary gland (24.9%), and tumors of the nerve sheath (18.7%), collectively representing 97% of California's benign tumor cases. The AAIRs for meningiomas, tumors of the pituitary gland, and tumors of the nerve sheath were 4.5, 2.0, and 1.5 per 100,000, respectively. Californian rates for meningiomas were similar to those reported by some other studies [11, 35, 38, 39, 42] but not all [43]. The rate of pituitary tumors in California was higher than that reported by CBTRUS, 1.37 per 100,000 [11], while the incidence rate for tumors of the nerve sheath was the same as that reported for the nation.

Cancer incidence is difficult to compare across geographical areas, time-periods and information sources. Data used in national and international incidence studies can differ in diagnostic and neuropathological assessment, case ascertainment practices [44–47]. Some studies are single institution or if population-based may lack a sufficient case population to calculate incidence rates or if rates can be calculated, the use of the world standard population for incidence rates standardization rather than the U.S. standard population [48, 49].

Among U.S. CNS tumor incidence studies, counts and rates can vary by data collection sources and tumor classifications systems. All national CNS tumor incidence statistics derived cases from one of four centralized data collection sources: the NPCR from the CDC; the North American Association of Central Cancer Registries (NAACCR); SEER and CBTRUS. Both NPCR and NAACCR are population-based and cover more than 95% of the U.S. population [8, 50], while SEER, a non-random sample of central cancer registries, represents 26% of the population [9]. CBTRUS differs from these agencies since it is a voluntary repository for CNS tumor data. In 1999, CBTRUS was estimated to cover 15% of the U.S. population with contributions from 16 state registries (excluding California) [11, 51]. All of these cancer data collection agencies use the ICD-O tumor classification system [7]; whereas neuropathologists use the WHO grading system, which is specific to classifying CNS tumors [52]. Both of these tumor malignancy scales were created by the World Health Organization and can differ substantially, one essential difference is in tumor behavior categories. The ICD-O category of uncertain tumor behavior applies to CNS tumors, whereas the WHO grading scheme does not have an option for coding tumors of uncertain behavior. Coding discrepancies can occur at the individual pathology report level. This issue is further complicated by the application of data collection agency specific coding rules. Pilocytic astrocytoma is considered benign using the WHO grading system and ICD-O-3, but it is classified as malignant for reporting purposes by NAACCR and SEER and thus all North American central tumor registries. Given that pilocytic astrocytoma is a high-incidence histology, its inclusion or exclusion could significantly sway pediatric PCNST statistics. On the other hand, some statistical sources choose not to partition histologies by tumor behavior, thus the incidence of CNS tumors calculated by these sources can appear higher than from other sources [11].

Other differences in CNS tumor incidence statistics can arise from the inclusion of all CNS tumors from a single case, regardless of tumor sequence (first primary tumors versus all primary tumors) and the organization of tumor histology codes. The CCR as well as all member central cancer registries of NPCR and NAACCR, use the SEER program's incidence site recode system that standardizes ICD-O histology subgroups [7, 9]. When comparing the incidence of pituitary gland tumors between sources, we

found wide variation in the ICD-O-3 histology codes used by CBTRUS and SEER. These code subgroup differences may explain a nearly two-fold difference in reported incidence in California compared to the nation, as reported by CBTRUS [11].

This is the first study to examine both malignant and benign PCNST in California. California is a large, heavily populated state with a diverse ethnic, cultural, and socioeconomic population. This diversity is reflected in the CCR, and we were able to conduct robust analyses and make comparisons that few others can perform. The CCR's epidemiologic value stems from the 1988 state-mandated comprehensive reporting of cancer cases from all physicians, hospitals, clinics, treatment facilities and pathology laboratories. Because a single standard is used for statewide data collection, quality assurance, and training and education for cancer registration, we acquire optimal case ascertainment and a high level of accuracy for many data items.

Our study and data source are not without limitations. This study was conducted solely using the CCR and was not supplemented with other data. The CCR data are collected for the purpose of surveillance and can be less detailed than those derived from medical records to support the design of a specific research study. Population-based cancer registry data are derived from many sources, thus, the quality of some variables may vary. Individual-level social indicators are not available to the CCR. Our SES measure is a composite of census-derived data and is more efficient for data analysis, and it avoids biases inherent in the use of individual component indicators. Another potential source of error is the misclassification of cases. Despite a rigorous data review and cleaning process, cases could have been misclassified based on tumor behavior, histology, and/or anatomical site.

Cancer surveillance identifies populations at greatest risk and which of their specific population attributes are associated with disease, providing valuable insights into disease etiology and prevention. This study of California PCNST establishes a foundation for future studies to examine age-group differences (i.e., children and seniors), specific histologies (i.e., glioblastoma and pituitary tumors), risk factors, and incidence trends over time.

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