Age at puberty and risk of testicular germ cell cancer (Ontario, Canada)

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Objectives: Incidence rates of testicular cancer are increasing among postpubescent men. This suggests that putative exposures may operate early in life and have changed over time. The age at which endocrine activity accelerates (age at puberty) may be such an exposure. This study was undertaken to investigate the relationship between age at puberty and testicular cancer risk.

Methods: A population-based case-control study was conducted in the province of Ontario, Canada which included males, aged 16 to 59 years, diagnosed with testicular germ cell cancer between 1987 and 1989, and age-matched controls. Data were collected on 502 cases, 346 case mothers, 975 controls, and 522 control mothers. Surrogate measures for age at puberty included age at starting to shave, appearance of hair, growth spurt, and voice change.

Results: A protective effect of later puberty was evident for all four measures of puberty as reported by both subjects and mothers, and greater protection was conferred when the greatest number of later puberty events were reported. Risk associated with earlier puberty was inconclusive.

Conclusions: As age at puberty is decreasing in the population, the proportion of boys experiencing the protective effect of later puberty may be diminishing. This may help explain the increasing incidence of testicular cancer. Cancer Causes and Control 1998, 9, 253-258

Key words: Canada, men, puberty, testicular cancer.

Introduction

Testicular germ cell cancer is predominantly a disease of young and middle-aged men. Age-specific incidence rates closely parallel endocrine activity, and appear to be increasing among post- but not prepubescent males. This increase has been observed in Ontario, Canada¹ as well as elsewhere in the world,²-⁵ and is likely due to a birth cohort effect operating in men born in the early part of this century.⁶⁻⁷

Undescended testicle is a strong and consistent risk factor for testicular germ cell cancer. Despite numerous investigations, little consistent information regarding other risk factors has emerged and the reason for the increasing incidence of this cancer remains unknown. Both the early age at onset and the increasing incidence suggest that putative exposures operate early in childhood or young adulthood, and may have changed over time. Age at puberty, and the acceleration of endocrine activity, may be such an exposure⁸⁻⁹ as it is consistent with the descriptive epidemiology of this cancer: a decline in age at puberty in boys,¹⁰ coincident with the

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Table 1. Puberty score based on subjects' responses and on mothers' responses independently, Ontario, Canada

<table>
<thead>
<tr>
<th>Puberty score</th>
<th>Definition of puberty score</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-4 early</td>
<td>3 or 4 variables reported as earlier</td>
</tr>
<tr>
<td>1-2 early</td>
<td>1 or 2 variables reported as earlier and a fewer number of variables reported as later</td>
</tr>
<tr>
<td>Same</td>
<td>3 or 4 variables reported as same or an equal number of variables reported as earlier and later</td>
</tr>
<tr>
<td>1-2 later</td>
<td>1 or 2 variables reported as later and a fewer number of variables reported as earlier</td>
</tr>
<tr>
<td>3-4 later</td>
<td>3 or 4 variables reported as later</td>
</tr>
</tbody>
</table>

birth cohort phenomenon observed in population-based incidence data on testicular germ cell cancer.

Several studies have been undertaken to examine the association between age at puberty and risk of testicular germ cell cancer, some of these report an association with others report no association. With no clear defining event, such as menarche for girls, to mark the onset of puberty in boys, these studies have relied on surrogate exposures (e.g., age at starting to shave, voice change, and appearance of body hair). Such surrogates only estimate the exposure of interest and are subject to an indeterminate amount of measurement error.

The present study was undertaken to test the hypothesis that advanced or delayed relative age at puberty is associated with risk of developing testicular germ cell cancer; and included two analytic strategies, both designed to help characterize the true effect of poorly measured exposures.

Materials and methods

A population-based case-control study was conducted in the province of Ontario, and included all histologically confirmed, newly incident cases of testicular germ cell cancer (ICD-9 code 186, ICD-O-M 906-910) diagnosed between 1987 and 1989, aged 16 to 59 years, and reported to the Ontario Cancer Registry by pathology reports. Controls were a random sample of the Ontario population, drawn from the Enumeration Composite Records of the Ontario Ministry of Revenue, and selected to have the same age distribution as that expected for cases based on Ontario cancer incidence data.

Data were collected through the use of a self-administered standardized questionnaire mailed to subjects. Another questionnaire was mailed to subject mothers, when they were available, and completed by telephone interview. Subjects provided information on sociodemographic factors, and occupational and medical histories, including treatment for undescended testicle. Both subjects and mothers were asked about events marking puberty in the subject: appearance of hair (pubic, chest, and axillary hair), starting to shave, growth spurt, and voice change. Ages at occurrence of these events were reported relative to peers: earlier than, later than, or at the same time as other boys. (A pre-test of the questionnaire revealed that subjects had difficulty recalling an actual age of these events.)

When information on at least three of the four puberty variables was available, two summary variables were created, one from subjects' responses and the other from mothers' responses, as shown in Table 1. In addition, a composite subject-mother report was created, adapted from a method described by Marshall. For the purpose of this analysis, subjects' and mothers' responses to relative time of puberty events, recorded as trichotomous response variables (earlier, same, later) were jointly classified as shown in Table 2. Discordant pairs (i.e., one reported later and the other reported earlier) were excluded from the analysis (n = 23 for growth spurt, 4 for voice change, 14 for starting to shave, and 18 for appearance of body hair).

Unconditional logistic regression modeling was used to calculate age-adjusted odds ratio estimates (AOR) and 95 percent confidence intervals (CI) using the statistical package EGRET. All reported odds ratio estimates were adjusted by five-year age groups.

Results

Of 621 eligible cases, 502 (80.8 percent) case subjects and 346 of their mothers completed questionnaires. A total of 1,438 controls were sent questionnaires; 95%