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Characterizing subsequent primary melanomas in adolescents and young adults: a population-based study from 1973-2011

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To the Editor

Melanoma is among the most common cancers diagnosed in adolescents and young adults (AYAs). Recent studies show an increasing incidence in young women and a worse prognosis in young men[1,2]. Prior studies have shown that a first diagnosis of melanoma elevates second malignancy risk, especially for melanoma[3]. We sought to characterize a population of male and female AYAs diagnosed with 2 or more primary melanomas between the ages of 15 and 39 [4]. Study of patients who develop multiple melanomas at a young age may help elucidate genetic and environmental factors that increase melanoma risk.

Methods

We used the Surveillance, Epidemiology and End Results (SEER) 18 cancer registry database (1973-2011), which has incorporated additional cancer registries to maximize sample size. We obtained patient demographic and clinical data on 551 AYAs with an

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invasive first primary melanoma (FPM) and subsequent primary melanoma (SPM) and 38,110 AYAs with only FPM[5]. Multivariable logistic regression was used to examine characteristics associated with developing a SPM.

Results

Most (67.7%) SPM developed within 5 years of FPM diagnosis and in females (65.3%). Females had more SPM on the extremities and were more likely to develop SPM at a different anatomical site (p=0.03). Males developed more SPM on the trunk and head/neck and were more likely to have an ulcerated SPM and/or present with regional or metastatic SPM (10.5% vs. 5.2%) (p=0.03) (Table 1). There was a trend towards thicker tumors in males for both FPM and SPM. In the multivariable comparison to AYAs with only one melanoma, non-Hispanic white race/ethnicity, younger age at FPM diagnosis, and female gender were associated with higher odds of SPM (Table 2).

Discussion

Prior studies show an increased risk for SPM in AYAs diagnosed with melanoma compared to middle-aged melanoma patients, and this increase is not merely a reflection of longer follow-up[6]. We found AYA females were more likely to develop a SPM, but males were more likely to present with advanced SPM. Biologic sex differences in host immunity or tumor factors could partially explain the latter finding, as evidenced by a prior study demonstrating a poorer prognosis in male AYAs with melanoma compared with females[1].

The association between SPM and younger age of FPM may relate to genetic predisposition or increased UV exposure at a younger age and tanning practices, particularly in women. The higher odds of SPM in those with ulcerated FPM was more commonly observed in men and may stem from the trend for thicker tumors in males, underlying genetic predisposition, or suboptimal screening access that could lead to more advanced presentation of FPM, while also contributing to increased risk for SPM.

Education regarding risk of new skin cancers and appropriate screening are especially important for AYAs, among whom the risk for SPM remains elevated for many years[3,6]. Determining whether AYAs who develop multiple melanomas before age 40 have associated germ-line mutations is an important area of future study.

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Table 1

Demographic and clinical characteristics of adolescents and young adults (AYAs) diagnosed with a 1st and subsequent primary melanoma between the age of 15 and 39 years, 1973-2011

Demographic and clinical characteristics	Total (n=551)		Male (n=191)		Female (n=360)		P
Age at diagnosis for the 1st melanoma							0.21
15-24	115	20.9%	33	17.3%	82	22.8%	
25-29	143	26.0%	45	23.6%	98	27.2%	
30-34	189	34.3%	74	38.7%	115	31.9%	
35-39	104	18.9%	39	20.4%	65	18.1%	
Age at diagnosis for the 2nd melanoma							0.08
15-24	45	8.2%	16	8.4%	29	8.1%	
25-29	107	19.4%	27	14.1%	80	22.2%	
30-34	144	26.1%	48	25.1%	96	26.7%	
35-39	255	46.3%	100	52.4%	155	43.1%	
Race/ethnicity							0.53
Non-Hispanic white	542	98.4%	187	97.9%	355	98.6%	
Other*/unknown	9	1.6%	<5	2.1%	5	1.4%	
Year of diagnosis for the 1st melanoma							0.48
1973-1983	54	9.8%	16	8.4%	38	10.6%	
1984-1993	90	16.3%	35	18.3%	55	15.3%	
1994-2003	203	36.8%	75	39.3%	128	35.6%	
2004-2011	204	37.0%	65	34.0%	139	38.6%	
Year of diagnosis for the 2nd melanoma							0.22
1973-1983	27	4.9%	7	3.7%	20	5.6%	
1984-1993	69	12.5%	31	16.2%	38	10.6%	
1994-2003	146	26.5%	48	25.1%	98	27.2%	
2004-2011	309	56.1%	105	55.0%	204	56.7%	
Time intervals between the 1st and 2nd melanoma							0.57
Under 3 months	36	6.5%	10	5.2%	26	7.2%	
4-11 months	35	6.4%	9	4.7%	26	7.2%	
Diagnosed within the same year, but interval unknown	<5	0.7%	<5	0.5%	<5	0.8%	
1 year	145	26.3%	50	26.2%	95	26.4%	
2-5 years	217	39.4%	85	44.5%	132	36.7%	
6-10 years	92	16.7%	30	15.7%	62	17.2%	
11+ years	22	4.0%	6	3.1%	16	4.4%	
Anatomical site for the 1st melanoma							<0.001
Head and neck	65	11.8%	39	20.4%	26	7.2%	

