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CLINICAL STUDY - PATIENT STUDY

Incidence of first primary central nervous system tumors in California, 2001–2005: children, adolescents and teens

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Abstract This study used data from the California Cancer Registry to comprehensively examine first primary central nervous system tumors (PCNST) by the International Classification of Childhood Cancers (ICCC) diagnostic groups and to compare their incidence by age groups, sex, race/ethnicity, socioeconomic status and tumor behavior. The study period, 2001–2005, represents the first 5 years of benign PCNST data collection in the state. The age-adjusted incidence rates were 2.1 for malignant and 1.3 for benign per 100,000. Children younger than 5 years old had the highest incidence of malignant PCNST (2.6 per 100,000). Teens aged 15–19 had the highest incidence of benign PCNST (1.8 per 100,000). Age-specific incidence rates were nearly the same for Hispanics, non-Hispanic whites, and Asian/Pacific Islanders for malignant PCNST among children younger than 5 (2.6–2.7 per 100,000); non-Hispanic whites had the highest rates in the 5–14 year-old age group (2.5 per 100,000) and Asian/Pacific Islanders the highest among the 15–19 year old age group (2.3 per 100,000). We found no statistically significant differences in the incidence of malignant PCNST by race/ethnicity in any age group. Astrocytoma had the highest incidence for both malignant and benign histology in most age groups.

Keywords Brain and other central nervous system neoplasms · Epidemiology · Cancer incidence · Childhood cancers · Ethnic groups

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Introduction

Primary tumors of the central nervous system (PCNST) among children, adolescents, and teens differ from those in adults in frequency, histological appearance, and clinical behavior [1]. PCNST are the second most common form of cancer among children aged 15 years and younger and the third most common among those 15–19 years old in California. While PCNST represent only 1.3% of incident cancers among adults 20 years and older, they represent from 26.4% (5–9 year olds) to 9.5% (15–19 year olds) of incident cancers among persons younger than 20 years old [2]. PCNST are the second leading cause of cancer deaths among children younger than 15 years old; they cause 32% (5–9 year olds) and 12.1% (15–19 year olds) of cancer deaths in children compared to 3% of cancer deaths for adults 20 years and older [2]. PCNST among children, adolescents, and teens tend to have short latent periods, often grow rapidly, and are aggressively invasive [1]. PCNST are a significant public health problem, they have a far more devastating effect on society,

communities and considering the potential years of productive life lost [3].

This study examined the incidence of malignant and benign first PCNST among children, adolescents, and teens using the population-based California Cancer Registry (CCR) from 2001 to 2005. This population is a subset of the population described in the authors' companion publication in this edition. Since 1988, California state law mandates the reporting of all newly diagnosed malignant cancers in California [4]. An amendment to this law enacted January 2001 provides for the additional reporting of benign and borderline behavior PCNST [5]. The 2001–2005 study period represents the first 5 years of complete PCNST data collection in California. The CCR provides a robust source of epidemiologic data for a densely populous geographic area. California can be viewed as a microcosm of United States reflecting the influence of its racial, ethnic and sociodemographic diversity on overall cancer incidence. Although pediatric PCNST incidence has been relatively well studied, this is the first study to comprehensively examine PCNST incidence by patient demographics and tumor behavior among children, adolescents and teens according to the International Classification of Childhood Cancers (ICCC).

Materials and methods

Materials and methods, including case identification, inclusion/exclusion criteria and tumor behavior assignment used in this study were identical to those described in the authors' companion publication in this edition. For these analyses, we divided cases into 4 age groups. Patients younger than 5 and patients 5–9 years old are referred to as children, those aged 10–14 years as adolescents, and those 15–19 years old as teens. Diagnostic groups were organized using the Surveillance, Epidemiology and End Results (SEER) Program's site/histology modification to the ICCC [6, 7]. Table 1 lists ICCC diagnostic groups by

Table 1 SEER recode of ICCC diagnostic groups and ICD-O-3 codes for California cases, 2001–2005

Diagnostic groups		ICD-O-3 code(s)	
		Morphology	Topography
IIIA	Ependymomas & choroid plexus tumor	9383, 9390–9394, 9390	C000–C809
IIIB	Astrocytomas	9380	C723
		9384, 9400, 9401, 9410, 9411, 9420, 9421, 9423, 9424, 9440–9442	C000–C809
IIIC1	Medulloblastomas	9470–9472, 9474, 9480	C000–C809
IIIC2	Primitive neuroectodermal tumors (PNET)	9473	C000–C809
IIIC9	Other intracranial & intraspinal embryonal tumors	9501–9503	C700–C729
		9508	C000–C809
IIID	Other gliomas	9380	C700–C722, C724–C729, C751, C753
		9381, 9382, 9430, 9450, 9451, 9460	C000–C809
IIIE	Other specified intracranial & intraspinal neoplasms	8270–8281, 8300, 9350–9352, 9360–9362, 9412, 9413, 9492, 9493, 9505–9507, 9530–9537, 9537–9539	C000–C809
XA	Intracranial & intraspinal germ cell tumors	9060, 9064, 9065, 9070–9072, 9080–9085, 9100	C700–C729, C751–C753
Z	Other	8000–8005, 9370	C700–C729, C751–C753
		9501–9503	C000–C699, C739–C768, C809
		8680, 8728, 8810, 8850, 8920, 9120, 9121, 9130, 9150, 9161, 9260, 9490, 9500, 9522, 9523, 9540–9571, 9590, 9591, 9650, 9670, 9671, 9675, 9680, 9684, 9687, 9690, 9691, 9695, 9698, 9699, 9702, 9705, 9714, 9719, 9727–9729, 9731, 9733, 9734, 9740, 9741, 9750	C000–C809

SEER Surveillance, Epidemiology and End Results

ICCC International Classification of Childhood Cancers, 3rd edition

ICD International Classification of Diseases, Oncology, 3rd edition

International Classification Diseases, Oncology, 3rd edition's (ICD-O-3) morphology and topography codes.

