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Brief communication

Birth weight, fetal growth, and risk of pediatric rhabdomyosarcoma: an updated record linkage study in California

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ABSTRACT

Purpose: The purpose of the study was to examine whether birth characteristics affect the risk of rhabdomyosarcoma (RMS) in children and adolescents younger than 19 years.
Methods: A total of 722 RMS cases diagnosed at the age of 0–19 years during 1988–2011 were identified from the California Cancer Registry and matched by birth date, sex, and race to 2,888 controls using California birth records. Conditional logistic regression was used to estimate the risk of RMS associated with birth weight, gestational age, and size for gestational age.
Results: High birth weight (odds ratio [OR]: 1.00; 95% confidence interval [CI]: 0.78–1.29) and large for gestational age (LGA; OR: 0.94, 95% CI: 0.72–1.23) were not associated with RMS risk overall. Among non-Hispanic whites, the ORs were 1.33 for high birth weight (95% CI: 0.94–1.89) and 1.17 for LGA (95% CI: 0.78–1.75); no indications of association were observed for other racial or ethnic groups (*P* interaction <.10). Compared with normal gestational age, preterm (<37 weeks) and post-term (>40 weeks) babies had 16%–18% lower risks of RMS overall, after adjusting for birth weight.
Conclusions: In the largest study to date, there was an indication of association between high birth weight, LGA, and increased RMS risk among non-Hispanic white children and adolescents, but not in other racial or ethnic groups.

Introduction

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma affecting children and adolescents (age, 0–19 years), with approximately five cases per million diagnosed annually in the United States [1]. Pediatric RMS arises from skeletal muscle tissue; two major subtypes, embryonal (eRMS) and alveolar RMS (aRMS), make up 60%–75% and 16%–30% of total cases, respectively [2–4].

Owing to the rarity of pediatric RMS, little is known about its etiology. Most RMS cases are sporadic, with a small proportion associated with genetic syndromes, including Li-Fraumeni, neurofibromatosis, and Beckwith-Wiedemann syndromes [5]. The incidence for embryonal subtype peaks before 5 years of age, and is more common in males than females (1.5:1), whereas alveolar incidence is evenly distributed throughout childhood and adolescence [5, 6]. Recent studies suggest an association with accelerated fetal growth. In a study of 27 cases, proportions of optimal birth weight and optimal weight for length were associated with increased risk, although associations were not statistically significant [7]. A record linkage study of 583 children (age, 0–5 years) diagnosed with RMS in California, Minnesota, New York, Texas, and Washington from 1988 to 1997 reported associations with high birth weight (odds ratio [OR]: 1.27, 95% confidence interval [CI]: 1.14–1.42) and the top decile of size for gestational age (OR: 1.42, 95% CI: 1.03–1.96) [8]. A statewide California study of 359 RMS cases aged 0–4 years, diagnosed from 1988 and up to 2008, showed a nonstatistically significant association between high birth weight and eRMS (OR: 1.21; 95% CI: 0.81–1.81), but not aRMS (OR: 0.60; 95% CI: 0.24–1.50) [9]. In contrast, an analysis of 322 matched cases and controls from the Intergroup Rhabdomyosarcoma Study Group (age, 0–20 years)

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Table 1
Risk of rhabdomyosarcoma associated with birth characteristics among 722 cases and 2888 controls in California (1988–2011)

Characteristic	All RMS (*n* cases = 722, *n* controls = 2,888)			eRMS (*n* cases = 444, *n* controls = 1,776)			aRMS (*n* cases = 197, *n* controls = 788)			*P* for interaction[†]
	Controls, *n* (%)	Cases, *n* (%)	OR[*] (95% CI)	Controls, *n* (%)	Cases, *n* (%)	OR[*] (95% CI)	Controls, *n* (%)	Cases, *n* (%)	OR[*] (95% CI)	
Birth weight (g)										
Low (<2,500)	164 (6)	48 (7)	1.05 (0.73–1.50)	95	27	0.99 (0.63–1.55)	53	13	0.97 (0.51–1.84)	.09
Normal (2,500–4,000)	2,362 (82)	585 (81)	1.00 (Ref.)	1,466	356	1.00 (Ref.)	635	164	1.00 (Ref.)	
High (>4,000)	362 (13)	89 (12)	1.00 (0.78–1.29)	215	61	1.09 (0.81–1.47)	100	20	0.89 (0.55–1.44)	
P-trend			.88			.61			.72	
Gestational age (wk)										
Preterm (<37)	278 (10)	67 (9)	0.84 (0.62–1.12)	175	40	0.82 (0.57–1.19)	76	16	0.66 (0.38–1.16)	.30
Normal (37–40)	1,300 (45)	355 (49)	1.00 (Ref.)	796	217	1.00 (Ref.)	363	103	1.00 (Ref.)	
Overdue (>40)	1,134 (39)	252 (35)	0.82 (0.68–0.98)	701	158	0.84 (0.67–1.05)	300	64	0.70 (0.50–0.97)	
Missing	176 (6)	48 (7)	1.01 (0.72–1.41)							
P-trend			.27			.51			.35	
Size for gestational age										
Small for gestational age	277 (10)	73 (10)	1.00 (0.76–1.32)	177	41	0.91 (0.64–1.30)	78	24	1.25 (0.78–1.98)	.22
Appropriate for gestational age	2,099 (73)	523 (72)	1.00 (Ref.)	1,294	325	1.00 (Ref.)	573	139	1.00 (Ref.)	
Large for gestational age	336 (12)	78 (11)	0.94 (0.72–1.23)	201	49	0.96 (0.69–1.33)	88	20	0.94 (0.58–1.53)	
Missing	176 (6)	48 (7)	1.10 (0.79–1.53)						0.38	
P-trend			.60			.84				

