Does a History of Melanoma Correlate with the Clinical Presentation of Dysplastic Nevi?

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ARTICLE

Abstract. In order to determine the prevalence of key features concerning nevocytic nevi (NN) in 150 consecutive Caucasian patients with dysplastic nevi (DN), total-body photographs were reviewed that revealed the following: 74% had ≧100 NN, 73% had NN 8 mm or more in diameter, and 81% had atypical NN. The patients were then divided into two subsets, those with a personal and/or family history of malignant melanoma (MM) and those without, to see if the proportion of these three features differed in these two groups. There were no statistically significant differences between the MM-history-positive and MM-history-negative subsets. J Dermatol Surg Oncol 1990; 16:538–542.

INTRODUCTION

It is known that certain subsets of the population are at increased risk for developing malignant melanoma (MM). Some of these risk factors have been identified.[1] Among these are the number of nevocytic nevi (NN), a personal and/or family history of MM, and dysplastic nevi (DN). We believe that a broad spectrum exists for the clinical presentation of DN. Experience has taught us that at one end of this spectrum are patients whom we have categorized as having "classic" DN fulfilling the following clinical triad: (1) a large number (≧100) of NN, (2) large-sized (≧8 mm) NN, and (3) atypical (dysmorphic) NN (Table 1). One purpose of this study was to see what percentage of DN patients had these three principal attributes.

Patients with DN also have been classified into groups based on the presence or absence of a personal and/or family history of MM; individuals who fall into those DN groups in which there is a personal and/or familial history of MM are reported to have a greater probability of developing MM.[2,3]

The other purpose of this study was to compare two subsets of DN patients, those with a personal and/or family history of MM and those without, to see if the prevalence of the three features mentioned above (eg, large number of NN, large-sized NN, dysmorphic NN) differed in these two groups of DN patients.

MATERIALS AND METHODS

Included in this study were 150 consecutive white patients with DN seen in the practice of one of us (A.W.K.). Only those between 20 and 40 years of age were included in order to reduce confounding NN with other pigmented lesions, such as seborrheic keratoses and solar lentigines, which are more common in older people. All patients were diagnosed both clinically and histologically[4] as having DN. Each had total-body photographs, with at least 24 exposures, taken as an aid to follow-up examinations.[5] The sex and age of each patient were recorded.

Information regarding a personal and/or family history of MM in the "modified nuclear pedigree" (parents, siblings, offspring, grandparents, aunts, uncles) was obtained from every patient. Patients were categorized into one of the four DN groups

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TABLE 1
Clinical Characteristics of "Classic" Dysplastic Nevi

Feature	Clinical Finding of Nevocytic Nevi
Number	More than 100
Size	Vary, but at least one ≧8-mm diameter
Color	Variegate; multiple shades of tans, browns, black, reds
Perimeter	Fades gradually into surrounding skin
Shoulder of lesion	Peripheral macular tan zone
Uniformity	Heterogeneous (variability from one lesion to another)

suggested by Rigel et al.[3] as follows: group 0 = no personal or family history of MM; group I = personal history of MM; group II = family history of MM in one nuclear-pedigree relative (excludes patient); group III = history of MM in more than one family member (may include patient).

The full set of photographs of each patient was projected and carefully scrutinized for NN. All photographs were taken at a fixed lens-to-skin distance in such a manner that the image on the rearview projector (EKTOGRAPHIC 460 Unit) is half of life size. The definition used for NN was all lesions 2 mm or greater in largest diameter that had the clinical appearance of NN. Those pigmented lesions that had the clinical features of ephelides, solar lentigines, seborrheic keratoses, verrucae, acrochordons, etc, were excluded. Previous studies from our group showed that there is consistency among observers in differentiating NN from other pigmented cutaneous neoplasms by this method.[6]

It was determined if the subject had less than 75 NN, between 75 and 99 NN, or 100 or more NN. The largest NN was measured, and, if the greatest diameter of any NN was 8 mm or more, it was determined how many of these "large" NN were present. Lastly, all NN were examined for irregular borders, marked play of colors, macular tan "shoulder," melanoma simulation, and heterogeneity (ie, variability from one lesion to another).

Patients who did not provide a family history (eg, orphans) were excluded from the study.

The data were entered into the IBM System-370 computer at the Courant Institute of Mathematics of New York University and analyzed by the SAS program.[7] After analysis of the 150 patients for presence/absence of the three principal clinical features [(1) large number of NN, (2) large-sized NN, and (3) atypical NN], patients were divided into two subsets, MM-history-positive DN patients and MM-history-negative DN patients. Comparisons were made between these two subsets for presence/absence of the three clinical features studied.

RESULTS

There were 72 men and 78 women included in the study. A personal and/or family history of MM was obtained in 87 (58%) of the patients. The distributions by sex and mean age of the DN patients in the MM-history-positive subset and MM-history-negative subset were not significantly different (Tables 2 and 3).