Results

There were 2,096 cases of PCNST among children, adolescents, and teens (from birth to 19 years old) in California from 2001 to 2005. Of those cases, 1,114 (53.1%) were malignant, 698 (33.3%) were benign, and 284 (13.6%) were of uncertain behavior. The resultant AAIR per 100,000 was 2.1 (CI: 2.0–2.2) for malignant, 1.3 (CI: 1.2–1.4) for benign, and 0.5 (CI: 0.5–0.6) for tumors of uncertain behavior.

As seen in Table 2, there was an increase in the proportion of cases by year for tumors of uncertain behavior for adolescents and teens, whereas the proportion of cases among the two groups of children, for both malignant and benign PCNST, appears to be stable over the study period. The ASIR for malignant PCNST decreased as age increased, starting from 2.6 per 100,000 among those younger than 5 years to 1.7 per 100,000 among 15 to 19-year olds. To compare with other studies, we calculated the AAIR per 100,000 for children and adolescents to be 2.2 for malignant and 1.2 for benign PCNST. The ASIR for benign PCNST fluctuated by age groups, ranging from 1.8 to 1.1 per 100,000. The incidence of tumors of uncertain behavior was very low. The pattern seen for malignant PCNST by age group was opposite that for tumors of uncertain behavior. Incident rates increased slightly as age group increased.

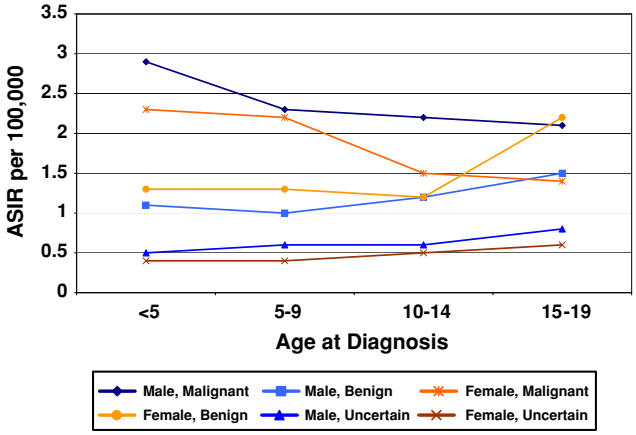

Fig. 1 Age-specific incidence rates (ASIR) of first primary malignant and benign first primary central nervous system tumors by age group and sex, California, 2001–2005

The highest incidence of PCNST was for malignant tumors in children and adolescents (Fig. 1). This pattern changed for teens, where incidence of benign PCNST was similar to that of malignant PCNST. The lowest incidence, at every age group, was for tumors of uncertain behavior. The ASIR for boys for malignant and uncertain behavior PCNST were higher than that for girls at all age groups. Incidence rates for girls with benign PCNST were higher than that for boys until adolescence, where they appeared

Table 2 Number of cases, percent and age-specific incidence rate* (ASIR) of first primary central nervous system tumors by age group, tumor behavior and year of diagnosis, California, 2001–2005

Age group	Behavior	2001		2002		2003		2004		2005		Total		
		n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	ASIR 95%CI
<5 years	Malignant	65	19.2	73	21.5	67	19.8	58	17.1	76	22.4	339	100.0	2.6 (2.4, 2.9)
	Benign	34	22.1	29	18.8	34	22.1	33	21.4	24	15.6	154	100.0	1.2 (1.0, 1.4)
	Uncertain	11	20.4	14	25.9	7	13.0	11	20.4	11	20.4	54	100.0	0.4 (0.3, 0.5)
	Total	110	20.1	116	21.2	108	19.7	102	18.6	111	20.3	547	100.0	4.2 (3.9, 4.6)
5–9 years	Malignant	70	23.6	59	19.9	61	20.5	53	17.8	54	18.2	297	100.0	2.3 (2.0, 2.5)
	Benign	28	18.9	30	20.3	37	25.0	30	20.3	23	15.5	148	100.0	1.1 (1.0, 1.3)
	Uncertain	7	10.8	13	20.0	15	23.1	14	21.5	16	24.6	65	100.0	0.5 (0.4, 0.6)
	Total	105	20.6	102	20.0	113	22.2	97	19.0	93	18.2	510	100.0	3.9 (3.6, 4.3)
10–14 years	Malignant	49	19.2	60	23.5	46	18.0	53	20.8	47	18.4	255	100.0	1.9 (1.6, 2.1)
	Benign	23	14.4	34	21.3	33	20.6	29	18.1	41	25.6	160	100.0	1.2 (1.0, 1.4)
	Uncertain	15	19.7	11	14.5	14	18.4	12	15.8	24	31.6	76	100.0	0.6 (0.4, 0.7)
	Total	87	17.7	105	21.4	93	18.9	94	19.1	112	22.8	491	100.0	3.6 (3.3, 3.9)
15–19 years	Malignant	37	16.6	45	20.2	34	15.2	60	26.9	47	21.1	223	100.0	1.7 (1.5, 2.0)
	Benign	41	17.4	46	19.5	45	19.1	50	21.2	54	22.9	236	100.0	1.8 (1.6, 2.1)
	Uncertain	14	15.7	17	19.1	18	20.2	20	22.5	20	22.5	89	100.0	0.7 (0.6, 0.8)
	Total	92	16.8	108	19.7	97	17.7	130	23.7	121	22.1	548	100.0	4.2 (3.9, 4.6)

