## LETTER TO THE EDITOR

Change in Dermoscopic Pattern of Naevi in Children: A Commentary

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Sir,

We read with interest the publication by Belloni Fortina et al. (1). In this observational study, 717 melanocytic naevi in 160 consecutive paediatric patients were followed for changes in dermoscopic pattern. Patients were 3–16 years of age at baseline and their naevi were followed for up to 7 years. Of the 717 naevi included in the study, 140 (19.5%) exhibited a change in dermoscopic pattern during follow-up. These changes were common in all paediatric age groups, but most frequent (25.3%) in the naevi of younger patients (age 3–6 years at baseline). Notably, of the 140 naevi with dermoscopic change, the most common type was from globular to globular-reticular pattern (35 of 119 naevi with globular pattern at baseline, 29.4%), from globular to reticular (14/119, 11.8%) and from globular-reticular to reticular (24 of 64 naevi with globular-reticular pattern at baseline, 37.5%). These observations are important and consistent with previous cross-sectional studies, which reported that, while a greater prevalence of globular naevi, including those with cobblestone pattern, was seen in children < 10 years, a predominance of reticular naevi was observed in adults (2–5).
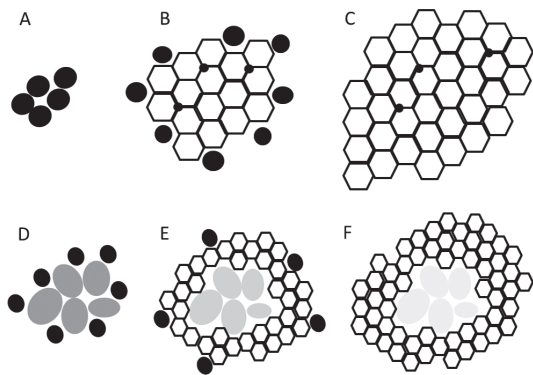

Fig. 1. Schematic showing change in dermoscopic pattern with growth of naevi. Globular to reticular pattern: (A) At the initial phase in the life of this naevus, the globular pattern represents peripheral globules (a dermoscopic hallmark of growing naevi) that are closely clustered together. (B) As the naevus increases in diameter, a network appears at the centre, while the peripheral globules mark the outer bounds of the growing naevus. (C) The naevus displays a reticular pattern, without peripheral globules, indicating that it has reached the senescent phase in its life-cycle. Globular to globular-reticular pattern: (D) Another type of growing naevus displays large cobblestone globules at the centre and smaller globules at the periphery. (E) As the naevus grows, the central cobblestone globules remain relatively unchanged or at time fade, while a centrifugally growing peripheral network follows the peripheral globules. (F) When growth arrests, the peripheral globules disappear. A variant of this pattern is the naevus with central homogenous area (central globules are indistinct) and peripheral network.

The authors interpret the above-mentioned findings as follows: "Our work instead shows several cases of a single naevus evolving from a globular pattern, characterized by a dermal proliferation to a reticular pattern consistent with an epidermal proliferation" (1). It is at this point that we would like to offer a different interpretation of their data.

First, while dermoscopy is an important bedside surrogate of the histopathological pattern of melanocytic neoplasms, there are limitations to the dermoscopic-pathological correlation. Pellacani et al. (6) have shown, using dermoscopic-reflectance confocal microscopy (RCM)-histopathological correlation, that naevi with globular dermoscopic pattern correlate either with a predominantly-junctional or a predominantly-dermal nested proliferation of melanocytes; furthermore, naevi with reticular dermoscopic pattern correlate with either predominantly-lentiginous or predominantly-nested junctional proliferation of melanocytes. Using RCM for longitudinal tracking of change in naevi, the authors have shown that, while some naevi changed dermoscopically from globular pattern to reticular pattern, they did not demonstrate a change in their overall RCM pattern; these naevi show a meshwork pattern on RCM throughout their evolution, consistent with a nested junctional proliferation of melanocytes (6). Initially, the naevus harbours large junctional nests, appearing globular on dermoscopy (Figs 1A and 2A), but with peripheral growth of the naevus, these junctional nests become elongated, appearing reticular on dermoscopy (Fig. 1B and 1C). In fact, we interpret Fig. 2 in the paper by Belloni Fortina et al. (1) as showing the growth pattern of a naevus with a predominantly-nested junctional proliferation of melanocytes. We posit that, while such growing naevi can show a dermoscopic change from globular to reticular pattern, the melanocytic proliferation is occurring within the same anatomic compartment.