Demographic and clinical characteristics	Total (n=551)		Male (n=191)		Female (n=360)		P
Trunk	237	43.0%	93	48.7%	144	40.0%	
Upper extremity	100	18.1%	29	15.2%	71	19.7%	
Lower extremity	138	25.0%	26	13.6%	112	31.1%	
Others/Unknown	11	2.0%	<5	2.1%	7	1.9%	
Anatomical site for the 2nd melanoma							<0.001
Head and neck	70	12.7%	43	22.5%	27	7.5%	
Trunk	231	41.9%	87	45.5%	144	40.0%	
Upper extremity	104	18.9%	30	15.7%	74	20.6%	
Lower extremity	138	25.0%	29	15.2%	109	30.3%	
Other or unknown	8	1.5%	<5	1.0%	6	1.7%	
Anatomical site same for the 2nd melanoma							0.03
Yes	220	39.9%	88	46.1%	132	36.7%	
No	331	60.1%	103	53.9%	228	63.3%	
Histopathologic subtype for the 1st melanoma							0.16
Superficial spreading	257	46.6%	84	44.0%	173	48.1%	
Nodular	28	5.1%	15	7.9%	13	3.6%	
Rare subtypes	25	4.5%	10	5.2%	15	4.2%	
Not otherwise specified	241	43.7%	82	42.9%	159	44.2%	
Histopathologic subtype for the 2nd melanoma							0.04
Superficial spreading	243	44.1%	75	39.3%	168	46.7%	
Nodular	18	3.3%	11	5.8%	7	1.9%	
Rare subtypes	25	4.5%	7	3.7%	18	5.0%	
Not otherwise specified	265	48.1%	98	51.3%	167	46.4%	
Tumor extension 1st mm							0.12
Cutaneous disease	490	88.9%	162	84.8%	328	91.1%	
Regional disease	43	7.8%	22	11.5%	21	5.8%	
Metastatic disease	<5	0.5%	<5	0.5%	<5	0.6%	
Unknown	15	2.7%	6	3.1%	9	2.5%	
Tumor extension 2nd mm							0.03
Cutaneous disease	486	88.2%	160	83.8%	326	90.6%	
Regional disease	29	5.3%	17	8.9%	12	3.3%	
Metastatic disease	10	1.8%	<5	1.6%	7	1.9%	
Unknown	26	4.7%	11	5.8%	15	4.2%	
Tumor thickness (1988 forward*), mm for 1st melanoma							0.01±
0.01-1.00	340	73.0%	105	65.2%	235	77.0%	
1.01-2.00	52	11.2%	21	13.0%	31	10.2%	
2.01-4.00	29	6.2%	18	11.2%	11	3.6%	
>4.01	7	1.5%	<5	2.5%	<5	1.0%	

Demographic and clinical characteristics	Total (n=551)		Male (n=191)		Female (n=360)		P
Unknown	38	8.2%	13	8.1%	25	8.2%	
Tumor thickness (1988 forward), mm for 2nd melanoma**							0.01±
0.01-1.00	358	76.8%	111	68.9%	247	81.0%	
1.01-2.00	27	5.8%	17	10.6%	10	3.3%	
2.01-4.00	12	2.6%	6	3.7%	6	2.0%	
>4.01	9	1.9%	5	3.1%	<5	1.3%	
Unknown	60	12.9%	22	13.7%	38	12.5%	
Ulcerated (2004 forward) 1st melanoma**							0.10±
No	173	84.8%	50	76.9%	123	88.5%	
Yes	21	10.3%	10	15.4%	11	7.9%	
Unknown	10	4.9%	5	7.7%	5	3.6%	
Ulcerated (2004 forward#) 2nd melanoma							<0.01±
No	182	89.2%	56	86.2%	126	90.6%	
Yes	7	3.4%	5	7.7%	<5	1.4%	
Unknown	15	7.4%	<5	6.2%	11	7.9%	

* Other race/ethnicity includes blacks, Asian/Pacific Islanders and American Indian/Alaskan Natives.