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

Table 3 Number of cases and percent of first primary central nervous system tumors, by age group, population demographic characteristics and tumor behavior, California, 2001–2005

Demographic Characteristics			Malignant		Benign		Uncertain		Total	
			n	%	n	%	n	%	n	%
< 5 years	Sex	Male	193	56.9%	72	46.8%	30	55.6%	295	53.9%
		Female	146	43.1%	82	53.2%	24	44.4%	252	46.1%
	Race/ethnicity	Non-Hispanic white	108	31.9%	62	40.3%	23	42.6%	193	35.3%
		Non-Hispanic black	21	6.2%	8	5.2%			32	5.9%
		Hispanic	168	49.6%	69	44.8%	25	46.3%	262	47.9%
		Asian-Pacific Islander	37	10.9%	11	7.1%			50	9.1%
		Other/Unknown	5	1.5%					10	1.8%
	Socioeconomic Status	Low	147	43.4%	72	46.8%	27	50.0%	246	45.0%
		Medium	62	18.3%	29	18.8%	12	22.2%	103	18.8%
		High	130	38.3%	53	34.4%	15	27.8%	198	36.2%
	Level of Urbanization	Urban	325	95.9%	144	93.5%	50	92.6%	519	94.9%
		Rural	14	4.1%	10	6.5%			28	5.1%
	Total		339		154		54		547	
5-9 years	Sex	Male	155	52.2%	68	45.9%	39	60.0%	262	51.4%
		Female	142	47.8%	80	54.1%	26	40.0%	248	48.6%
	Race/ethnicity	Non-Hispanic white	113	38.0%	74	50.0%	25	38.5%	212	41.6%
		Non-Hispanic black	17	5.7%	9	6.1%			28	5.5%
		Hispanic	138	46.5%	55	37.2%	30	46.2%	223	43.7%
		Asian-Pacific Islander	24	8.1%	8	5.4%	8	12.3%	40	7.8%
		Other/Unknown	5	1.7%			0	0.0%	7	1.3%
	Socioeconomic Status	Low	134	45.1%	52	35.1%	31	47.7%	217	42.5%
		Medium	53	17.8%	34	23.0%	11	16.9%	98	19.2%
		High	110	37.0%	62	41.9%	23	35.4%	195	38.2%
	Level of Urbanization	Urban	283	95.3%	138	93.2%	61	93.8%	482	94.5%
		Rural	14	4.7%	10	6.8%			28	5.5%
	Total		297		148		65		510	
10-14 years	Sex	Male	154	60.4%	82	51.3%	43	56.6%	279	56.8%
		Female	101	39.6%	78	48.8%	33	43.4%	212	43.2%
	Race/ethnicity	Non-Hispanic white	113	44.3%	78	48.8%	33	43.4%	224	45.6%
		Non-Hispanic black	10	3.9%	10	6.3%	8	10.5%	28	5.7%
		Hispanic	104	40.8%	61	38.1%	31	40.8%	196	39.9%
		Asian-Pacific Islander	27	10.6%	6	3.8%			37	7.5%
		Other/Unknown			5	3.1%	0	0.0%	6	1.2%
	Socioeconomic Status	Low	104	40.8%	58	36.3%	37	48.7%	199	40.5%
		Medium	42	16.5%	35	21.9%	10	13.2%	87	17.7%
		High	109	42.7%	67	41.9%	29	38.2%	205	41.8%
	Level of Urbanization	Urban	243	95.3%	151	94.4%	69	90.8%	28	5.7%
		Rural	12	4.7%	9	5.6%	7	9.2%	463	94.3%
	Total		255		160		76		491	
15-19 years	Sex	Male	138	61.9%	101	42.8%	52	58.4%	291	53.1%
		Female	85	38.1%	135	57.2%	37	41.6%	257	46.9%
	Race/ethnicity	Non-Hispanic white	102	45.7%	105	44.5%	40	44.9%	247	45.1%
		Non-Hispanic black	12	5.4%	9	3.8%	7	7.9%	28	5.1%
		Hispanic	73	32.7%	103	43.6%	36	40.4%	212	38.7%
		Asian-Pacific Islander	35	15.7%	17	7.2%	5	5.6%	57	10.4%
		Other/Unknown								
	Socioeconomic Status	Low	85	38.1%	105	44.5%	32	36.0%	222	40.5%
		Medium	42	18.8%	49	20.8%	16	18.0%	107	19.5%
		High	96	43.0%	82	34.7%	41	46.1%	219	40.0%
	Level of Urbanization	Urban	207	92.8%	223	94.5%	81	91.0%	511	93.2%
		Rural	16	7.2%	13	5.5%	8	9.0%	37	6.8%
	Total		223		236		89		548	

