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Baldness, acne and testicular germ cell tumors

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Abstract

Androgen levels during critical periods of testicular development may be involved in the etiology of testicular germ cell tumors (TGCT). We evaluated the roles of adolescent and early adult life correlates of androgen exposure and TGCT in a hospital-based case control study. TGCT cases (n=187) and controls (n=148), matched on age, race and state of residence, participated in the study. Unconditional logistic regression was used to estimate associations between TGCT and male pattern baldness, severe acne, markers of puberty onset and body size. Cases were significantly less likely to report hair loss than controls (OR, 0.6; 95% CI, 0.4, 1.0). Amount of hair loss, increasing age at onset and increasing rate of loss were all inversely associated with TGCT (rate of hair loss: p-trend=0.03; age at onset: p-trend=0.03; amount of hair loss: p-trend=0.01). History of severe acne was inversely associated with TGCT (OR, 0.5; 95% CI, 0.3, 0.9) and height was positively associated with TGCT (p-trend=0.02). Increased endogenous androgen levels during puberty and early adulthood may be associated with decreased risk of TGCT. Additional studies of endogenous hormone levels during puberty and early adult life are warranted, especially studies evaluating the role of androgen synthesis, metabolism and uptake.

Keywords

Testicular germ cell tumors; baldness; acne; hospital-based; case-control

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INTRODUCTION

Testicular germ cell tumors (TGCT) are the most commonly occurring tumors in young adult men aged 15 to 39 years in the United States (U.S.), although they account for less than 2 percent of male malignant neoplasms (Altekruse *et al.*, 2010). Based on data from 2003-2007, TGCT incidence rates among white men in the U.S. was 5.9 per 100,000 men (Altekruse *et al.*, 2010). TGCT is suggested to develop as a result of the neoplastic transformation of germ cells into testicular carcinoma *in situ*. It is believed that these neoplasms arise early in fetal life and progress to invasive cancer under the influence of adult gonadotropic and androgenic hormones (Rajpert-De & Skakkebaek, 1993; Skakkebaek *et al.*, 1998). It is further hypothesized that the progression of these pre-neoplastic lesions occurs due to some unknown perturbation of the hypothalamic-pituitary-gonadal axis at critical periods of testicular development (Forman *et al.*, 1994).

There are few established risk factors for TGCT beyond age, race/ethnicity, adult stature, history of cryptorchidism, and family history of TGCT (McGlynn & Cook, 2009). Research on early life exposures and TGCT risk has primarily focused on perinatal and early postnatal exposure to endogenous and exogenous estrogens. The role of androgen levels during adolescence and early adult life has received less attention. However exposures associated with increased androgen levels, such as male pattern baldness and severe acne (Hamilton, 1942; Strauss *et al.*, 1962), have been inversely associated with risk of TGCT (Depue *et al.*, 1983; Petridou *et al.*, 1997). To evaluate possible surrogates of androgenic sex hormone levels, we examined data from a hospital based case-control study of TGCT patients at The University of Texas M. D. Anderson Cancer Center (UTMDACC) in Houston, TX and adult male friends of patients. Specifically, we evaluated whether markers of increased androgen exposure, male pattern baldness and severe adolescent acne were associated with TGCT risk; we also evaluated markers of early puberty onset and body size as TGCT risk factors. Finally, we assessed whether risk estimates for these factors varied by TGCT histology.

MATERIALS AND METHODS

TGCT cases and friend controls were enrolled into a hospital-based case-control study conducted at UTMDACC. Full details of the study design have been described elsewhere (Sigurdson *et al.*, 1999; Sonke *et al.*, 2007; Walcott *et al.*, 2002). Men with incident primary TGCT registered at UTMDACC between January 1990 and October 1996 through the Genitourinary Oncology clinic or men that had been previously treated and were recruited from The University of Texas M. D. Anderson Tumor Registry (January 1990 – August 1994) were identified as cases. To assemble a control population, cases were asked to provide the name of at least one adult male friend who had never had cancer and was of similar age and race. All participants were between the ages of 18 and 50 at the time of the cases diagnosis and resided in Texas, Louisiana, Arkansas, or Oklahoma.

