The spectrum of morphologic patterns of nodular melanoma: a study of the International Dermoscopy Society

Editor

Nodular melanoma (NM) is the most aggressive melanoma subtype and is considered as responsible for more than 40% of melanoma deaths.[1–4] Early detection of NM is a major challenge, as most NMs lack the ABCD diagnostic criteria and display a non-specific clinical pattern that may mimic other benign lesions.[5]

The aim of our study was to identify distinct morphologic patterns among NMs. In the context of a study[6] conducted on behalf of the IDS, a data set of clinical and dermatoscopic images of histologically confirmed NMs was collected. For the present study, 165 macroscopic images were included. After excluding cases with available dermatoscopic, but missing clinical images (n = 10), and those with poorly discriminated clinical images (n = 9), the final sample consisted of 146 NMs. Those were evaluated by six independent dermatologists (AS, HT, GA, CL, HK and AL), who were blinded for the histopathologic diagnosis or any clinical information, using an online platform (Survey Monkey, San Mateo, CA, USA). Lesions were assigned into predefined diagnostic categories based on morphology, which have been determined via consensus among the authors, based on available literature and preliminary analysis of the data set: seborrheic keratosis-like, non-melanoma (NMSC)-like including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), pyogenic granuloma–angioma–angiokeratoma-like, dermatofibroma-like, blue naevus-like, dermal naevus-like, pigmented naevus-like, spitz-like, pigmented nodular melanoma-like, hypo/amelanotic melanoma-like, polypoid-like and miscellaneous. An agreement threshold of 4 out of 6 evaluators was set, with lesions meeting this threshold be classified to the respective morphologic category, so specific morphologic clusters emerged. An agreement was reached in 80 of 146 evaluated NMs (54.8%), which were categorized into eight morphologic patterns (Table 1). Most nodular lesions have been characterized as pigmented nodular melanoma-like (n = 46), followed by NMSC-like (n = 13), hypo/amelanotic melanoma-like (n = 8), seborrheic keratosis-like (n = 8), pyogenic granuloma–angioma–angiokeratoma-like (n = 2), dermatofibroma-like (n = 1), pigmented naevus-like (n = 1) and Spitz-like (n = 1). In 66 (45.2%) NMs, the agreement threshold was not reached.

Our data suggest at least five morphologic patterns of NM, reflecting its clinical diversity and ability to mimic benign and other malignant nodular skin lesions. NMs with a typical clinical appearance, mainly pigmented (Fig. 1a), have a high likelihood of being identified by a dermatologist, which is consistent with prior findings.[7] Furthermore, clinicians may consider including NMSC (BCC or SCC) (Fig. 1e-f) along with hypo/amelanotic melanoma (Fig. 1b) in the differential diagnosis. These findings confirm the fact that a significant proportion of NMs lacks pigmentation.[5,8] Finally, it is interesting to note that NMs may clinically mimic benign lesions such as inflamed seborrheic keratosis (Fig. 1c) or pyogenic granuloma (Fig. 1d).[9] A melanoma presenting a keratotic surface may often misdiagnosed as a benign lesion, and this has been previously supported by case reports of verrucous–keratotic melanomas.[10] Moreover, the fact that several morphologic patterns did not achieve an important scoring among the evaluators could be attributed to the overlap between clinically relevant categories, i.e. naevus-like lesions. In addition, the fact that no agreement was reached for a significant number of NMs (45.2%) highlights the significant challenges related to the non-specific clinical appearance of the tumour.

The distinct patterns of NM identified are of great importance to address the early detection of this melanoma subtype in clinical practice. Our study provides a further insight in the diversity of the morphology of early NM, consisting of lesions that may mimic more common benign or malignant entities. The detection of NM, therefore, requires a high grade of alertness and the consideration of NM within the differential of more common

Table 1 Distribution of nodular melanoma cases into morphologic patterns based on the agreement among evaluators (n = 146)