Shaded cells categories with less than 5 cases were omitted

to be same; later ASIRs increased among teen girls, where they exceed the malignant PCNST rate in boys. Adolescents showed the widest sex-specific gulf for malignant PCNST. The ASIR among girls starts to decline dramatically from 5 to 14 years old; incidence rates for boys declined as well but not as dramatically. When PCNST incidence rates were compared by age group, sex, and tumor behavior, we found that there were no significant

differences except among adolescents. The ASIR for malignant PCNST for adolescent boys was 2.2 (CI: 1.9–2.6) and for adolescent girls was 1.5 (CI: 1.2–1.8). Malignant PCNST incidence among teen boys and girls was 2.1 (CI: 1.7–2.5) and 1.4 (CI: 1.1–1.7), respectively. Benign PCNST among teen boys and girls was 1.5 (CI: 1.2–1.8) and 2.2 (CI: 1.8–2.6), respectively.

Table 3 shows the study population by age groups, demographic characteristics, and tumor behavior. For nearly all age groups, boys were more often diagnosed with malignant PCNST and tumors of uncertain behavior; girls, proportionally, had more benign PCNST. The exception was for adolescents, where boys were proportionally diagnosed more often with benign PCNST.

Hispanic children, younger than 5, had proportionally more PCNST. Non-Hispanic white adolescents and teens had proportionally more PCNST. In the 5–9 age group, Hispanic children had more malignant and uncertain behavior PCNST while non-Hispanic white children had more benign PCNST.

Among children younger than 5, more cases were from lower socioeconomic status (SES) regardless of tumor behavior. For children 5–9, more cases of malignant and uncertain PCNST were in low SES, while benign cases were from high SES. For adolescents and teens, all cases of malignant PCNST were from high SES. For adolescents, more benign cases were from high SES while uncertain cases were from low SES. For teens, the opposite was seen—more uncertain cases were from high SES while more benign cases were from low SES. Lastly, overwhelmingly, more cases, regardless of tumor behavior were from urban areas of California than from rural.

Incidence rates were calculated for race/ethnic groups by tumor behavior in Table 4. For many subgroups by age, race/ethnicity, or tumor behavior, incidence rates could not be calculated due to the small number of cases. Where incidence rates could be calculated and compared, we found no statistically significant differences by race/ethnicity for any age group by tumor behavior. Incidence rates for all tumor behaviors were highest in non-Hispanic white children aged 5–9 years and in adolescents with the exception of malignant tumors, which were highest in Asian/Pacific Islander children younger than 5 and teens.

At every age group, astrocytomas (IIIB), ependymomas, and choroid plexus (IIIA) predominated (Table 5). For both malignant and benign PCNST, at nearly every age group, astrocytoma had the highest incidence. Among children younger than 5 years old, the primary malignant diagnoses were ependymomas and choroid plexus (IIIA), while for children 5–9 years old, other gliomas (IIID) was

Table 4 Age-specific incidence rate[a] (ASIR) with 95% confidence interval (CI) of first primary central nervous system tumors by age group, tumor behavior and race/ethnicity, California, 2001–2005

Age Group	Race	Malignant		Benign	
		ASIR	95%CI	ASIR	95%CI
< 5 years	Non-Hispanic White	2.6	(2.2, 3.2)	1.5	(1.2, 1.9)
	Non-Hispanic Black	2.3	(1.4, 3.5)		
	Hispanic	2.6	(2.2, 3.0)	1.1	(0.8, 1.4)
	Asian-Pacific Islander	2.7	(1.9, 3.8)		
	Total	2.6	(2.4, 2.9)	1.2	(1.0, 1.4)
5-9 years	Non-Hispanic White	2.5	(2.1, 3.1)	1.7	(1.3, 2.1)
	Non-Hispanic Black	1.7	(1.0, 2.8)		
	Hispanic	2.2	(1.9, 2.6)	0.9	(0.7, 1.2)
	Asian-Pacific Islander	1.8	(1.1, 2.6)		
	Total	2.3	(2.0, 2.5)	1.1	(1.0, 1.3)
10-14 years	Non-Hispanic White	2.3	(1.9, 2.7)	1.6	(1.2, 1.9)
	Non-Hispanic Black				
	Hispanic	1.7	(1.4, 2.1)	1.0	(0.8, 1.3)
	Asian-Pacific Islander	1.8	(1.2, 2.7)		
	Total	1.9	(1.6, 2.1)	1.2	(1.0, 1.4)
15-19 years	Non-Hispanic White	2.0	(1.6, 2.5)	2.1	(1.7, 2.5)
	Non-Hispanic Black				
	Hispanic	1.4	(1.1, 1.8)	2.0	(1.6, 2.4)
	Asian-Pacific Islander	2.3	(1.6, 3.2)	1.1	(0.7, 1.8)
	Total	1.7	(1.5, 2.0)	1.8	(1.6, 2.1)

[a] Age-specific incidence rates are per 100,000 population. Rates are standardized to the 2000 US population

Shaded cells rates could not be calculated if number of cases were less than 15 and/or the underlying population was less than 100,000

Table 5 Number of cases, percent and age-specific incidence rate[a] (ASIR) of first primary central nervous system tumors by diagnositic group, age group and tumor behavior, California, 2001–2005

