Seborrheic Keratosislike Melanoma With Folliculotropism

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Background: Seborrheic keratosislike melanoma could be one of the most problematic melanoma simulators, and it may be incorrectly treated by electrocautery or cryotherapy. Dermoscopic examination of pigmented tumors improves the diagnostic accuracy in these challenging lesions. In these tumors, numerous comedolike openings are present.

Observations: A 34-year-old man was seen for a conspicuous pigmented lesion on his back that clinically resembled a seborrheic keratosis because of the presence of multiple comedolike openings. Findings from dermoscopic examination showed distinct melanoma criteria (atypical pigmented network, asymmetric globules and dots, and a blue-whitish veil), in addition to multiple comedolike openings. Histopathological examination confirmed a peculiar melanoma variant characterized by prominent folliculotropism and minimal radial spreading. This tumor was not associated with chronic sun-damaged skin.

Conclusion: Dermoscopy was useful in identifying a particular case of seborrheic keratosislike melanoma with folliculotropism, thus avoiding incorrect treatment.

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Early and accurate melanoma diagnosis is probably the most challenging task for dermatologists and dermatopathologists. It is well-known that several benign lesions are melanoma simulators, and that some melanomas may mimic benign tumors, mainly melanocytic nevi, but also seborrheic keratosis, pigmented basal cell carcinomas, or even infectious or inflamed warts.

Dermoscopy is a noninvasive technique that improves the diagnostic accuracy of skin tumors, and it is especially useful in the differential diagnosis of classic clinical simulators of melanoma. Although dermoscopic criteria have been described for differentiating melanocytic and nonmelanocytic skin lesions, some observed features may be confusing when they present together in the same lesion. In fact, several authors have just enhanced the possibility of missing melanomas when specific dermoscopic findings for nonmelanocytic lesions are observed (eg, multiple comedolike openings and mililike cysts mimicking seborrheic keratosis), as well as when specific melanoma findings are not present.

Several clinical and/or histopathological variants of melanoma have been described to date. A poorly known and rare histopathological type is the verrucous nevoid melanoma or seborrheic keratosislike melanoma, which has only been reported in a few publications. It is characterized by prominent epidermal hyperplasia, hyperkeratosis, and even pseudofollicular plugs, so clinically and even histopathologically, it may resemble a benign lesion.

On the other hand, follicular invasion known as folliculotropism is a well-recognized condition in melanoma and nonmelanoma cutaneous neoplasias, such as cutaneous T-cell lymphoma, in situ Bowenoid carcinoma, and lentigo maligna, to name the better known examples.

We report herein a single case of a young adult affected by an extremely rare variant of folliculotropic cutaneous melanoma. An illustrating clinical-dermoscopic and histopathological correlation is shown, highlighting its importance in challenging melanoma cases.

Report of a Case

A 34-year-old male patient from Spain presented with a pigmented lesion on his back that had been growing during recent months. He remembered it had bled 2
years before. His brother, 6 years older, was affected by atypical mole syndrome and multiple primary melanoma (an in situ melanoma diagnosed at age 36 years and a superficial spreading malignant melanoma [Breslow depth of 0.6 mm] at age 37 years).

On physical examination, the patient had a symmetric, slightly raised lesion of 6 mm in diameter, with brown-blackish pigmentation, in the middle of his back. The clinical appearance resembled a pigmented seborrheic keratosis because it showed prominent pseudofollicular openings on its surface (Figure 1). Findings from dermoscopic examination showed that it was a 1-axis asymmetric and pigmented lesion with bluish, dark to light brown, and black coloration. It showed areas with disarranged prominent pigmented network, multiple asymmetric pigmented globules and dots on the periphery, and a conspicuous blue-whitish veil on the elevated center of the lesion. Spectacular follicular openings can be identified related to the most pigmented and raised area of the lesion.