Of the 150 DN patients in this study, 111 (74%) had ≧100 moles, 15 (10%) had 75–99 moles, and 24 (16%) had less than 75 moles (Table 4). An analysis

TABLE 2
Sex Distribution of Dysplastic Nevi Patients with a Personal and/or Family History of Malignant Melanoma and Those Without

	Men	Women	Total
DN patients with a family and/or personal history of MM	41 (47.1%)	46 (52.9%)	87 (58%)
DN patients without a family and/or personal history of MM	31 (49.2%)	32 (50.8%)	63 (42%)
Total	72 (48%)	78 (52%)	150 (100%)

TABLE 3
Age Distribution of All Patients

	Mean Age (years)
Patients with a personal and/or family history of MM	31.1
Patients without a personal and/or family history of MM	31.6
Men	31.1
Women	31.4

TABLE 4
Number of Nevocytic Nevi

	<75	75–99	≧100
DN patients with a family and/or personal history of MM	13 (14.9%)	7 (8%)	67 (77%)
DN patients without a family and/or personal history of MM	11 (17.5%)	8 (12.7%)	44 (69.8%)
Total	24 (16%)	15 (10%)	111 (74%)

p = 0.552.

comparing the MM-history-positive subset to the MM-history-negative subset for the number of moles ≧100 showed that there was no significant difference (p = 0.552) between the two groups.

The largest NN was ≧8 mm in 108 (72.5%) of the DN patients. When compared for prevalence of NN 8 mm or larger, no statistically significant difference was found between the MM-history-positive DN patients and the MM-history-negative DN patients (p = 0.620) (Table 5). It was then determined how many moles ≧8 mm were present on each patient (Table 6). No significant difference was found when the MM-history-positive DN patients were compared to the MM-history-negative DN patients (p = 0.571).

A total of 122 (81.3%) had NN with 2 or more of the distinctive features described above (Table 7). No significant difference (p = 0.342) was found when the MM-history-positive subset was compared to the MM-history-negative subset to see if there was a difference in prevalence of dysmorphic features of NN between these groups.

It should be noted that although there was no statistically significant difference in the prevalence of the three "classic" features studied, a greater percentage of patients in the MM-history-positive subset had these attributes.

TABLE 5
Largest Nevocytic Nevus

	Greatest Diameter		
	1–7 mm	≧8 mm	Total
DN patients with a family and/or personal history of MM	25 (29.1%)	61 (70.9%)	86 (57.7%)
DN patients without a family and/or personal history of MM	16 (25.4%)	47 (74.6%)	63 (42.3%)
Total	41 (27.5%)	108 (72.5%)	149 (100%)

p = 0.620.

DISCUSSION

One purpose of this study was to identify what percentage of the 150 consecutive patients with DN had the three principal clinical attributes of patients who have "classic" DN, namely, 100 or more NN, NN 8 mm or more in diameter, and dysmorphic NN. Our study showed that 74% had 100 or more NN, 73% had NN 8 mm or more in diameter, and 81% had dysmorphic NN. All three characteristics were present in 53% of the patients, while 81% had at least two of these characteristics. The second purpose of the study was to compare two subsets of DN patients, those with a personal and/or family history of MM and those without, to see if the prevalence of the three principal features mentioned above differed in these two groups. There were no statistically significant differences between the MM-history positive and negative groups.

Others have reported on the definition and recognition of DN based on descriptive clinical criteria (Table 8). Lynch et al.[8] observed that MM was associated with a distinguishing cutaneous phenotype characterized by the presence of multiple large moles that were irregular in shape, reddish-brown to pink, and exhibited evidence of "leakage" of pigment. They suggested this disorder be named the familial atypical multiple mole melanoma (FAMMM) syndrome. Clark et al.,[9] in their discussion of the B-K mole syndrome, stated that an af-

TABLE 6
Comparison Between Melanoma-History-Positive and Melanoma-History-Negative Patients Based on Number of Nevocytic Nevi ≧8 mm Diameter

	Number of Nevocytic Nevi ≧8 mm Diameter						
	0	1	2–3	4–5	6–9	10+	Total
DN patients with a family and/or personal history of MM	25 (29.7%)	19 (21.8%)	25 (29.7%)	10 (11.5%)	7 (8%)	1 (1.1%)	87 (58%)
DN patients without a family and/or personal history of MM	16 (25.4%)	15 (23.8%)	17 (27%)	8 (12.7%)	3 (4.8%)	4 (6.3%)	63 (42%)
Total	41 (27.3%)	34 (22.7%)	42 (28%)	18 (12%)	10 (6.7%)	5 (3.3%)	150 (100%)

p = 0.571.