Secondly, Belloni Fortina et al. (1) segregated naevi with globular dermoscopic pattern from naevi with cobblestone pattern. It has been shown that naevi with cobblestone pattern display a predominantly-dermal nested proliferation of melanocytes on RCM and histopathology (6). A change from cobblestone pattern to reticular pattern would lend strong support to the notion that dermal proliferations of melanocytes evolve into junctional proliferations. However, of the cobblestone naevi, very few (2/110=1.8%) became reticular (1). An interesting pattern of growth can be seen in naevi with
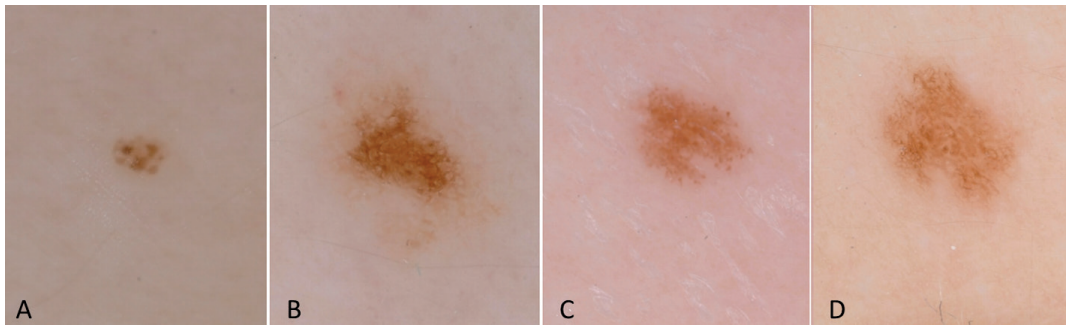
Fig. 2. Change in dermoscopic pattern in growing naevi on the back. Globular to reticular pattern: (A) At baseline (age 11 years), a back naevus, 1.5 mm in diameter, displays at globular pattern, akin to that shown in Fig. 1A. (B) At follow-up (age 14 years), the naevus has grown to 4 mm in diameter and displays a reticular pattern, without peripheral globules, akin to the pattern shown in Fig. 1C. Globular to globular-reticular pattern: (C) At baseline (age 11 years), a back naevus, 2.5 mm in diameter, displays a globular pattern with peripheral globules, as shown in Fig. 1D. (D) At follow-up (age 14 years), the naevus has grown to 4.4 mm in diameter and displays a central globular and peripheral reticular pattern, without peripheral globules, as shown in Fig. 1F. Of note, the central area has remained globular, while the surrounding area that displayed peripheral globules (C) has evolved into a reticular pattern (D).

central cobblestone globules and peripheral network. At their inception, these naevi can appear as wholly globular in pattern, consisting of central cobblestone globules and smaller peripheral globules (Figs 1D and 2C). As these naevi grow, they become reticular-globular; the peripheral portion centrifugally grows, developing a network, while the central cobblestone component remains more constant (Figs 1 E, F and 2D).

Thirdly, we recently published a longitudinal observational study of back naevi in 443 children (39% females) residing in Framingham, MA, USA (7). Dermoscopic imaging of up to 4 index back naevi was performed at age 11 years (baseline) and repeated at age 14 years (follow-up). Of 936 naevi imaged dermoscopically, 31% (291 naevi) changed in dermoscopic classification. Notably, only 4% (*n* = 13) of naevi assessed as globular at baseline were classified as reticular at follow-up. However, we acknowledge the differences in age range and follow-up range between our cohort (7) and that of Belloni Fortina et al. (1). In addition, there is a substantial difference in distribution of naevi by dermoscopic classification between the 2 studies: Belloni Fortina et al. (1) classified 16/717 naevi (2.2%) as homogenous, while we classified 468/936 naevi (50%) as homogenous (7). As dermoscopic pattern has been shown to be related to skin phenotype (8, 9), we suspect that our population of children may be of paler complexion than the population in Padua, Italy.

Finally, dermoscopy offers a window for better understanding naevogenesis by observing naevus growth *in vivo*. While dermoscopy by itself may be limited in distinguishing junctional from dermal proliferation of melanocytes, the correlation of dermoscopic patterns of naevi with RCM and histopathological findings (6) points to the existence of distinct subsets of naevi. These subsets include naevi with reticular pattern that comprise mostly-lentiginous proliferation of melanocytes; naevi with reticular pattern that transiently display peripheral globules during growth – these naevi consist of a predominantly nested-junctional proliferation of melanocytes; and naevi with cobblestone globular pattern that show a mostly nested-dermal proliferation of melanocytes. Naevi with composite patterns also exist (e.g. naevus with central cobblestone globules and peripheral network; Fig. 2D). As naevi are among the most important known risk factors for melanoma, we hope that a better understanding of naevogenesis will constitute an important step towards reducing melanoma incidence and mortality.