Regardless of ethnicity, tumor stage, or tumor histology, all men diagnosed with TGCT during the given time period were eligible for inclusion. Tumors were grouped as pure seminomas, nonseminomas (teratoma, embryonal carcinoma, and choriocarcinoma) and mixed germ cell tumors (both seminomatous and nonseminomatous elements) based on pathology report review. Because it is not clear that gonadal and extragonadal germ cell tumors share common etiologies we excluded men diagnosed with extragonadal germ cell tumors to avoid introducing heterogeneity into the case group.

Cases and controls completed a self-administered questionnaire ascertaining information on demographics, lifestyle habits, medical history and diet. Information on adolescent and adult surrogates of androgen exposure was also collected. The questionnaire ascertained whether

participants had experienced any hair loss prior to the diagnosis for cases or a comparable reference date for controls. Additional questions asked participants to report the age they first started to lose hair, and to characterize their rate of hair loss (slow/gradual, moderate or rapid) and amount of hair loss (just a little, about a quarter, about half, or about three quarters). They were also asked to classify their hair loss based on the Hamilton-Norwood pictorial stage of baldness scale included in their questionnaire (Figure 1) (Hamilton, 1951; Norwood, 1975). Additional questions ascertained whether participants had severe acne during their teenage years and asked participants to report the age at which they first noticed that their voice began to deepen, the age they began to shave, and the age at the first appearance of pubic hair. Participants were also asked to self-report their current height in feet and inches and to report their weight in pounds at ages 16 and 20 and then at one year prior to interview. We calculated body mass index (BMI in kg/m²) at ages 16, 20 and one year prior to interview and categorized BMI into underweight, normal, overweight and obese according to WHO cut points. In addition to reporting information on height and weight, participants were asked to classify their body build at different time periods during development (age 12, age 16, age 20 and one year prior to interview) into one of four anthropomorphic categories: 1. average build, balanced bone, muscle, fat distribution, 2. lean build, thinner muscle and fat distribution, 3. husky build, thicker muscle and bone structure overall, 4. central adiposity, greater fat thickness around abdomen.

Statistical Analysis

Analyses were conducted for all cases combined and for cases classified by histologic type: seminomas, nonseminomas and mixed germ cell tumors. We categorized male pattern baldness using the Hamilton-Norwood scale into two variables: pattern of hair loss (frontal/ temples (II, IIa, III, IIIa, IVa) vs. vertex hair loss (III-vertex, IV, V, Va, VI, VVI)) and amount of hair loss (None/I; II, IIa; III, IIIa, III-vertex, IV, IVa; V, Va, VI, VII) as used by Petridou *et al.* (1997).

A number of cases did not have a matched control because a name was not provided or the individual named was unwilling to participate. To avoid the loss of information by excluding unmatched cases we evaluated the results using a matched analysis (conditional logistic regression) and an unmatched analysis (unconditional logistic regression adjusting for age and race). The point estimates for the two models were not substantially different (data not shown) and did not change the interpretation of the results, thus we present the results from the unmatched analysis. Odds ratios (OR) and 95% confidence intervals (CI) were calculated as estimates of relative risk using unconditional logistic regression. Polytomous logistic regression models were used to compare controls with each of the case groups defined by histologic type. All analyses were adjusted for race, income and history of cryptorchidism as well as participants' age at diagnosis for cases and at time of interview for controls. Education was also considered as a potential confounding factor; however, the addition of education to a model controlling for age, race, income and history of cryptorchidism did not substantially change the ORs (less than 10% change in risk estimate); thus, education was not included as an adjustment factor in the final analysis. First or second degree family history of testicular cancer was reported in less than 4% of the study population, therefore we did not include it as a potential confounding factor. Because we were concerned about the possibility that the reporting of cases hair loss could be affected by chemotherapy or hair re-growth after treatment, we excluded (n=15) cases whose age of diagnosis was younger or within two years of the age of baldness onset in sensitivity analyses. All analyses were performed in Stata/SE (Stata Statistical Software, version 10.1; StataCorp, College Station, TX).