	< 5 years												5-9 years											
	Malignant				Benign				Uncertain		Total			Malignant				Benign				Uncertain		Total			
Diagnostic Groups	n	%	ASIR	95% CI	n	%	ASIR	95% CI	n	%	n	%	ASIR 95% CI	n	%	ASIR	95% CI	n	%	ASIR	95% CI	n	%	n	%	ASIR	95% CI
IIIA Ependymomas & Choroid Plexus Tumor	74	21.8%	0.6	(0.4, 0.7)	21	13.6%	0.2	(0.1, 0.2)			99	18.1%	0.8 (0.6, 0.9)	28	9.4%	0.2	(0.1, 0.3)	11	7.4%			6	9.2%	45	8.8%	0.3	(0.3, 0.5)
IIIB Astrocytomas	67	19.8%	0.5	(0.4, 0.7)	119	77.3%	0.9	(0.8,1.1)			189	34.6%	1.5 (1.3, 1.7)	72	24.2%	0.6	(0.4, 0.7)	102	68.9%	0.8	(0.6, 0.9)	8	12.3%	182	35.7%	1.4	(1.2, 1.6)
IIIC1 Medulloblastomas	64	18.9%	0.5	(0.4, 0.6)	0	0.0%			0	0.0%	64	11.7%	0.5 (0.4, 0.6)	68	22.9%	0.5	(0.4, 0.7)	0	0.0%			0	0.0%	68	13.3%	0.5	(0.4, 0.7)
IIIC2 PNET	47	13.9%	0.4	(0.3, 0.5)	0	0.0%			0	0.0%	47	8.6%	0.4 (0.3, 0.5)	29	9.8%	0.2	(0.1, 0.3)	0	0.0%			0	0.0%	29	5.7%	0.2	(0.1, 0.3)
IIIC9 Other Intracranial & Intraspinal	16	4.7%	0.1	(0.1, 0.2)	0	0.0%			0	0.0%	18	3.3%	0.1 (0.1, 0.2)					0	0.0%			0	0.0%				
IIID Other Gliomas	40	11.8%	0.3	(0.2, 0.4)	0	0.0%			0	0.0%	40	7.3%	0.3 (0.2, 0.4)	73	24.6%	0.6	(0.4, 0.7)	0	0.0%			0	0.0%	73	14.3%	0.6	(0.4, 0.7)
IIIE Other Specified Intracranial & Intraspinal	4								36	66.7%	43	7.9%	0.3 (0.2, 0.5)					22	14.9%	0.2	(0.1, 0.3)	46	70.8%	71	13.9%	0.5	(0.4, 0.7)
XA Intracranial & Intraspinal Germ Cell	8	2.4%			5	3.2%			0	0.0%	13	2.4%		13	4.4%							0	0.0%	14	2.7%		
Z Other	17	5.0%	0.1	(0.1, 0.2)	6	3.9%			11	20.4%	34	6.2%	0.3 (0.2, 0.4)	9	3.0%			12	8.1%			5	7.7%	26	5.1%	0.2	(0.1, 0.3)
Total	339	100.0%	2.6	(2.4, 2.9)	154	100.0%	1.2	(1.0, 1.4)	54	100.0%	547	100.0%	4.2 (3.9, 4.6)	297	100.0%	2.3	(2.0, 2.5)	148	100.0%	1.1	(1.0, 1.3)	65	100.0%	510	100.0%	3.9	(3.6, 4.3)

	10-14 years												15-19 years											
IIIA Ependymomas & Choroid Plexus Tumor	23	9.0%	0.2	(0.1, 0.3)	5	3.1%			12	15.8%	40	8.1%	0.3 (0.2, 0.4)	21	9.4%	0.2	(0.1, 0.2)					12	13.5%	37	6.8%	0.3	(0.2, 0.4)
IIIB Astrocytomas	66	25.9%	0.5	(0.4, 0.6)	89	55.6%	0.7	(0.5, 0.8)	7	9.2%	162	33.0%	1.2 (1.0, 1.4)	71	31.8%	0.6	(0.4, 0.7)	61	25.8%	0.5	(0.4, 0.6)	5	5.6%	137	25.0%	1.1	(0.9, 1.3)
IIIC1 Medulloblastomas	28	11.0%	0.2	(0.1, 0.3)	0	0.0%			0	0.0%	28	5.7%	0.2 (0.1, 0.3)	23	10.3%	0.2	(0.1, 0.3)	0	0.0%			0	0.0%	23	4.2%	0.2	(0.1, 0.3)
IIIC2 PNET	17	6.7%	0.1	(0.1, 0.2)	0	0.0%			0	0.0%	17	3.5%	0.1 (0.1, 0.2)	11	4.9%			0	0.0%			0	0.0%	11	2.0%		
IIIC9 Other Intracranial & Intraspinal	0	0.0%			0	0.0%			0	0.0%	0	0.0%		0	0.0%			0	0.0%			0	0.0%	0	0.0%		
IIID Other Gliomas	51	20.0%	0.4	(0.3, 0.5)	0	0.0%			0	0.0%	51	10.4%	0.4 (0.3, 0.5)	35	15.7%	0.3	(0.2, 0.4)	0	0.0%			0	0.0%	35	6.4%	0.3	(0.2, 0.4)
IIIE Other Specified Intracranial & Intraspinal					41	25.6%	0.3	(0.2, 0.4)	46	60.5%	91	18.5%	0.7 (0.5, 0.8)	6	2.7%			138	58.5%	1.1	(0.9, 1.3)	56	62.9%	200	36.5%	1.6	(1.3, 1.8)
XA Intracranial & Intraspinal Germ Cell	59	23.1%	0.4	(0.3, 0.6)					0	0.0%	62	12.6%	0.5 (0.3, 0.6)	43	19.3%	0.3	(0.2, 0.4)					0	0.0%	45	8.2%	0.3	(0.3, 0.5)
Z Other	7	2.7%			22	13.8%			11	14.5%	40	8.1%	0.3 (0.2, 0.4)	13	5.8%			31	13.1%			16	18.0%	60	10.9%	0.5	(0.3, 0.6)
Total	255	100.0%	1.9	(1.6, 2.1)	160	100.0%	1.2	(1.0, 1.4)	76	100.0%	491	100.0%	3.6 (3.3, 3.9)	223	100.0%	1.7	(1.5, 2.0)	236	100.0%	1.8	(1.6, 2.1)	89	100.0%	548	100.0%	4.2	(3.9, 4.6)