TABLE 7
Number of Distinctive Features in Nevocytic Nevi*

	≧2	<2	Total
DN patients with a family and/or personal history of MM	73 (83.9%)	14 (16.1%)	87 (58%)
DN patients without a family and/or personal history of MM	49 (77.8%)	14 (22.2%)	63 (42%)
Total	122 (81.3%)	28 (18.7%)	150 (100%)

$p = 0.342$.
*Distinctive features: irregular borders, marked play of colors, heterogeneity among the nevocytic nevi, macular tan shoulder, melanoma simulation.

fected patient may have fewer than 10 B-K moles or more than 100. They described the prototypic B-K mole as about 10 mm in diameter, irregular in outline, and haphazardly pigmented (tan, brown, black, and pink). Elder et al.[10] characterized DN as larger than the "common" acquired NN, irregular in outline and color, with variability from one lesion to another. In 1984, Swerdlow et al.[11] reported that there is a significant risk of developing MM associated with NN that have color variation and irregular edges, as well as with increased number of NN and large NN (over 7 mm diameter). Kelly et al.[12] found that, in 75% of all subjects in whom "melanocytic dysplasia" of any degree was diagnosed clinically, "dysplasia" was found histologically. These authors delineated the clinical features of these DN by looking at 175 color enlargements of histologically confirmed lesions. They found that 90% of the DN had ill-defined borders, 84% had irregularly distributed pigmentation, 72% had a diameter over 5 mm, 64% exhibited erythema, 63% had accentuated skin markings, and 46% had irregular borders. Of all subjects screened, 95% had 3 of these 6 features, while all had at least 2. They emphasized the importance of having clinical criteria for the diagnosis of DN, if screening by clinical inspection is to be possible.

Counts of moles have been performed in past studies, in both the general population and in patients with DN and/or MM. Mackie et al.[13] counted the number of benign pigmented NN in a British population in order to provide a range of normal numbers of NN for a Caucasion population in a temperate climate. These investigators examined people from 4 days to 96 years of age, with no personal and/or family history of MM. This provides data on the prevalence of NN in various age groups including individuals in the 20 to 40-year-old span, which is the range of ages included in our study. They found that in the age group of 20–29 years old, the mean number of moles in women was 33 and in men 22. From the ages of 30–39, the mean number of moles in women was 25, and in men 11. Cooke et al.[14] also examined the number of moles present in a predominantly Anglo-Saxon population in sunny New Zealand. For the pertinent age decade of 20–29, women had an average of 53 NN and men had an average of 47. In the other pertinent age decade, 30–39 years of age, women had an average of 52 NN and men 43. In our study of DN patients, the total NN count was ≧100 in 74% of patients. The finding of a higher average number of NN in our DN patients is consistent with other similar reports indicating that DN patients have a greater number of NN compared to controls that do not have DN.[11,15]

Nordlund et al.[15] found that patients with MM and atypical NN had more NN than patients with only atypical NN but no MM, and this difference was statistically significant. Although in our study a greater percentage of MM-history-positive patients had ≧100 NN compared to the MM-history-negative patients, this difference was not statistically significant.

A personal and/or family history of MM did not seem to influence, to statistical significance, the clinical presentation of NN using the parameters

TABLE 8
Descriptive Clinical Criteria of Dysplastic Nevi Published in the Literature

Criteria	Lynch[8]	Clark[9]	Elder[10]	Swerdlow[11]	Kelly[12]	Nordlund[15]
Increased number of NN	X			X		
Increased size of NN	X	X	X	X	X	X
Irregular shape of NN	X	X	X	X	X	X
Color variability	X	X	X	X	X	X
Shoulder	X				X	
"Atypical" appearance			X			
Heterogeneity			X			

applied in the population we studied. It is probable that the risk for MM is dependent on the total number of risk factors that a person has.[1] Our study was limited to looking at the clinical presentation of NN and did not address the issue of other risk factors for MM. Additional work needs to be done to quantitate other risk factors such as phenotype (eg, hair color, eye color, and complexion) to determine if patients in DN group III (who are at highest risk for MM[16]) have the same combination of additional risk factors as those in the other DN groups. Although there were no statistically significant differences in the prevalence of clinical features of NN in the MM-history-positive and MM-history-negative subsets in this study, this does not imply that the risk for MM is similar. Indeed, based on published data, DN patients of the D-2 type (ie, two or more family members have MM) have been shown to have a near 100% risk of developing MM, while other types are at much less risk.[2] Thus, a personal and/or family history of MM is an additive risk factor for MM in patients with DN.

Greene[16] recently reviewed a number of laboratory abnormalities that have been reported in D-2 type DN patients. It would be interesting to compare MM-history-positive DN patients with MM-history-negative DN patients to see if there are any significant biologic, genetic, immunologic, or cytologic differences between these two groups.

The clinical characteristics of NN as outlined in this study (≧100 NN, plus NN ≧8 mm diameter, plus dysmorphic NN) are useful in identifying one end of a broad clinical spectrum of patients with DN. Using these criteria, the clinical identification of this subset of DN patients is relatively easy. More work is necessary to characterize patients toward the other end of the DN spectrum, that is, those with fewer moles, that are not as large, and/or not dysmorphic.

The overriding goal is to identify individuals who are at increased risk for developing MM. Physicians and the general public should be alerted to the possibility of an increased risk for developing MM if the person has >100 moles, and, especially, if some are large (≧8 mm). Even if no nevocytic nevus is dysmorphic, having a combination of these two clinical attributes increases one's risk for MM.[11] Patients thought to be at increased risk for malignant melanoma should be examined at regular intervals, by physicians and by themselves, since early diagnosis and prompt removal of MM is the only current method of curing such patients.

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