RESULTS

The distributions of selected demographic and health characteristics for the TGCT cases and controls are provided in Table 1. The median age for friend controls and all cases combined was similar. As expected, the median age for nonseminoma cases was approximately 10 years younger than seminoma cases. Cases were more likely than controls to have a history of cryptorchidism (13.4% all cases vs. 2.0 % controls; age- and race-adjusted odds ratio (OR), 7.8; 95% confidence interval (CI), 2.3-26.5). Compared to controls, cases tended to report somewhat lower annual incomes and were less likely to have more than a high school education. Marital status did not differ between cases and controls.

Overall, any hair loss was reported by 33.2% of cases and 50.0% of controls (OR, 0.6; 95% CI, 0.4, 1.0) (Table 2). Compared to participants with no hair loss, increasing age at onset of hair loss was inversely associated with TGCT (p-trend=0.03). Increasing rate of hair loss and amount of hair loss were also inversely associated with TGCT (rate of hair loss: p-trend=0.03; amount of hair loss: p-trend=0.01). In addition, based on the Hamilton-Norwood scale, frontal or temporal hair loss was inversely associated with TGCT (OR, 0.5; 95% CI, 0.3, 0.9) compared to participants with no hair loss.

In analyses by histologic subtype, nonseminoma cases were significantly less likely than controls to have experienced any hair loss (OR, 0.4; 95% CI, 0.2, 0.8) (Table 2). Increasing age at onset of hair loss was inversely associated with nonseminomas (p-trend=0.01). Increasing rate of hair loss and increasing amount of hair loss were significantly more common in the nonseminoma cases than the controls (rate of hair loss: p-trend<0.01; amount of hair loss: p-trend<0.01). Frontal or temporal hair loss, as based on the Hamilton-Norwood scale, was inversely associated with nonseminomas (OR, 0.4; 95% CI, 0.2, 0.8).

In sensitivity analyses restricted to cases with onset of hair loss reported at least two years prior to case diagnosis, the inverse associations seen for all of the hair loss variables and TGCT were strengthened (results not shown).

Adjusted odds ratios for androgen related correlates and TGCT are shown in Table 3. Cases were half as likely to report a history of severe acne in adolescence (OR, 0.5; 95% CI, 0.3, 0.9). Factors indicative of puberty onset (age at first appearance of pubic hair and age began shaving) were not strongly associated with TGCT. Another factor indicative of puberty onset, increasing age when voice deepened was inversely associated with TGCT (p-trend = 0.05); however, none of the age categories were statistically significant. Increasing height was positively associated with TGCT (OR for a one inch increase in adult height, 1.1; 95% CI, 1.0, 1.2; p-trend=0.02). In analyses by histologic subtype, cases with nonseminoma and with mixed germ cell tumors were significantly less likely to report a history of severe acne in adolescence (nonseminoma: OR, 0.4; 95% CI, 0.2, 1.0; mixed germ cell tumors: OR, 0.3; 95% CI, 0.1, 1.0). Factors indicative of puberty onset were not associated with histologic subtype of TGCT. Increasing height was positively associated with nonseminoma TGCT (OR per one inch increase in adult height, 1.2; 95% CI, 1.0, 1.3; p-trend=0.01).

BMI was not associated with TGCT overall or by histologic subtype (results not shown). Similarly, there were no patterns suggesting that body build was associated with TGCT overall or by histologic subtype beyond the association reported with height.

DISCUSSION

We observed an inverse association between TGCT and self-reported male pattern baldness and severe adolescent acne. The association with TGCT was most pronounced for increasing age at hair loss and frontal or temporal hair loss. Increasing rate of hair loss and increasing

amount of hair loss were also inversely associated with TGCT. In histologic specific analyses, the associations were primarily limited to nonseminoma, however that could be due to insufficient sample sizes for the other histologic subtypes as the associations were in the same directions as those for nonseminoma. The reported associations were independent of known risk factors for TGCT, age, race and prior cryptorchidism, as well as income, an indicator of socioeconomic status.