Morphologic patterns	Description	Agreement among >4/6 evaluators
Seborrheic keratosis-like	A lesion characterized by a hyperkeratotic or verrucous surface	8 (5.5%)
NMSC-like	A red or slightly pigmented nodular lesion with vascularity, translucency and possible ulceration/crusting	13 (8.9%)
Pyogenic granuloma–angioma–angiokeratoma-like	Purple-black to red colour, haemorrhage or ulceration with well-defined borders and/or collarette of scale	2 (1.4%)
Dermatofibroma-like	Papule or nodule, reddish or skin-coloured	1 (0.7%)
Blue naevus-like	A nodule with homogeneous or predominantly bluish coloration	0
Dermal naevus-like	A homogeneously pinkish or flesh-coloured lesion with smooth surface	0
Pigmented naevus-like	A nodular lesion with predominantly brownish coloration, occasionally with reddish halo and "irritated" appearance	1 (0.7%)
Spitz-like	A reddish-brown nodule	1 (0.7%)
Pigmented nodular melanoma-like	A nodule with homogeneous or predominantly black colour (with or without other colours)	46 (31.5%)
Hypo/amelanotic melanoma-like	A non-to-lightly pigmented nodule, often asymmetric, with potential speckles of pigment, not conforming to any of the above categories	8 (5.5%)
Polypoid-like	A pedunculated nodule	0
Miscellaneous	Lesions that could not be binned to any of the previous categories (e.g. a multinodular lesion)	0
No agreement		66 (45.2%)

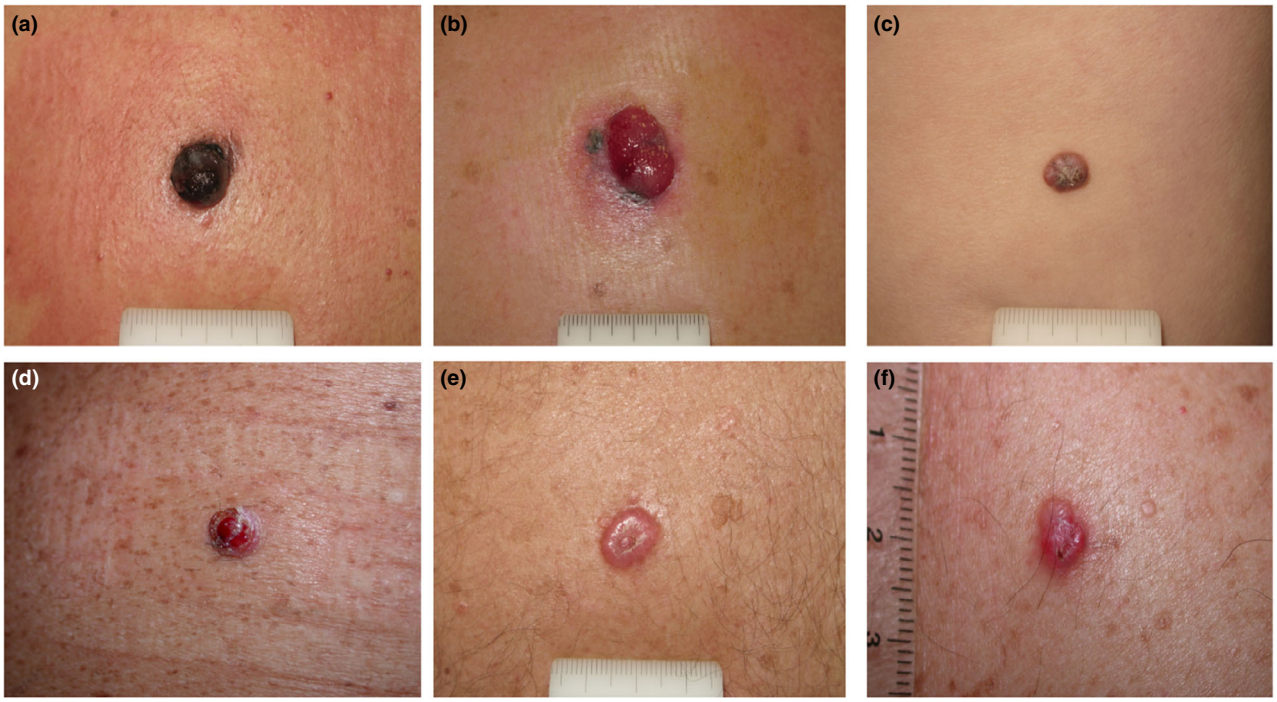

Figure 1 Nodular melanomas presenting with a typical clinical morphology as arises from an agreement of 4 out of 6 evaluators: (a) pigmented nodular melanoma-like, (b) hypo/amelanotic melanoma-like and nodular melanomas imitating benign and malignant non-melanoma lesions, (c) seborrheic keratosis-like, (d) pyogenic granuloma–angioma–angiokeratoma-like and (e)-(f) non-melanoma skin cancer-like.

nodular lesions among dermatologists. Conclusively, a more precise categorization of NM's clinical morphology to enhance their early diagnosis is warranted.

