

LETTERS TO THE EDITOR

On the Age When Malignant Transformation of Congenital Melanocytic Nevi Occurs

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We read with interest the article published in issue 3 of *Actas Dermosifiliográficas* corresponding to April 2008,¹ which reviewed the always controversial subject of congenital melanocytic nevi (CMN), and which discussed the results of a systematic review published in 2006 by Krengel et al.² It was surprising to read that the greatest risk of CMN becoming malignant occurs during adolescence, since this contrasts with our experience in the Melanoma Unit of the Hospital San Cecilio, Spain, where most malignant transformations of CMN occur during the first 3 or 4 years of life, in agreement with other series published on the subject.³⁻⁶ This led us to refer to the source article to attempt to clarify the reason for this difference, and we believe that this inconsistency originates from an incorrect interpretation of the data.

In fact, the article analyzes 14 series that included 6571 patients with CMN, among which 46 cases of melanoma were detected, representing a total of 0.7% of cases. The mean age at the time of melanoma diagnosis was 15.5 years (median, 7 years), and thus the authors of the source article and its aforementioned reviewers concluded that the greatest risk of malignancy would occur during adolescence and not during the first years of life.

However, we believe that this conclusion is incorrect, and a more thorough analysis of the data would yield different results. The original article contains a table in which all the series and the age of melanoma onset are presented, and there is no doubt that the mean and median are those presented, but we believe that in this

case they are not appropriate measures to faithfully represent the meaning of the data, for the following reasons.

If we divide the 46 cases of melanoma into 3 age groups (group 1: onset ≤ 4 years; group 2: onset 4-18 years; and group 3: onset ≥ 18 years) we can see that the great majority of the 46 cases of melanoma were detected in the first age group (≤ 4 years), as presented in the Table.

Thus, there were 21 cases of melanoma in group 1, 8 cases in group 2, and 17 cases group 3. However, if we are stricter in our analysis, we could exclude those melanomas appearing on normal skin, extracutaneous ones, or those with an unknown primary site. Thus, there would be 3 extracutaneous cases in group 1 (Hale et al) and 2 more with an unknown primary site (Hale et al and Greeley et al); there would be 2

Table. Distribution of Melanomas Reported in the Different Series

Age Groups	≤ 4 y	4-18 y	≥ 18 y
Cases and Age at Diagnosis			
Greeley et al (1965)	1 y, 1 y ^a	10 y, ^a 10 y ^a	38 y, 30 y ^a
Lorentzen et al (1977)			28 y, 38 y, 40 y
Arons and Hurwitz (1983)			
Quaba and Wallace (1986)		7 y, 10 y	
Ruiz-Maldonado et al (1992)	8 mo, 2 y	14 y	
Swerdlow et al (1995)			18 y, 20 y
Dawson et al (1996)	0 y, 0 y		
Sahin et al (1998)			26 y, ^a 42 y, ^a 57 y ^a
Egan et al (1998)	2 y, 3 y		
Foster et al (2001)			
Berg and Lindelöf (2003)	1 y	7 y	
Ka et al (2005)			
Hale et al (2005)	1 y, ^a 1 y, ^a 1 y, ^a 3 y ^a		
Bett (2005)	0 mo, 3 mo, 6 mo, 4 y 7 mo, 9 mo, 1 y, 3 y	7 y, 2 y	24 y, ^a 39 y, 58 y 20 y, 26 y, 34 y ^a 39 y
Total	21 cases	8 cases	17 cases
Cases of malignancy in CMN (corrected)	16 cases	6 cases	10 cases

Abbreviation: CMN, congenital melanocytic nevus

^aExtracutaneous melanoma, on normal skin, or with an unknown primary site.

cases with an unknown primary site in group 2 (Greeley et al); and, finally, there would be 3 cases (Sahin et al) on normal skin in group 3, another 2 extracutaneous cases (Bett et al) and 1 case (Lorentzen et al) with an unknown primary site. These adjustments would result in there being 10 real cases of malignant transformations of CMN in adults, 6 in the intermediate group, and 16 in group 1, an analysis which clearly points to early malignancy.

On the other hand, the difference in age results in a distorted mean of 15.5 years. Nor would the median be a suitable measure here, since although there are a sufficient number of cases of adults, they have a much wider age range (with onset of malignancy between 18 and 58 years of age) than that included in group 1 (cases with onset during the first 4 years of life). Thus, in this case, neither the median nor the mean faithfully represent the meaning of the data reviewed by the authors, and neither would the conclusions based on these be valid.

There are other data in support of our assertion. The series studied by Hale et al,⁴ which was based on the largest current registry of large CMN (the NYU-LCMN), in fact reported more cases of melanoma than those reviewed by the authors. This was a series of 205 patients with CMN in

whom 10 cases of melanoma were found. Of these, 7 appeared in the first 3 years of life, and the other 3 appeared in those aged 35 years or more. Krengel et al appear to justify the exclusion of 6 of these melanomas because they were already diagnosed at the time of study enrollment, but this has no bearing on the age of onset, which is the subject under discussion.

Neither do the authors' arguments appear valid when justifying the data from other series supporting early malignancy due to a possible selection bias, since most studies include information on patients of pediatric age. In our opinion, this fact does not invalidate the observation that a large number of melanomas do indeed appear in the first years of life. Longer follow-up time may have led to the detection of a greater number of melanomas in adults; however, as presented by the authors, the incidence of melanomas did not change during the follow-up period, and in fact the series in which this was longer did not find higher rates of malignancies (Lorentzen et al and Swerdlow et al).

Nevertheless, the subject addressed continues to be a matter of debate, and new prospective studies based on a much wider series of patients are needed with a much longer follow-up period.

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