In the literature, the role of androgen levels during adolescence and early adult life has received less attention than *in utero* or early life exposures to estrogen. However to our knowledge, two studies have evaluated androgenic sex hormone correlates and TGCT risk (Depue *et al.*, 1983; Petridou *et al.*, 1997). In a case-control study of 97 incident TGCT cases and 198 age-matched controls in Athens Greece enrolled between 1993 and 1997, Petridou and colleagues reported an inverse association of TGCT with baldness as determined by the Hamilton-Norwood score (Petridou *et al.*, 1997). The authors reported that the inverse association with baldness was more pronounced among nonseminomas than among seminomas (Petridou *et al.*, 1997). Consistent with the findings of Petridou and colleagues, our results were supportive of an inverse association of nonseminoma, as well as overall TGCT, with increasing hair loss on the Hamilton-Norwood scale.

In a case-control study of 108 testicular cancer cases in men 16-30 years old and 108 age-matched neighborhood controls in Los Angeles County California, Depue and colleagues also reported an inverse association between TGCT and report of severe acne around the time of puberty (Depue *et al.*, 1983). The authors also collected information on the onset of puberty including age started shaving and age of voice change and found no association between TGCT and these factors; the authors did not report information on baldness or body size (Depue *et al.*, 1983). Our findings of an inverse association with severe acne but no association with onset of puberty are supportive of the results reported by Depue and colleagues.

It has been hypothesized that puberty may be a period of development during which exogenous or endogenous hormonal factors increase the risk of TGCT (Richiardi *et al.*, 2007). Hormonal exposures during this time may be more relevant to nonseminoma risk, given that the peak incidence of nonseminomas is ten-years earlier than the peak incidence of seminomas, and within a biologically relevant time period after puberty. However we cannot rule out the fact that we may not have seen an association between male pattern baldness and severe adolescent acne in the other histologic subtypes because of the limited sample size. It is plausible that increased androgen exposure, specifically 5-alpha-dihydrotestosterone (DHT), during puberty or early adulthood could potentially decrease risk of TGCT. The oily secretion of sebaceous glands is under the control of androgens; further, increases in androgen receptors and DHT production have been reported in patients with severe acne compared to normal subjects (Bonne *et al.*, 1977; Boudou *et al.*, 1995; Hay & Hodgins, 1974; Sansone & Reisner, 1971; Strauss *et al.*, 1962). Androgenic alopecia, the most common type of male pattern baldness, is characterized by recession of the hairline and is considered a part of the normal male secondary sexual characteristics (Hamilton, 1951; Sawaya, 1999). An absence of androgenic alopecia is observed in patients who lack 5 alpha-reductase, indicating that DHT, the 5 alpha-reduced metabolite of testosterone is the principle mediator of androgen-dependent hair loss (Balducci *et al.*, 1996; Hamilton, 1942). Research has also shown that 5 alpha-reduced metabolites of testosterone are increased in balding areas of the human scalp (Sawaya & Price, 1997). In human males, 5 alpha-reductase is expressed in the prostate, skin, epididymis, seminal vesicle and liver at high levels (Imperato-McGinley & Zhu, 2002). Therefore it is plausible that the gonadal dysfunction contributing to decreased testosterone and increased DHT in men with severe acne or male pattern baldness may also contribute to decreased TGCT risk. It is also

plausible that the onset of puberty may be programmed during the time period of organogenesis. The puberty markers evaluated may therefore be proxy variables for exposures operating during the prenatal period.