Response to "Change in Dermoscopic Pattern of Naevi in Children" by Scope et al.

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We read with interest the Commentary by Scope et al., in which the authors propose a different interpretation of our data (1).

As correctly highlighted by Scope et al., our cohort differs in both age and follow-up from the Framingham cohort (7). Scope et al. report that only 4% of globular

naevi evolved into a reticular pattern in their study, which included patients followed up from age 11 to age 14 years. This is not surprising, as most of our globular naevi evolve into reticular from age 3 to age 10 years and consequently at age 11 years have already changed their pattern. In an as-yet unpublished larger cohort of patients only 3 out of 47 globular naevi observed at age 11 years changed into reticular after a follow-up of 4–5 years.

With regard to the comment on cobblestone naevi, we also segregated this group from the group of globular naevi on the basis that both histology and reflectance confocal microscopy (RCM) pattern are different from those of globular naevi (6). In our updated cohort of patients 90% (208 out of 231) of cobblestone naevi observed at the first visit were detected in older ages, i.e. in patients > 7 years old, with only one in patients aged 4 years or less. Most of the cobblestone naevi that changed pattern evolved into reticular/globular pattern (17 out of 231 (–7.3%)) and only 5 into reticular pattern. Most of these changes occurred in patients older than 11 years. The study on globular naevi by Pellacani et al. (6) analysing the correlation between dermatoscopy, RCM and histology and the longitudinal follow-up was conducted in patients much older than ours.

With regard to the comment on homogeneous pattern, our data are in line with those reported by Zalaudek et al. (2). The different results reported in the Framingham' study (7) could be explained not only by the different age of our cohort, but also by the different skin type as suggested by Scope et al.; in fact more than 85% of our patients had skin type 3 or darker, while 67% of Framingham population had been classified as "fair" or "very fair".

REFERENCES (for both papers)

1. Belloni Fortina A, Zattra E, Bernardini B, Alaibac M, Peserico A. Dermoscopic changes in melanocytic naevi in children during digital follow-up. Acta Derm Venereol 2012; 92: 427–429.
2. Zalaudek I, Grinschgl S, Argenziano G, Marghoob AA, Blum A, Richtig E, et al. Age-related prevalence of dermoscopy patterns in acquired melanocytic naevi. Br J Dermatol 2006; 154: 299–304.
3. Changchien L, Dusza SW, Agero AL, Korzenko AJ, Braun RP, Sachs D, et al. Age- and site-specific variation in the dermoscopic patterns of congenital melanocytic nevi: an aid to accurate classification and assessment of melanocytic nevi. Arch Dermatol 2007; 143: 1007–1014.
4. Seidenari S, Pellacani G, Martella A, Giusti F, Argenziano G, Buccini P, et al. Instrument-, age- and site dependent variations of dermoscopic patterns of congenital melanocytic naevi: a multicentre study. Br J Dermatol 2006; 155: 56–61.
5. Zalaudek I, Schmid K, Marghoob AA, Scope A, Manzo M, Moscarella E, et al. Frequency of dermoscopic nevus subtypes by age and body site: a cross-sectional study. Arch Dermatol 2011; 147: 663–670.
6. Pellacani G, Scope A, Ferrari B, Pupelli G, Bassoli S, Longo C, et al. New insights into nevogenesis: in vivo characterization and follow-up of melanocytic nevi by reflectance confocal microscopy. J Am Acad Dermatol 2009; 61: 1001–1013.
7. Scope A, Dusza SW, Marghoob AA, Satagopan JM, Braga Casagrande Tavoloni J, Psaty EL, et al. Clinical and dermoscopic stability and volatility of melanocytic nevi in a population-based cohort of children in Framingham school system. J Invest Dermatol 2011; 131: 1615–1621.
8. Zalaudek I, Argenziano G, Mordente I, Moscarella E, Corona R, Sera F, et al. Nevus type in dermoscopy is related to skin type in white persons. Arch Dermatol 2007; 143: 351–356.
9. Scope A, Marghoob AA, Dusza SW, Satagopan JM, Agero AL, Benvenuto-Andrade C, et al. Dermoscopic patterns of naevi in fifth grade children of the Framingham school system. Br J Dermatol 2008; 158: 1041–1049.