[a] Age-specific incidence rates are per 100,000 population. Rates are standardized to the 2000 US population

PNET Primitive Neuroectodermal Tumors

Shaded cells rates could not be calculated if number of cases were less than 15 and/or the underlying population was less than 100,000

ranked first only slightly ahead of astrocytomas (IIIB), which was followed closely by medulloblastomas (IIIC1). For adolescents, germ cell tumors (XA) ranked a close second to astrocytomas (IIIB). Among teens, benign PCNST classified as other specified intracranial and intraspinal tumors (IIIE) were ranked first; the majority of patients in that sub-category were diagnosed specifically with pituitary adenoma (66.7%). Overall, pituitary adenoma comprised 20.1% of all diagnoses in teens. In all age groups, the majority of tumors of uncertain behavior were classified as other specified intracranial and intraspinal tumors (IIIE) classification. In nearly every age group, the majority of those patients were diagnosed specifically with gangliogliomas, representing between 37.0% (5–9 year olds) and 47.8% (10–14 year olds) of those cases. Among children younger than 5 years old, nearly an equal number of patients were diagnosed with craniophargiomas and gangliogliomas (36.1 and 38.9%, respectively).

Table 6 shows the distribution of astrocytomas; both malignant and benign numbered nearly the same for boys and girls younger than 15 years old, while among teens, they predominated in boys. Further, boys had the most ependymomas and choroid plexis tumors, medulloblastomas, and PNET. Although astrocytomas and PNET tumors were distributed nearly equally among non-Hispanic white and Hispanic children; all other histologies were more frequently seen in adolescent and teen non-Hispanic whites. In the low SES group, ependymomas and choroid plexis tumors, medulloblastomas, and PNET were found most often among children younger than 10 years old. Astrocytomas were found mostly among low SES children younger than 5, with a near even distribution among those 5–9 and among high SES adolescents and teens. Furthermore, benign astrocytomas were found mainly in the low SES group for children younger than 5 and in teens. In high SES groups however astrocytoma were found mainly among those 5–14 years old.

Discussion

This is the first study to examine both malignant and benign PCNST among children, adolescents, and teens in California. Fifty-three percent of PCNST among those younger than 20 years old were malignant, 33.3% benign, and the remainder was of uncertain behavior. The AAIR of malignant PCNST in this age group was 2.1 cases per 100,000 persons and for benign PCNST, 1.3 per 100,000. Among children and adolescents younger than 15 years old, the malignant PCNST was 2.2 per 100,000 and for benign PCNST, 1.2 per 100,000.

In the present study, the incidence of malignant tumors decreased with increasing age. The highest incidence for malignant PCNST was found among children younger than 5 years old [8–11], whereas teens had the highest incidence of benign and uncertain behavior PCNST. Post-mortem studies on younger brains have found a higher relative concentration of neural stem cells [12, 13], which suggests that the immature brain might possess an increased capacity to generate malignant neuroepithelial tumors through increased populations of neural stem and progenitor cell types, supporting the stem cell hypothesis for tumor formation [14].

Consistent with results found for adults, boys at every age group had a higher incidence of malignant tumors, while girls generally had a higher incidence of benign tumors [11, 15]. Significant sex-specific differences were not found for malignant PCNST in the 5–9 year age group or for benign PCNST among adolescents. The incidence of malignant PCNST in girls dropped sharply starting in the 5–9 year old age group while the incidence of benign PCNST rose just as dramatically starting in the adolescence. Age- and sex-specific tumor frequency and tumor behavior transition are postulated to be hormone-related, coinciding with the onset of puberty, although the specific mechanism has yet to be determined [16]. For example, in a case report, the growth and regression of a pilocytic astrocytoma was found to be related to exogenous human growth hormone (hGH) [17].

In our study, astrocytomas were the prominent diagnoses for malignant PCNST in most age groups, which is consistent with other national and international studies [8, 10, 11, 15, 18–29]. Ependymomas and choroid plexus tumors were highest among children younger than 5 years old [19, 20, 26, 27], while other gliomas and medulloblastomas had a similar incidence to astrocytomas in the 5–9 age group [11, 20]. We noted a surge in germ cell tumors for adolescents, which declined for teens concurrent with an increase in pituitary tumors [16, 30, 31]. The proportional incidence of pituitary adenomas in our study population was similar to that reported by CBTRUS, although our methods varied [21].