Although our results are consistent with those of prior studies, there are several limitations to our study. The study relied on self-report, rather than measurement of baldness, severe acne, onset of puberty, height, weight and body build. It is possible that cases may more accurately or critically report these exposures; however, the bulk of these exposures were inversely associated with TGCT and thus case over-reporting is not likely to have occurred. Compared to trained observers, validation studies cited kappas of 0.47-0.55 for self-reported baldness (Littman & White, 2005; Taylor *et al.*, 2004) and 0.48 for self-reported acne (Jagou *et al.*, 2006) suggesting that self-report of these features is quite reliable. The study evaluating the reliability of self-reported baldness using the Hamilton-Norwood scale also demonstrated that men's self assessment of baldness at early ages was adequate (Littman & White, 2005). The inverse association between balding and TGCT could have been related to hair re-growth after chemotherapy, especially if the age at onset of balding was close to the age of diagnosis/treatment. Further, if at the time of the interview those who experienced hair loss due to cancer treatment experienced difference in hair re-growth (curlier, coarser, color change) the cases might be more likely to report on current hair patterns rather than hair patterns prior to diagnosis. We examined the age at which balding reportedly occurred in the controls, and this age predated cancer diagnosis for the majority of cases in the matched sets (80.4%). In a sub-analysis restricting to cases with onset of hair loss reported at least two years prior to case diagnosis the inverse associations seen for all of the hair loss variables and TGCT risk were strengthened; suggesting that misclassification of hair patterns due to cancer treatment and hair re-growth did not substantially affect our results. It is likely that this study did not find an association between puberty onset and TGCT, because puberty onset in males occurs over a span of time and is not marked by one specific event, as a result there may be a large amount of variability with respect to the self-report of age at onset of puberty that contributes to the lack of association.

Controls, as a comparison group, are selected to represent the exposure distribution in the source population that gave rise to the cases. Whether friend controls provide this distribution is unknown and may be unlikely. Friend controls as the referent group in any study raises the concern that controls are too similar to cases, especially when considering behavioral exposures (cigarette smoking and alcohol consumption), as cases may nominate a friend control with similar behavior characteristics. If the friend controls in this study, in fact, are too similar to cases in terms of the exposures of interest, then it is likely that our estimates of risk would be underestimates of the true relationship between these factors and TGCT. In our study, however, the controls were older and reported higher incomes than cases, suggesting that over-matching was not present, at least for these factors. While we attempted to match on age, the cases tended to nominate friend controls who were generally older than they were, therefore as a matching factor, we adjusted for age in all of our analyses. We also adjusted for income as a potential confounding factor. Further the exposures we have examined, baldness, severe acne and indicators of puberty onset, are not behavioral factors and may be less subject to the bias described above. The specificity of our finding, that the association between male pattern baldness as well as severe acne and TGCT was primarily limited to nonseminoma, may be due to the limited numbers of seminoma and mixed germ cell tumors.

In summary, our findings of an inverse association between male pattern baldness and TGCT, particularly among men with nonseminoma, as well as, severe adolescent acne and TGCT are consistent with the findings of previous reports (Depue *et al.*, 1983; Petridou *et al.*, 1997). Increased endogenous androgen levels, specifically DHT, during puberty and

early adulthood may directly affect TGCT risk by altering testicular development. Additional studies of endogenous hormone exposure during puberty and early adult life are warranted, especially studies evaluating the role of androgen synthesis and metabolism and the androgen receptor in TGCT.

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Figure 1.
Male balding patterns based on the Hamilton-Norwood scale of hair loss.

Selected characteristics of controls and testicular cancer cases by histology: The University of Texas M. D. Anderson Cancer Center, January 1990 - October 1996.

