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Cutaneous Melanoma—Season and Invasion?

A Preliminary Report

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Histological diagnosis of superficial spreading melanoma (SSM) of invasive type was found to vary significantly with season, such cases being most numerous in April–September. Cases of *in situ* type were evenly distributed throughout the year. This distinction has not been made previously. It suggests that different mechanisms may be involved in the development of these two lesions. The results as a whole support the theory that the development of invasive melanoma is related to periodic sun exposure, and are in keeping with the proposed role of ultraviolet radiation as a late-stage promoter. The possibility of virus-related initiation is also discussed. (Received February 4, 1988.)

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The incidence of cutaneous melanoma has been reported to vary with season, possibly due to the influence of sunlight on pre-existing lesions, such as benign nevi (1–7). Recently, Schwartz et al. (8) verified this seasonality for various anatomical sites and found that the superficial spreading type of cutaneous melanoma (SSM) showed the strongest association with time of the year, while the nodular (NM) type showed no significant pattern. Their results indicate that sunlight may have a late-stage promotional effect on melanoma, being most pronounced for the SSM type, as suggested previously (9). Seasonal patterns in connection with melanoma *in situ* versus *invasive* melanoma have not been reported hitherto. This paper documents such a variation in the time of histological diagnosis of these two lesions.

MATERIAL AND METHODS

Between 1981 and 1986 a total of 419 patients from Western Norway with *in situ* and *invasive* cutaneous melanoma were diagnosed at this Institute. All had been classified on routine histology according to Clark's method with regard to histological type (10). *In situ* cases were coded separately. Furthermore, the month of histological diagnosis was recorded. χ^2 statistics were used for comparison between proportions, and age was compared using the Mann-Whitney test. For the evaluation of seasonality, we used Hewitt's non-parametric rank-test (11).

RESULTS

The major finding in this study was the difference in season of diagnosis, between SSM of *in situ* type and its invasive counterpart. As shown in Fig. 1 the diagnosis of the former was evenly distributed throughout the year, while the latter tended to peak between April and September. Further details are given in the Tables.

Table I shows the distribution of cases according to sex and histological type. The highest number was recorded in females (57% of all cases), with a female/male ratio of 1.3. Superficial spreading melanoma (both *in situ* and invasive) was found in 52% of the cases, with a female/male ratio of 1.2. Among all cases of SSM, 76% were invasive in males, compared with 65% in females ($\chi^2=2.98$, $p<0.10$). Nodular melanoma was found in 22%

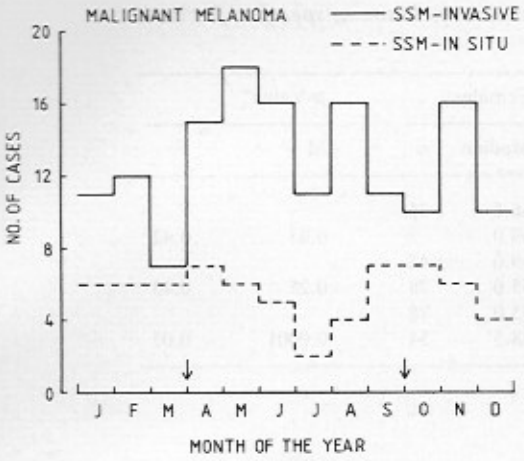

Fig. 1. Seasonal distribution of all cases of Superficial Spreading Melanoma (SSM), specified for *in situ* and *invasive* cases (n=219); combined data for 6 years). Note: the drop in number of cases in July is probably related to the summer holiday season.

of the cases, also without sex predilection. Altogether 10% of cutaneous melanomas remained unclassified.

Age at diagnosis was compared between the different types, as shown in Table II. There was no difference between SSM *in situ* and *invasive*, either in males or females, and no sex difference. However, statistical significances (Table III) appeared between patients with NM and invasive SSM. The former were older, especially the males.

Seasonal variation is further documented in Table III. While no seasonal pattern was seen for SSM *in situ*, the invasive type showed a clear seasonal variation, being most frequently diagnosed in April–September. This result in the total material was due to marked seasonality among females, 64% of cases occurring in April–September ($p<0.002$). A larger proportion of all SSM cases were invasive in April–September, 74% versus 65%. The corresponding figures in females were 72% and 55%. We also found seasonality among females with nodular melanoma: 63% of the cases occurring in May–October ($p<0.05$). Seasonality was further present in lentigo maligna (LM), with a peak in February–July, but not with lentigo maligna melanoma (LMM, Table III). The numbers for the latter were low.