California's unique race/ethnic population allows analyses of the distribution of cancer incidence in groups that might otherwise be overlooked or inaccurately counted. California's younger population (<20 years old) is predominantly Hispanic (45.8%). Hispanics represent 50.2% of children younger than 5 years old, 47.8% of those in the 5–9 age group, and 44.3% of the adolescent group. However, in the teen group, the Hispanic population is nearly equal to the non-Hispanic white population (40.9 and 39.5%, respectively) [32]. Therefore not surprisingly, in our study the highest proportional incidence of malignant PCNST was among Hispanic children younger than 10 years old; non-Hispanic whites had the highest incidence among 10–19 year olds. The ASIR reported for

Table 6 Number of cases and percent of first primary malignant and benign central nervous system tumors by age group, population demographics and diagnostic group, California, 2001–2005

Demographic Characteristics			Malignant												Benign					
			IIIA Ependymomas & Choroid Plexus Tumor		IIIB Astrocytomas		IIIC1 Medullo-blastomas		IIIC2 PNET		IIID Other Gliomas		XA Intracranial & Intraspinal Germ Cell		Z Other		Total		IIIB Astrocytomas		IIIE Other Specified Intracranial & Intraspinal		Z Other		Total	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
< 5 years	Sex	Male	41	55.4%	40	59.7%	43	67.2%	26	55.3%	18	45.0%			25	53.2%	193	56.9%	60	50.4%			12	34.3%	72	46.8%
		Female	33	44.6%	27	40.3%	21	32.8%	21	44.7%	22	55.0%			22	46.8%	146	43.1%	59	49.6%			23	65.7%	82	53.2%
	Race/ethnicity	Non-Hispanic white	22	29.7%	24	35.8%	20	31.3%	13	27.7%	12	30.0%			17	36.2%	108	31.9%	47	39.5%			15	42.9%	62	40.3%
		Hispanic	41	55.4%	25	37.3%	38	59.4%	24	51.1%	19	47.5%			21	44.7%	168	49.6%	54	45.4%			15	42.9%	69	44.8%
		Other/Unknown	11	14.9%	18	26.9%	6	9.4%	10	21.3%	9	22.5%			9	19.1%	63	18.6%	18	15.1%			5	14.3%	23	14.9%
	Socioeconomic Status	Low	36	48.6%	25	37.3%	27	42.2%	20	42.6%	21	52.5%			18	38.3%	147	43.4%	61	51.3%			11	31.4%	72	46.8%
		Medium	12	16.2%	13	19.4%	14	21.9%	10	21.3%	5	12.5%			8	17.0%	62	18.3%	19	16.0%			10	28.6%	29	18.8%
		High	26	35.1%	29	43.3%	23	35.9%	17	36.2%	14	35.0%			21	44.7%	130	38.3%	39	32.8%			14	40.0%	53	34.4%
5-9 years	Sex	Male	13	46.4%	36	50.0%	42	61.8%	16	55.2%	35	47.9%			13	48.1%	155	52.2%	46	45.1%			22	47.8%	68	45.9%
		Female	15	53.6%	36	50.0%	26	38.2%	13	44.8%	38	52.1%			14	51.9%	142	47.8%	56	54.9%			24	52.2%	80	54.1%
	Race/ethnicity	Non-Hispanic white	6	21.4%	32	44.4%	28	41.2%	12	41.4%	26	35.6%			9	33.3%	113	38.0%	51	50.0%			23	50.0%	74	50.0%
		Hispanic	14	50.0%	34	47.2%	36	52.9%	13	44.8%	30	41.1%			11	40.7%	138	46.5%	37	36.3%			18	39.1%	55	37.2%
		Other/Unknown	8	28.6%	6	8.3%					17	23.3%			7	25.9%	46	15.5%	14	13.7%			5	10.9%	19	12.8%
	Socioeconomic Status	Low	17	60.7%	30	41.7%	28	41.2%	14	48.3%	34	46.6%			11	40.7%	134	45.1%	35	34.3%			17	37.0%	52	35.1%
		Medium			11	15.3%	15	22.1%			13	17.8%			7	25.9%	53	17.8%	21	20.6%			13	28.3%	34	23.0%
		High	8	28.6%	31	43.1%	25	36.8%	11	37.9%	26	35.6%			9	33.3%	110	37.0%	46	45.1%			16	34.8%	62	41.9%
10-14 years	Sex	Male			34	51.5%					25	49.0%	49	83.1%	46	58.2%	154	60.4%	42	47.2%	22	53.7%	18	60.0%	82	51.3%
		Female			32	48.5%					26	51.0%	10	16.9%	33	41.8%	101	39.6%	47	52.8%	19	46.3%	12	40.0%	78	48.8%
	Race/ethnicity	Non-Hispanic white			33	50.0%					24	47.1%	19	32.2%	37	46.8%	113	44.3%	47	52.8%	17	41.5%	14	46.7%	78	48.8%
		Hispanic			24	36.4%					21	41.2%	27	45.8%	32	40.5%	104	40.8%	28	31.5%	21	51.2%	12	40.0%	61	38.1%
		Other/Unknown			9	13.6%					6	11.8%	13	22.0%	10	12.7%	38	14.9%	14	15.7%					21	13.1%
	Socioeconomic Status	Low			30	45.5%					17	33.3%	21	35.6%	36	45.6%	104	40.8%	29	32.6%	16	39.0%	13	43.3%	58	36.3%
		Medium			10	15.2%					13	25.5%	9	15.3%	10	12.7%	42	16.5%	17	19.1%	11	26.8%	7	23.3%	35	21.9%
		High			26	39.4%					21	41.2%	29	49.2%	33	41.8%	109	42.7%	43	48.3%	14	34.1%	10	33.3%	67	41.9%
15-19 years	Sex	Male			44	62.0%					17	48.6%	35	81.4%	42	56.8%	138	61.9%	36	59.0%	44	31.9%	21	56.8%	101	42.8%
		Female			27	38.0%					18	51.4%	8	18.6%	32	43.2%	85	38.1%	25	41.0%	94	68.1%	16	43.2%	135	57.2%
	Race/ethnicity	Non-Hispanic white			30	42.3%					17	48.6%	15	34.9%	40	54.1%	102	45.7%	33	54.1%	55	39.9%	17	45.9%	105	44.5%
		Hispanic			23	32.4%					11	31.4%	12	27.9%	27	36.5%	73	32.7%	22	36.1%	68	49.3%	13	35.1%	103	43.6%
		Other/Unknown			18	25.4%					7	20.0%	16	37.2%	7	9.5%	48	21.5%	6	9.8%	15	10.9%	7	18.9%	28	11.9%
	Socioeconomic Status	Low			33	46.5%					15	42.9%	14	32.6%	23	31.1%	85	38.1%	26	42.6%	64	46.4%	15	40.5%	105	44.5%
		Medium			12	16.9%					8	22.9%	9	20.9%	13	17.6%	42	18.8%	17	27.9%	25	18.1%	7	18.9%	49	20.8%
		High			26	36.6%					12	34.3%	20	46.5%	38	51.4%	96	43.0%	18	29.5%	49	35.5%	15	40.5%	82	34.7%