Table 1

Characteristic	Controls (n = 148)		All Cases (n = 187)		Tumor Type					
					Seminoma (n = 50)		Nonseminoma (n = 95)		Mixed Germ Cell (n = 42)	
Age in 1996										
median (min, max)	34	(18, 63)	33	(18, 57)	38.5	(24, 57)	29	(18, 51)	33.5	(20, 51)
	n	%	n	%	n	%	n	%	n	%
18-24	11	7.4	27	18.2	1	0.7	19	12.8	7	4.7
25-34	66	44.6	82	55.4	12	8.1	53	35.8	17	11.5
35-44	45	30.4	63	42.6	30	20.3	18	12.2	15	10.1
45-54	21	14.2	14	9.5	6	4.1	5	3.4	3	2.0
55-64	5	3.4	1	0.7	1	0.7	0	0.0	0	0.0
Race										
White	130	87.8	151	80.8	41	82.0	75	79.0	35	83.3
Hispanic	14	9.5	28	15.0	7	14.0	13	13.7	7	16.7
Other	4	2.7	8	4.2	2	4.0	7	7.4	0	0.0
History of cryptorchidism										
Yes	3	2.0	25	13.4	7	14.0	12	12.6	6	14.3
No	145	98.0	162	86.6	43	86.0	83	87.4	36	85.7
Income										
<\$25,000	20	14.3	55	31.6	11	23.4	30	34.1	14	35.9
\$25,000 - \$54,999	43	30.7	52	29.9	12	25.5	34	38.6	6	15.4
\$55,000 - \$74,999	36	25.7	29	16.7	8	17.0	13	14.8	8	20.5
\$75,000 +	41	29.3	38	21.8	16	34.0	11	12.5	11	28.2
Years of education										
12	31	21.0	58	31.0	12	24.0	30	31.6	16	38.1
> 12	117	79.1	129	69.0	38	76.0	65	68.4	26	61.9
Body mass index (kg/m ²) one year prior to diagnosis										
< 25.0	56	37.8	85	45.5	21	42.0	48	50.5	16	38.1
25.0 - 25.9	71	48.0	75	40.1	22	44.0	35	36.8	18	42.9

Characteristic	Controls (n = 148)	All Cases (n = 187)	Tumor Type		
			Seminoma (n = 50)	Nonseminoma (n = 95)	Mixed Germ Cell (n = 42)
30.0	21	14.2	27	14.4	7
			14.0	12	12.6
			8		19.0

* Columns may not sum to total because of missing data.

Table 2

Associations of testicular germ cell tumors and male pattern baldness according to histology: The University of Texas M. D. Anderson Cancer Center, January 1990 - October 1996.

Characteristic	Controls n = 148			All Cases n = 187			Seminoma n = 50			Nonseminoma n = 95			Mixed Germ Cell Tumors n = 42					
	n	%		n	%	OR* (95% CI)	n	%	OR* (95% CI)	n	%	OR* (95% CI)	n	%	OR* (95% CI)			
Self-reported baldness	74	50.0	125	66.8	1.0	reference	32	64.0	1.0	reference	70	73.7	1.0	reference	23	54.8	1.0	reference
No	74	50.0	62	33.2	0.6	(0.4, 1.0)	18	36.0	0.7	(0.3, 1.3)	25	26.3	0.4	(0.2, 0.8)	19	45.2	0.9	(0.5, 1.9)
Yes	74	50.0	62	33.2	0.6	(0.4, 1.0)	18	36.0	0.7	(0.3, 1.3)	25	26.3	0.4	(0.2, 0.8)	19	45.2	0.9	(0.5, 1.9)
Age at onset of hair loss	74	39.6	125	66.8	1.0	reference	32	64.0	1.0	reference	70	73.7	1.0	reference	23	54.8	1.0	reference
No self-report baldness	39	20.9	31	16.6	0.6	(0.3, 1.0)	10	20.0	0.7	(0.3, 1.6)	12	12.6	0.4	(0.2, 0.8)	9	21.4	0.9	(0.4, 2.1)
18-25	26	13.9	25	13.4	0.7	(0.3, 1.4)	5	10.0	0.5	(0.2, 1.5)	11	11.6	0.5	(0.2, 1.2)	9	21.4	1.3	(0.5, 3.4)
26-35	7	3.7	3	1.6	0.2	(0.1, 1.3)	2	4.0	0.7	(0.1, 3.9)	0	0.0	--	--	1	2.4	--	--
36 +																		0.75
p-trend						0.03				0.19			0.01					0.75
Rate of hair loss	74	50.0	125	66.8	1.0	reference	32	64.0	1.0	reference	70	73.7	1.0	reference	23	54.8	1.0	reference
No self-report baldness	56	37.8	53	28.3	0.7	(0.4, 1.1)	14	28.0	0.7	(0.3, 1.4)	22	23.2	0.5	(0.3, 0.9)	17	40.5	1.1	(0.5, 2.3)
Slow	13	8.8	4	2.2	0.2	(0.1, 0.7)	2	4.0	0.4	(0.1, 2.0)	2	2.2	0.2	(0.1, 0.8)	0	0.0	--	--
Moderate/rapid																		0.28
p-trend						0.01				0.12			< 0.01					0.28
Amount of hair loss	74	50.0	125	66.8	1.0	reference	32	64.0	1.0	reference	70	73.7	1.0	reference	23	54.8	1.0	reference
No self-report baldness	47	31.8	42	22.5	0.7	(0.4, 1.2)	11	22.0	0.7	(0.3, 1.5)	20	21.1	0.6	(0.3, 1.2)	11	26.2	0.9	(0.4, 2.1)
A little	16	10.8	15	8.0	0.6	(0.3, 1.4)	4	8.0	0.6	(0.2, 2.0)	5	5.3	0.4	(0.1, 1.1)	6	14.3	1.4	(0.5, 4.0)
About a quarter	11	7.4	5	2.7	0.3	(0.1, 0.9)	3	6.0	0.6	(0.1, 2.4)	0	0.0	--	--	2	4.8	0.5	(0.1, 2.8)
Half or greater																		0.78
p-trend						0.02				0.25			< 0.01					0.78
Pattern of hair loss - Hamilton-Norwood Scale†	74	50.0	125	66.8	1.0	reference	32	64.0	1.0	reference	70	73.7	1.0	reference	23	54.8	1.0	reference
None	48	32.4	34	18.2	0.5	(0.3, 0.9)	10	20.0	0.6	(0.3, 1.3)	15	15.8	0.4	(0.2, 0.8)	9	21.4	0.7	(0.3, 1.8)
Frontal/temples	26	17.6	27	14.4	0.7	(0.4, 1.5)	8	16.0	0.8	(0.3, 1.9)	10	10.5	0.5	(0.2, 1.2)	9	21.4	1.1	(0.4, 2.9)
Vertex																		
Amount of hair loss - Hamilton-Norwood Scale‡	74	50.0	125	66.8	1.0	reference	32	64.0	1.0	reference	70	73.7	1.0	reference	23	54.8	1.0	reference
I																		

