Nested Melanoma, a New Morphological Variant of Superficial Spreading Melanoma with Characteristic Dermoscopic Features

A new morphological variant of superficial spreading melanoma (SSM) was first described by Kutzner *et al*. (1) and named "melanoma composed exclusively or predominantly of large nests"; it was later named "nested melanoma" (NM) (2,3). Clinically, lesions are larger in diameter (>6 mm), mostly showing typical clinical features of melanoma (the ABCD rule), and significantly different from all other pigmented lesions (the "ugly duckling sign") (1). The majority of NM is found on the trunk and limbs of patients older than 60 years (1-9). Dermoscopy shows typical features of melanoma (asymmetry, irregular blotches, atypical pigmented network, multicomponent structure, irregular dots, and globules) followed by the "typical" dermoscopic finding of a globular pattern with globules varying in shape, color, and distribution (1,3). It is known that flat nevi in the elderly present with a reticular or structureless dermoscopic global pattern, along with the fact that total nevi count decreases with advancing age due to involution of nevi (4,5). Therefore, a globular pattern is uncommon in the elderly, and this finding should always invoke a high suspicion of melanoma.

Histological diagnosis may be difficult because of the predominantly nested pattern, and the condition may be confused histologically with a benign junctional nevus (6). However, these large junctional nests of different sizes, with bridging and cytonuclear atypias together with lesion asymmetry, are the hallmark of this special kind of melanoma (6). Pathologically, NM presents with large intraepidermal melanocytic nests, which are more or less the same size and shape and equally distributed along the dermoepidermal junction, with a focal tendency to confluence. Melanocytes in nests show moderate to significant cytological atypia (1). Since most NMs were found on sun-damaged skin, solar elastosis can be present. Pagetoid spread of atypical melanocytes along the epidermis is rare, but may be found (1-3). In most case reports there was discrepancy between clinical and dermoscopic features – both favoring melanoma – and histopathology, which at first glance appeared nevoid (9). Although the majority of analyzed NMs were in situ, an invasive dermal component was also found. The atypical nevus in the elderly is an unstable nevus, and one variation also observed is the hypercellular nested variant described by authors; these have been reported as in situ nevoid melanomas, with cellular morphology usually associated with crowded small-to-medium hyperchromatic melanocytes. The progression of these atypical nested melanomas is often to a small cell (nevoid) melanoma, which may become desmoplastic (9). Although the term "superficial spreading melanoma" is appropriate for NM from a clinical perspective, at least some of these tumors may be linked to an aberrant nevus pathway seen in elderly individuals, explaining their unusual pattern resembling a bizarre nevus (9).

Additional tests can be performed due to clinicopathological discrepancy, including confocal microscopy, immunohistochemistry, array comparative genomic hybridization (aCGH), and in situ hybridization (FISH). Reflectance confocal microscopy may be useful in cases of such difficult lesions in order to proceed to surgical excision with more confidence, and can reveal the presence of dense nests at the dermoepidermal junction with cytologic atypia and pagetoid cells (3,7). In confocal microscopy, a grossly regular clod pattern (at low magnification) with atypical cells within nests (at higher magnification) was found if the NM was in situ (3,7,9). aCGH showed multiple chromosomal aberrations in all cases (1,2). Processing with the FISH technique showed a variation in range from 40% to 87% FISH-positive NM, depending on different authors (1,2). Once the diagnosis of NM is established, further treatment, including re-excision, is highly recommended (2).

All the authors who described NM consider NM a special variant of SSM in the elderly, and according to their opinion this should lead to modification of histopathological criteria for SSM. We would stress that the "elderly" criterion is not mandatory given the numerous cases reported in people under 60 years of

age (6). This is important and should henceforth reduce misinterpretation of this variant of melanoma due to the lesion's nevoid appearance (9). Dermoscopic criteria for NM should also be established so clinicians consider NM in differential diagnosis, which would further help the pathologist establish the correct diagnosis, since it is crucial not to misdiagnose a malignant lesion. Dermoscopy is very helpful in all cases, and globules are typically found in conjunction with other melanoma-specific criteria (1,3).

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