[*] Odds ratios are adjusted for plurality.
[†] *P* for interaction from likelihood-ratio test comparing eRMS versus aRMS.

enrolled from 1982 to 1988 observed statistically significant associations between both low (OR: 4.46; 95% CI: 1.41–14.1) and high (OR: 2.41; 95% CI: 1.09–5.35) birth weight and aRMS, although no statistically significant associations were seen for the more common embryonal subtype [5].

The present analysis is an update to previous analyses of RMS cases conducted in California; it includes diagnoses spanning 24 years (1988–2011) and ages to 19 years, more than doubling the sample size of earlier studies [8, 10]. This is the largest study examining the association between birth weight, measures of fetal growth, and risk of RMS overall and by race and ethnic group and histologic subtype.

Methods

Study population

We conducted a population-based case-control study of 722 cases of pediatric RMS (*International Classification of Childhood Cancer, third edition*, recode 91; *International Classification of Diseases for Oncology, third edition* (ICD-O-3), codes 8900–8905, 8910, 8912, 8920, 8991) and 2,888 matched controls by linking cancer diagnosis records from the California Cancer Registry (CCR) to birth records maintained by the vital statistics unit of the California Department of Public Health. Cases were diagnosed from 1988 (the earliest year the CCR data were electronically available) through 2011 (when the linkage was conducted) and born in or after 1978 (the earliest year the California birth data were electronically available), and each case was linked to statewide birth records and matched by year and month of birth, sex, race, and ethnicity (i.e., Hispanic vs. non-Hispanic) to four controls from the birth records who had not been linked to the CCR. Using first and last name, date of birth, mother's name, and social security number (when available), 76% of RMS cases were linked to a California birth certificate. This study was approved by Institutional Review Boards at the University of California, Berkeley and the California Department of Public Health.

Data collection

The California birth records included data on sociodemographic, birth, and pregnancy characteristics, including birth weight (in grams) and gestation length (in days), birth order, plurality, race and ethnicity (child, maternal, and paternal), parental age and years of education, geographic location at birth, month when prenatal care began, and principal source of payment for prenatal care and delivery. The CCR data included information on the date of cancer diagnosis and tumor characteristics.

Gestational age was calculated from the date of last menstrual period through birth date. Outlier values less than 20 weeks or greater than 43 weeks were removed ($n = 73$). Size for gestational age was calculated according to the methodology described in Alexander et al. [11]. Briefly, information from the pool of all available "healthy" controls was used to establish standards stratified by week of gestation, sex, and race. Any child above the 90th or below the 10th percentile for birth weight in their gestational week, sex, and race-specific strata was considered to be large for gestational age (LGA) or small for gestational age (SGA).

Cancer histologic type was classified as embryonal (ICD-O-3: 8910, 8912, 8991), alveolar (8920), or unclassified (8900–8902). Cancer site was classified according to the ICD-O-3 Surveillance Epidemiology and End Results (SEER) Site/Histology Validation List codes (http://seer.cancer.gov/icd-o-3/sitetype.icdo3.d20150918.pdf), as connective and soft tissue (ICD-10: C470–C476, C478–C479, C490–C496, C498–C499), testis (C620–C6221, C629), orbit (eye; C690–C691, C693, C695–C698), nasopharynx (C110–C113, C118–C119), and others.

Statistical analysis

Statistical analyses used both univariate and multivariate conditional logistic regression to calculate ORs and 95% CIs for each measure of fetal growth, including birth weight (<2,500, 2,500–4,000, >4,000 g), gestational age (premature, <37 weeks; normal, 37–40 weeks; overdue, >40 weeks), and size for