BIRTH DEFECTS ARE ASSOCIATED WITH GERM CELL TUMORS AMONG MALE BUT NOT FEMALE ADOLESCENTS IN THE CHILDREN'S ONCOLOGY GROUP GERM CELL TUMOR EPIDEMIOLOGY (GAMETES) STUDY

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Keywords: germ cell tumors; birth defects; epidemiology; sex; effect modification; cancer predisposition

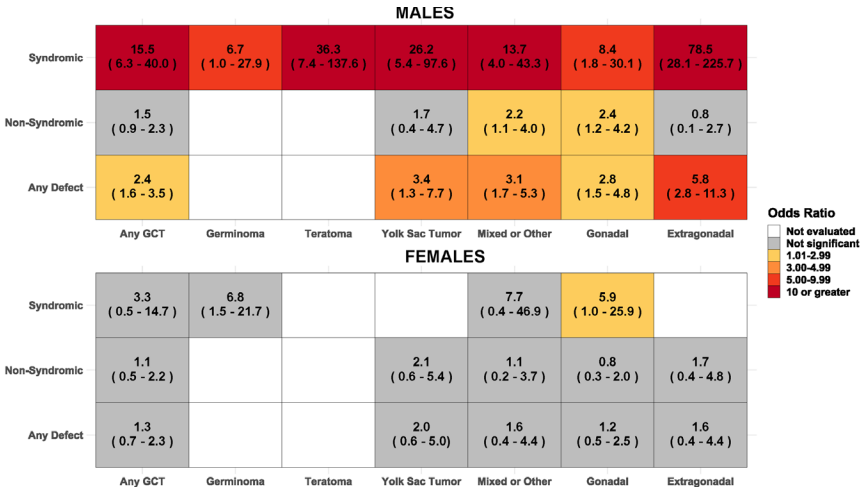
Background: Studies suggest birth defects are associated with germ cell tumors (GCTs). However, few investigations have evaluated associations by sex, type of birth defect, tumor histologic subtype, or location. Therefore, we performed a detailed analysis of the associations between birth defects and GCTs among participants in the Children's Oncology Group Germ Cell Tumor Epidemiology (GaMETES) Study.

Materials/Methods: Cases (N=638) were diagnosed with GCTs between July 2008 and December 2015 and aged <20 years. Ten controls per case, matched on sex and maternal race/ethnicity, were randomly selected from births in three U.S. states (Oklahoma, North Carolina, and Texas). Information on birth defects diagnoses were obtained from parental interview (cases) and statewide birth defects registries (controls), then classified using ICD-9 codes. Birth defects were classified as syndromic (attributable to a chromosomal or genetic diagnosis) or non-syndromic. Logistic regression was used to calculate odds ratios and 95% confidence intervals (ORs; 95% CIs) for associations between birth defects and GCTs, overall as well as by sex, tumor subtype, and type of birth defect.

Results: Prevalence of any birth defect or syndrome was 8% in GCT cases and 4% in controls (OR 2.0, 95% CI 1.4-2.7). Among all cases of GCTS, non-chromosomal defects were associated with the mixed/other (OR 1.9, 95% CI 1.0-3.3) and yolk sac tumor subtypes (OR 1.9, 95% CI 0.8-3.9). Genitourinary defects were associated with yolk sac tumors (OR 3.4, 95% CI 1.0-8.6), gonadal tumors (OR 2.2, 95% CI 0.9-4.5), and extracranial/extragonadal tumors (OR 2.2, 95% CI 0.5-6.0). In sex-stratified analyses, non-syndromic defects were associated with mixed/other and gonadal tumors among males, whereas they were not associated with GCTs among females (Figure 1).

Conclusions: Our results suggest that non-chromosomal birth defects, particularly genitourinary defects, are associated with GCTs in children and adolescents. Associations were strongest for yolk sac or mixed/other tumors, and may be specific to males. Effect modification by sex may be attributable to differences in the distributions of tumor subtypes by sex. Our findings may assist in discovery of risk factors for these tumors, and improve understanding of sex ratio disparities.

Images / Graph / Table


MALES
Syndromic
15.5 (6.3 - 40.0)
6.7 (1.0 - 27.9)
36.3 (7.4 - 137.6)
26.2 (5.4 - 97.6)
13.7 (4.0 - 43.3)
8.4 (1.8 - 30.1)
78.5 (28.1 - 225.7)
Non-Syndromic
1.5 (0.9 - 2.3)
1.7 (0.4 - 4.7)
2.2 (1.1 - 4.0)
2.4 (1.2 - 4.2)
0.8 (0.1 - 2.7)
Any Defect
2.4 (1.6 - 3.5)
3.4 (1.3 - 7.7)
3.1 (1.7 - 5.3)
2.8 (1.5 - 4.8)
5.8 (2.8 - 11.3)
Any GCT
Germinoma
Teratoma
Yolk Sac Tumor
Mixed or Other
Gonadal
Extragonadal
FEMALES
Syndromic
3.3 (0.5 - 14.7)
6.8 (1.5 - 21.7)
7.7 (0.4 - 46.9)
5.9 (1.0 - 25.9)
Non-Syndromic
1.1 (0.5 - 2.2)
2.1 (0.6 - 5.4)
1.1 (0.2 - 3.7)
0.8 (0.3 - 2.0)
1.7 (0.4 - 4.8)
Any Defect
1.3 (0.7 - 2.3)
2.0 (0.6 - 5.0)
1.6 (0.4 - 4.4)
1.2 (0.5 - 2.5)
1.6 (0.4 - 4.4)
Any GCT
Germinoma
Teratoma
Yolk Sac Tumor
Mixed or Other
Gonadal
Extragonadal
Odds Ratio
Not evaluated
Not significant
1.01-2.99
3.00-4.99
5.00-9.99
10 or greater