Characteristic	Controls n = 148		All Cases n = 187		Seminoma n = 50		Nonseminoma n = 95		Mixed Germ Cell Tumors n = 42									
II, IIa	39	26.4	27	14.4	0.5	(0.3, 0.9)	8	16.0	0.6	(0.2, 1.4)	11	11.6	0.4	(0.2, 0.8)	8	19.0	0.8	(0.3, 2.0)
III, IIIa, III-vertex, IV, IVa	27	18.2	28	15.0	0.7	(0.4, 1.4)	8	16.0	0.8	(0.3, 1.9)	11	11.6	0.5	(0.2, 1.2)	9	21.4	1.2	(0.4, 3.0)
V, Va, VI, VII	8	5.4	6	3.2	0.5	(0.2, 1.7)	2	4.0	0.6	(0.1, 3.2)	3	3.2	0.5	(0.1, 1.9)	1	2.4	0.4	(0.1, 3.6)
<i>p</i> -trend			0.10		0.37		0.03		0.74									

* Adjusted for age in 1996, race, history of cryptorchidism, and income.

[†] Frontal/temples included Hamilton-Norwood categories II, IIa, III, IIIa, and IVa; Vertex included categories III-vertex, IV, V, Va, VI and VII

[‡] Hamilton-Norwood Scale groupings based on same categories in Table 1 of Petridou et al. (1997)

Associations of testicular germ cell tumors and selected correlates of androgen sex hormone exposure according to histology: The University of Texas M. D. Anderson Cancer Center, January 1990 – October 1996.