** Tumor thickness data is only available for cases diagnosed after 1988; Information on depth for cases diagnosed before 1988 may be available in different versions of coding but are complicated to incorporate.

Ulceration information is available for cases diagnosed after 2004 only.

± p for difference from chi-square test excludes patients before 1988 for tumor thickness and patients before 2004 for ulceration.

Table 2

Demographic and clinical factors associated with subsequent primary melanoma (SPM) (versus only a first primary melanoma (FPM)) in Adolescents and Young Adults (AYAs): multivariable* odds ratios (OR) with 95% confidence intervals (CI), 1973-2011

	AYAs with only FPM, N=38110		AYAs with SPM N=551		P difference**	OR (95% CI)
Year of diagnosis for the 1st (or only) melanoma					<0.01	
1973-1983	4205	11.0%	54	9.8%		Reference
1984-1993	6508	17.1%	90	16.3%		1.14 (0.81-1.61)
1994-2003	12830	33.7%	203	36.8%		1.34 (0.99-1.81)
2004-2011	14567	38.2%	204	37.0%		1.19 (0.88-1.61)
Age at diagnosis for the 1st (or only) melanoma (years)					<0.01	
15-24	5971	15.7%	115	20.9%		Reference
25-29	7755	20.3%	143	26.0%		0.96 (0.75-1.23)
30-34	10617	27.9%	189	34.3%		0.93 (0.73-1.17)
35-39	13767	36.1%	104	18.9%		**0.39 (0.30-0.51)**
Race					<0.01	
Non-Hispanic white	35322	92.7%	542	98.4%		Reference
Other[#]/unknown	2788	7.3%	9	1.6%		**0.20 (0.10-0.39)**
Sex					0.01	
Male	15267	40.1%	191	34.7%		Reference
Female	22843	59.9%	360	65.3%		**1.21 (1.01-1.45)**
Anatomical site for the 1st (or only) melanoma					0.08	
Head and neck	4419	11.6%	65	11.8%		Reference
Trunk	15000	39.4%	237	43.0%		1.07 (0.81-1.42)
Upper extremity	7885	20.7%	100	18.1%		0.87 (0.63-1.20)
Lower extremity	9347	24.5%	138	25.0%		0.98 (0.72-1.32)
Other/unknown	1459	3.8%	11	2.0%		0.56 (0.29-1.07)
Histopathologic subtype for the 1st (or only) melanoma					0.25	
Superficial spreading	16215	42.5%	257	46.6%		Reference
Nodular	2212	5.8%	28	5.1%		0.80 (0.54-1.19)
Rare subtypes	1664	4.4%	25	4.5%		1.03 (0.68-1.56)
Not otherwise specified	18019	47.3%	241	43.7%		0.86 (0.72-1.03)
Tumor thickness (1988 forward [±]), mm for the 1st (or only) melanoma					0.04	
0.01-1.00	21464	68.1%	340	73.0%		Reference
1.01-2.00	3834	12.2%	52	11.2%		0.86 (0.64-1.15)
2.01-4.00	1672	5.3%	29	6.2%		1.12 (0.75-1.68)

	AYAs with only FPM, N=38110		AYAs with SPM N=551		P difference**	OR (95% CI)
>4.01	810	2.6%	7	1.5%		0.60 (0.28-1.30)
Unknown	3757	11.9%	38	8.2%		0.69 (0.49-0.98)
Ulcerated (2004 forward ∞) 1st (or only) melanoma					0.08	
No	12319	84.6%	173	84.8%		Reference
Yes	1061	7.3%	21	10.3%		1.65 (0.99-2.76)
Unknown	1187	8.1%	10	4.9%		0.97 (0.48-1.97)

* Odds ratios adjusted for all variables in the table.

** p for difference from chi-square test excludes patients before 1988 for tumor thickness and patients before 2004 for ulceration.

Other race/ethnicity includes blacks, Asian/Pacific Islanders and American Indian/Alaskan Natives.

± Tumor thickness data is only available for cases diagnosed after 1988.

∞ Ulceration information is only available for cases diagnosed after 2004.