Histopathological examination demonstrated an asymmetric lesion, formed by the proliferation of atypical melanocytes mostly at the dermoepidermal junction, but almost limited to the follicular structures, sparing the interfollicular space. Follicular infundibula were dilated and filled with keratin debris resembling horny plugs. Beside this, there was minimal proliferation of atypical melanocytes above the dermoepidermal junction and mild papilar dermis invasion, but both were less prominent than the follicular infiltration. Intradermal melanocytic nevus remnant was identified adjacent to the main lesion. Lamellar fibrosis around follicular structures, sparse infiltrate of melanophages, lymphoid inflammatory infiltrate, and neovascularization were found focally. Melanocytic cells were epitheloid and dendritic type, with prominent nucleolus and cellular pleomorphism. The mitotic index was raised—approximately 5 mitosis per high-power field. A diagnosis of superficial spreading melanoma with prominent folliculotropism over preexisting melanocytic nevus, with mild regression phenomena, was concluded. Breslow depth measured 0.6 mm, and the Clark level was II (papillar dermis) (Figure 3 and Figure 4).

Additional immunohistochemical studies were performed. Staining with HMB45 (prediluted; DAKO, Glostrup, Denmark) and melan-A (1:50; DAKO) confirmed the melanocytic origin of neoplastic cells and also helped to limit the melanoma extension (Figure 5). Reexcision with appropriate surgical margin (1 cm) was carried out. During the 4 years of follow-up, there was no sign of local or regional recurrence, and the patient remained free of disease. Both brothers were investigated for CDKN2A exon 2 and CDK4 gene defects, but no mutation has been found to date.

COMMENT

We report herein an unusual presentation of seborrheic-like melanoma with folliculotropism. In clinical practice, seborrheic keratosis is considered to be a clinically easily identifiable tumor. Unfortunately, some melanomas can resemble this banal tumor. Because the standard treatment for seborrheic keratosis is cryotherapy or electrocautery without histopathological study, in the case of a wrong diagnosis, the prognosis of the patient with
melanoma is obviously affected. In biopsy specimens of tumors with the clinical diagnosis of seborrheic keratosis, 0.5% were found to be melanomas. In addition, some cases of seborrheic keratosis-like melanoma have been documented in different reports. In most cases, dermoscopy has been found to be a useful tool for distinguishing melanoma and seborrheic keratosis mainly when specific criteria of melanocytic lesions are observed. Clinically, our case could be confused with a pigmented seborrheic keratosis, mainly due to the presence of horny plugs; however, dermoscopic features (pigmented network and multiple pigmented globules and dots) strongly suggested a melanocytic lesion, and pigmented keratosis could immediately be ruled out.

In an attempt to coin the correct denomination, a critical review of the literature was performed to conclude 2 differential diagnoses: the rare variant of verrucous-hyperkeratotic melanoma and follicular melanoma (FM). Verrucous-hyperkeratotic melanoma was described in 1982 by Kuehnl-Petzoldt et al as a variant of melanoma that might often be diagnosed, both clinically and histopathologically, as benign verrucoid lesions, especially seborrheic keratosis. It is usually observed in the extremities of women and characterized by marked verrucous hyperplasia and hyperkeratosis of the epidermis. Histopathologically, these authors described, as additional typical features, the proliferation of neoplastic cells mostly at the dermoepidermal interface rather than in the upper reaches of the epidermis and the absence of nodule formation. The prognosis of verrucous-hyperkeratotic melanoma did not differ from that of nonverrucose melanomas matched for sex, anatomic site, and thickness of the neoplasm. In 1993, Blessing et al reported a series of 20 cases of verrucous-nevoid melanoma, and they found them more often on the back and limbs of male patients with a mean age of 57 years. Clinical diagnosis of benign lesions (warty nevi, papillomas, seborrheic keratosis, and cysts) had been made in more than 50% of the cases. Histopathologically, these lesions were characterized by a spectrum of nevoid features, combined with marked epidermal hyperplasia, elongation of rete ridges, and overlying hyperkeratosis. At the same time, lesions showed typical melanoma findings, such as intraepidermal invasion and pleomorphism. They emphasize that histopathological classification may be very difficult, since more than 50% of their cases were initially labeled unclassifiable and 10% were histopathologically diagnosed as benign lesions. In these 2 retrospective clinicopathological studies, the contradictory epidemiologic data that were found probably reflects an insufficient number of cases because this is not a common type of melanoma. To date, only extremely rare additional cases have been reported, such as melanomas associated with pseudoepitheliomatous hyperplasia, or other entities that combine biphenotypic characteristics in the same neoplasm. The histopathological appearance of our case obviously differs from verrucous-hyperkeratotic melanoma, since the lack of epidermal hyperplasia and hyperkeratosis is evident.