Table 3

Characteristic	Controls n = 148				All Cases n = 187				Seminoma n = 50				Nonseminoma n = 95				Mixed Germ Cell Tumors n = 42			
	n	%	n	%	OR [*]	(95% CI)	n	%	OR [*]	(95% CI)	n	%	OR [*]	(95% CI)	n	%	OR [*]	(95% CI)	n	%
Severe adolescent acne	113	76.4	164	87.7	1.0	reference	41	82.0	1.0	reference	84	88.4	1.0	reference	39	92.9	1.0	reference		
No	35	23.6	23	12.3	0.5	(0.3, 0.9)	9	18.0	0.7	(0.3, 1.7)	11	11.6	0.4	(0.2, 1.0)	3	7.1	0.3	(0.1, 1.0)		
Yes																				
Age voice deepened																				
< 13 years	40	27.0	39	20.9	0.6	(0.3, 1.2)	15	30.0	0.8	(0.3, 1.9)	15	15.8	0.5	(0.2, 1.2)	9	21.4	0.5	(0.2, 1.5)		
13 years	45	30.4	43	23.0	0.6	(0.3, 1.2)	8	16.0	0.4	(0.2, 1.1)	25	26.3	0.7	(0.3, 1.5)	10	23.8	0.7	(0.2, 1.8)		
14 years	14	9.5	30	16.0	1.2	(0.5, 2.8)	6	12.0	0.9	(0.3, 2.9)	17	17.9	1.4	(0.6, 3.7)	7	16.7	1.3	(0.4, 4.2)		
>14 years	32	21.6	52	27.8	1.0	reference	15	30.0	1.0	reference	27	28.4	1.0	reference	10	23.8	1.0	reference		
<i>p</i> -trend						0.05				0.39				0.06				0.13		
Age at first appearance of pubic hair																				
< 12 years	16	10.8	21	11.2	1.2	(0.5, 2.8)	6	12.0	1.1	(0.3, 3.5)	11	11.6	1.5	(0.5, 4.2)	4	9.5	0.7	(0.2, 3.1)		
12 years	32	21.6	51	27.3	1.5	(0.7, 3.0)	12	24.0	1.1	(0.4, 3.0)	26	27.4	1.7	(0.7, 3.9)	13	31.0	1.6	(0.6, 4.5)		
13 years	48	32.4	48	25.7	0.9	(0.4, 1.7)	10	20.0	0.5	(0.2, 1.4)	26	27.4	1.1	(0.5, 2.5)	12	28.6	0.9	(0.3, 2.5)		
>13 years	31	20.9	42	22.5	1.0	reference	14	28.0	1.0	reference	19	20.0	1.0	reference	9	21.4	1.0	reference		
<i>p</i> -trend						0.32				0.60				0.23				0.75		
Age began shaving																				
< 15 years	28	18.9	30	16.0	1.1	(0.6, 2.3)	7	14.0	0.7	(0.2, 2.0)	17	17.9	1.5	(0.6, 3.4)	6	14.3	1.3	(0.4, 3.8)		
15 years	29	19.6	44	23.5	1.4	(0.8, 2.7)	9	18.0	1.0	(0.4, 2.4)	27	28.4	2.0	(0.9, 4.1)	8	19.0	1.3	(0.4, 3.7)		
16 years	29	19.6	43	23.0	1.2	(0.6, 2.2)	12	24.0	1.0	(0.4, 2.4)	16	16.8	0.9	(0.4, 2.0)	15	35.7	2.3	(0.9, 5.7)		
>16 years	54	36.5	65	34.8	1.0	reference	20	40.0	1.0	reference	32	33.7	1.0	reference	13	31.0	1.0	reference		
<i>p</i> -trend						0.48				0.53				0.13				0.79		
Adult height																				
5' 6"	10	6.8	16	8.6	1.0	reference	5	10.0	1.0	reference	10	10.5	1.0	reference	1	2.4	1.0	reference		
5' 7" - 5' 11"	86	58.1	86	46.0	1.6	(0.6, 4.5)	23	46.0	1.0	(0.2, 3.8)	40	42.1	1.6	(0.5, 5.3)	23	54.8	4.2	(0.5, 37.8)		
6'	52	35.1	84	44.9	2.3	(0.8, 6.7)	22	44.0	1.3	(0.3, 5.5)	45	47.4	2.7	(0.8, 9.1)	17	40.5	4.9	(0.5, 45.6)		
<i>p</i> -trend [†]						0.02				0.24				0.01				0.32		

* Adjusted for age in 1996, race, history of cryptorchidism, and income.
 † p-trend based on continuous (rather than categorical) variable coding