PNET Primitive Neuroectodermal Tumors

Shaded cells categories with less than 5 cases; age groups that represented less than 25 of a histology group and/or no meaningful information could be gleaned due to small case numbers, were omitted

malignant PCNST for children younger than 5 (2.6–2.7 per 100,000) was nearly the same for Hispanics, non-Hispanic whites, and Asian/Pacific Islanders. Non-Hispanic whites had the highest incidence among 5–14 year olds (2.5 per 100,000) and Asian/Pacific Islanders had the highest incidence among teens (2.3 per 100,000). The differences in these incidence rates were not statistically significant.

This is the first study to examine the proportions of PCNST incidence by SES in this age group. We found that children younger than 10 years old in the lowest SES group had a higher proportional incidence of malignant PCNST, while children and adolescents 5–19 years old in the highest SES group had a higher incidence of benign PCNST compared to other SES groups. This finding may be related to unique class level exposures or indirectly related to race/ethnicity population distribution, specifically those groups that are more likely at the lower SES levels and/or differential healthcare coverage [33]. Cancer incidence has been found to be highest among those with more education, greater income, and with private insurance [34, 35]. Reasons for this are unclear. Some have advanced the theory, least in childhood leukemia, that higher SES groups are immunologically shielded by hyperhygienic environments, leading to naïve immune systems which are more prone to cancer development [36, 37].

Common causes for differences in CNS tumor incidence statistics between epidemiologic studies were discussed at length in the authors' companion publication in this edition. Unique to comparisons of pediatric CNS tumor incidence statistics is the variation in the selection of age groupings across sources and the use of the ICCC. The ICCC was designed specifically for childhood cancers and is based on tumor morphology in conjunction with primary anatomical site, rather than histology and anatomical site separately as is common [6, 7]. Additionally, SEER created a recode system for the ICCC [6, 7], as it did for the ICD-O [38]. The ICCC SEER site recode is used by the CCR, all North American central cancer registries, NPCR and SEER to organize histologies but not by CBTRUS or in international studies. Even when the ICCC was used, valid comparisons between studies and statistical sources could not be made because many of those studies used cases from a single institution or if population-based, did not calculate incidence rates [39–41]. When rates were available, the detail necessary for valid comparison was not the same [18, 42]. We found the use of the ICCC to have limitations. Although appropriate for showing transitioning tumor occurrence by age groups, the ICCC was inadequate for delineating PCNST among teens. For example, 20% of benign PCNST among teens were pituitary adenomas, which were otherwise hidden in the category of "other intracranial and intraspinal", since they are nearly nonexistent among children and adolescents younger than 15 years old.

Our study's strengths and weakness have been discussed in the authors' companion publication in this edition. Specific to this study, even though 5 years of benign data had been collected, due to the small numbers of cases, stable and accurate incidence rates could not be calculated for many sex-race/ethnic-age group combinations among children, adolescents, and teens.

Primary central nervous system tumors are a major source of cancer morbidity and mortality among children, adolescents, and teens. While PCNST incidence has been relatively well-researched, this is the first study to comprehensively examine benign PCNST by ICCC diagnostic groups and age groups, and to compare them to malignant PCNST. In addition, this is one of the few studies to examine PCNST among adolescents [22, 24, 30, 43]. This study of California PCNST among children, adolescents, and teens provides a basis for future basic, translational and clinical brain tumor research and for both healthcare and public health in California.

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