Another consideration is the histopathological resemblance with a recently described melanoma variant, FM. In 2004, Hantschke et al reported a series of 5 cases of invasive melanomas that clinically resembled comedo or pigmented cysts that developed on actinically damaged skin, with an inconspicuous picture. Histopathological fea-
tures consisted of a deep-seated follicular structure in which atypical melanocytic cells extend downward along the follicular root sheath epithelium, permeating the inner and lower portions of the follicular structure as well as the adjacent dermis and parts of the sebaceous apparatus, and constitute nests to a variable degree. They proposed that FM is a variant of lentigo maligna melanoma because both present on actinically damaged skin of elderly patients, with similar architectural arrangement and with the same malignant cytologic features (i.e., atypically shaped polygonal and epithelioid cells invading the whole follicular structure). The main differences found by authors between FM and lentigo maligna melanoma are the clinical appearance; the almost exclusive affection of the follicular structure in FM, which only rarely could show secondary involvement of the adjacent epidermis; and the earlier invasive growth of FM. Hantschke et al14 even proposed that by definition, epidermal involvement of each side of FM should not exceed the depth of the follicular structure and should not show regression features.

Despite clinical and histopathological resemblances between our case and FM, we also found important differences: clinically, the young age of the patient and the melanoma location on sun-protected skin without a high pilosebaceous density. Histopathologically, it presented overlying a previous melanocytic nevus, and mild regression signs were shown. Thus, our case is not related to lentigo maligna melanoma and chronic sun-damaged skin.

We suggest that our case is the same histopathological variant of melanoma described as FM by Hantschke et al.14 However our case is different from the previously described cases of FM with the typical localization on sun-damaged skin, the small size of the lesions, and the consideration of this melanoma as an aggressive variant of lentigo maligna melanoma. Since only 5 cases were included in this series, it is possible to speculate that the histopathological finding of folliculotropism may be more evident in the head and face than in the rest of the body surface because of the high follicular density.

Another interesting feature in the present case is that it was within a familial multiple melanoma setting. Familial melanoma is estimated to account for 10% of all cases of melanoma. In these families, the presence of patients with multiple primary melanomas and early age at onset is characteristic, and the risk of melanoma development in another relative increases by about 15%. However, no special melanoma type has been identified in familial cases; neither clinical nor histopathological findings are characteristic; and nowadays, it is not possible to distinguish them from sporadic cases. Germline defects in several genes involved in cell cycle regulation, mainly the CDKN2A tumor suppressor gene, have been demonstrated in some Spanish familial melanoma kindred, which predisposes to early melanoma development. However, there are large numbers of melanoma families without any identifiable mutations.16

In conclusion, we present herein an exceptionally rare melanoma case in the context of familial multiple melanoma with a clinical-dermoscopic-histopathological correlation that shows an almost exclusive affection of the follicular structure. This histopathological finding presented a diagnostic challenge because clinically it resembled seborrhic keratosis. We would like to emphasize that the dermoscopic observation of these difficult lesions is essential to avoid an initial incorrect diagnosis and thus inappropriate therapy such as electrocauterization or cryotherapy.

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