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Use of self-applied sculptured gel nails may increase the risk of allergy to (meth)acrylates in children and adolescents

Editor

Gel nails are a new type of artificial nails containing UV-curing acrylates and methacrylates, here referred to as (meth)acrylates.[1] They are known to be more fashionable and long lasting than conventional nail polishes. Until a few years ago, gel nails were applied only by nail technicians, but recently several and inexpensive home-use UV-curing kits have been placed on the market, increasing the risk of complications induced by these nail cosmetics.[1] Among complications, allergic contact dermatitis (ACD) due to (meth)acrylates is a well known issue for adults, both beauty technicians and consumers.[2] For the latter, the use of home kits for UV-curing gel nails is most likely worse than aesthetician procedures performed in professional nail salons. During self-application or during application by untrained people, there is a higher risk that the gel containing acrylate monomers overflows from the nail plate and comes in contact with the periungual skin, enhancing sensitization. ACD to (meth)acrylates is rarely described in childhood and adolescence.[1,3,4,5]

A 14-year-old non-atopic girl referred to us with a 1-week-history of itchy eczematous dermatitis of the hands, particularly involving periungual regions of all fingers and some fingertips (Fig. 1a,b,c). Face, mainly eyelids and lips, was also involved (Fig. 1d). The history revealed that for 6 months she was applying gel nails every 20 days to herself utilizing a home UV-curing kit received as a birthday gift. Dermatitis cleared within 2 weeks after removing the gel nail and with mometasone furoate cream (once daily) and cetirizine tablets (10 mg/day). One month later, patient was patch tested with SIDAPA (Società Italiana di Dermatologia Allergologica, Professionale e Ambientale) baseline series and with acrylates series; readings were done on day (D)2, D4 and D7.[6] At D4, we observed positive reactions to 2-hydroxyethyl methacrylate 2% pet. (+++) contained in baseline series and to all tested (meth)acrylates: ethylene glycol dimethacrylate 2.0% pet. (+++), hydroxypropyl methacrylate 2.0% pet. (+++), urethane dimethacrylate 2.0% pet. (++), triethylene glycol dimethacrylate 2.0% pet. (++) and methyl methacrylate 2% pet. (++). No new positive reactions at D7 were observed.

(Meth)acrylates are reactive monomers that polymerize spontaneously or on UV-light exposure to form products, such as plastics, glues, textiles, medical devices and artificial nails.[2,3,7,8] These polymers are normally inert and non-sensitizing, and sensitization can occur in case of incomplete curing of the monomers, sometimes present as impurities in the final product. Regarding artificial nails, the availability of UV-light emitting home-curing kits increased this risk. In fact, these cheap kits without any calibration or service advice, may not allow a complete polymerization with the residual monomers able to induce sensitization. Moreover, the (meth)acrylates concentration in gel nails can be higher than 90%[1] and users apply and remove these artificial nails themselves, as our young patient.

Only exceptional cases of ACD due to nail (meth)acrylates were described in children and they are also very rare in adolescents.[1,3,4,5] To the best of our knowledge, 8 females were reported, including ours 2 children and 6 adolescents (mean age: 13.8; range: 10–17 years) (Table 1).[1,3,4,5] Only in 2 cases, the face was also affected, probably due to accidental contact with contaminated hands or to airborne exposure during the gel nail removing phase. Conversely to what observed in adults,[1] in these 8 young patients onycholysis, paronychia or permanent nail dystrophy were not reported. Occupational exposure was identified only in 1 of them: an English girl employed as beauty technician. Even if the 8 subjects were not homogeneously tested, 2-HEMA resulted the most frequently positive (meth)acrylate. 2-HEMA is the best single patch test allergen to detect ACD from (meth) acrylates in gel nails.[9] Other patch test reactions are frequent, both due to cross-reactions and possible concomitant sensitization, as gel nails contain many different (meth)acrylates.