The seasonal difference was also evident when each year (1981–86) was analysed separately. In 5 of the 6 years, more cases of invasive SSM presented between April and September than in the rest of the year. In the 6th year the numbers were equal. In contrast,

Table I. *Distribution of 419 cases of cutaneous melanoma with respect to sex and histological type, specified for in situ and invasive cases*

Histology	Males (%) *n*	Females (%) *n*	Total (%)
Lentigo maligna	18 (9.9)	30 (12.7)	48 (11.5)
Lentigo maligna melanoma	7 (3.8)	7 (3.0)	14 (3.3)
Superficial melanoma in situ	24 (13.2)	42 (17.7)	66 (15.8)
Superficial melanoma	75 (41.2)	78 (32.9)	153 (36.5)
Nodular melanoma	39 (21.4)	54 (22.8)	93 (22.2)
Unclassified	19 (10.4)	26 (11.0)	45 (10.7)
Total number of cases	182	237	419

Table II. *Comparison of age in different types of cutaneous melanoma, specified for both sexes (N=419)*

Histology	Males		Females		*p*-Value[a]	
	Median	*n*	Median	*n*	M	F
Lentigo maligna	69.5	18	66.5	30		
Lentigo maligna melanoma	59.0	7	69.0	7	0.05	0.42
Superficial melanoma in situ	53.5	24	49.0	42		
Superficial melanoma	50.0	75	55.0	78	0.25	0.43
Superficial melanoma	50.0	75	55.0	78		
Nodular melanoma	67.0	39	58.5	54	0.0001	0.05

[a] Mann-Whitney rank-sum test, M = males, F = females.

in situ cases showed the greatest number between April and September in 2 of 6 years, the greatest number in the rest of the year in 3 years and equal numbers in one.

DISCUSSION

Our results verify (1–7) seasonality in the histological diagnosis of cutaneous melanoma, with a summer peak, especially for the SSM type. Further they also indicate, in keeping with previous reports (1, 2, 12), that there is a distinct sex difference, seasonality being

Table III. *Seasonality in occurrence of different types of cutaneous melanoma, specified for both sexes (N=419)*

Numbers occurring in significant seasonal periods, total numbers and seasons are given.

Type	Number/total in period	Period	*p*-Value
Lentigo maligna			
females	20/27	Feb–July	0.056
males	14/18	Feb–July	<0.05
total	34/45	Feb–July	<0.05
Lentigo maligna melanoma			
females	–/7	–	NS
males	–/7	–	–
total	–/14	–	NS
Superficial spreading melanoma in situ			
females	–/42	–	NS
males	–/24	–	NS
total	–/66	–	NS
Superficial spreading melanoma			
females	50/78	Apr–Sep	<0.002
males	–/75	–	NS
total	87/153	Apr–Sep	<0.05
Nodular melanoma			
females	34/54	May–Oct	<0.05
males	–/39	–	NS
total	–/93	–	NS

present only in females. The explanation for this is not clear. Sun exposure habits and possibly cyclical hormones may contribute (1, 2, 5), but the question remains open.

When *invasive* and *in situ* cases of SSM in our series were analysed separately, new information became evident. *In situ* cases showed no significant seasonal variation, whereas the diagnosis of *invasive* SSM was most frequent in the summer period (April–September). The summer peak in incidence of cutaneous melanoma is thought to be the result of intermittent sun exposure, and seems to favour a short-term induction period (4–6, 13). As indicated by the present results, this may be the case only for invasive melanomas. Their non-invasive counterpart is more evenly distributed through the year. Thus, the development of invasion is somehow connected with periodic sun exposure, perhaps as a rather late-stage *promoter* in melanoma development (8, 9). This is strengthened by the lack of age difference between *in situ* and *invasive* cases, indicating an association with season and seasonal events rather than age and tumour duration. Furthermore, the age difference between invasive SSM and NM support the proposed action of sun exposure as a late-stage promoter, and also the hypothesis that NM is an end-stage result of SSM (9). However, seasonal variation of NM in females would also be in keeping with the idea of a short-term transition between SSM and NM, the peak season for this lagging slightly behind that for SSM. The results are also in line with previous reports of seasonal variation in proliferative activity in melanoma (14), breast carcinoma (15) and bladder carcinoma (16).

Reports on the role of sunlight in initiation and promotion of cutaneous melanoma have been conflicting (9, 12–14), but they seem to favour a late-stage promotional effect. As regards initiation, recent results from this Institute suggest a link between cutaneous melanoma and cervical neoplasia, possibly involving a common risk factor, i.e. human papilloma virus (17, 18).

In conclusion, our results indicate a relationship between season and the development of invasion in malignant melanoma, which must be further verified. They delineate new biological fields that may be pertinent to the understanding of melanoma development, as well as being of practical use in preventive efforts.

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