The "Hidden-Wolf among the Lambs": Proposal of a New Phenomenon through a Camouflaged-melanoma among Pigmented Seborrheic Keratoses

B Tas[1], A Caglar[2], US Tetikkurt[2]

ABSTRACT

Malignant melanoma (MM) is the most malignant skin cancer whose classical clinical types include lentigo maligna (LM), superficial spreading melanoma (SSM), nodular (NM) and acral lentiginous melanoma (ALM). Superficial spreading melanomas constitute approximately 70% of melanomas. For the early diagnosis of MM, the ABCD rule and the "ugly duckling" sign are the most utilized criteria. We present a 72-year-old man with a SMM which was located among numerous pigmented and non-pigmented seborrheic keratosis (SK). We also propose a new mnemonic to describe camouflaged-melanomas among pigmented SKs, as well as other benign non-melanocytic lesions through our case.

Keywords: Malignant melanoma, pigmented seborrheic keratosis, superficial spreading melanoma

From: [1]Department of Dermatology, Health Science University and [2]Department of Pathology, Health Science University, Istanbul Bagcilar Research and Training Hospital, Turkey.

Correspondence: Dr B Tas, [1]Department of Dermatology, Health Science University, Istanbul Bagcilar Research and Training Hospital, Bagcilar Research and Training Hospital, Atakoy 7-8. Kısım, Martı Sitesi, 14/105, Bakirkoy/Istanbul, Turkey. Fax: (+90) 212-4404000.
Email: betulavc@yahoo.com

INTRODUCTION

In the early diagnosis of a MM, education of persons is very important in that they can notice an existing unusual lesion, or subsequent changes in appearance in the lesion. Indeed, it has been shown that, acquiring the habit of regular self skin-examinations by patients, decreased the deeper invasion of MM lesions at the time of diagnosis. Some guiding tips have been proposed for the purpose of early identification of MM. One of them is the "ugly duckling" sign which is defined as a MM lesion unlike the surrounding benign moles (1, 2). Here, we report a SSM which was hidden among numerous non-pigmented and pigmented SKs. Although it was similar to the surrounding pigmented SKs in general, noticing of the lesion by the patient due to its "bizarre" appearance was made the early diagnosis of the lesion possible. Thus, based on the interesting expression of our patients we propose a new term to describe MM hidden among pigmented SKs, as well as other non-melanocytic lesions, which is "hidden-wolf among the lambs".

CASE REPORT

A 72-year-old man was admitted to our dermatology clinic due to his dark-colored back lesion. According to the patient's history, he worked as a farmer for many years and has had numerous pigmented skin lesions located on his back, from his 40s. Some of the lesions were yellow or yellowish-brown while some included more darker-brown areas. Because all lesions looked similar to each other in general appearance, he was not concerned about them. However, he noticed some changes in color and shape of one of them, six months ago, and he expressed his complaint as " I think I found the treacherous-wolf".

On dermatological examination, the skin type of the patient was Fitzpatrick II, and there were hundreds of lesions sized 2-14mm, pigmented and non-pigmented SKs on the whole back. Among these lesions, a darker-brown to black colored lesion was seen (Fig.1a). On dermatoscopic examination, it had very heterogen, irregular bordered, asymmetric (18X28mm in diameter) and maculo-papular appearance. It included more than one color (yellow, light and dark-brown, black, pink and reddish), an irregular reticulated background pigmentation, a small and slightly ulcerated focus on papular part, tongue-like extentions, globules, fine irregular and asymmetric vessels, pigment regression areas, and structureless areas on the macular area (Fig.1b).

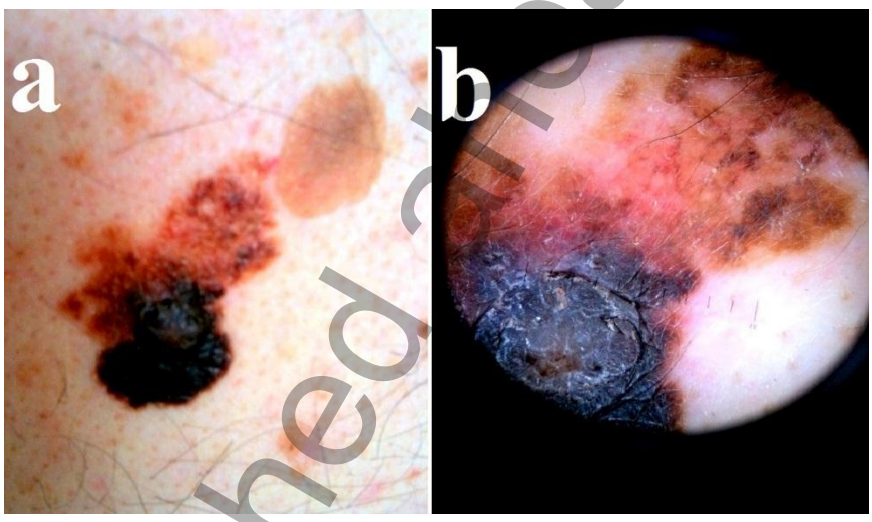

Fig. 1: Clinical appearances of the melanoma and surrounding seborrheic keratoses (a), and dermatoscopic (b) view of the melanoma.

The rest of the skin and mucous membranes did not show any other similar lesion or additional pathology. There was no regional or systemic lymphadenomegaly or hepatosplenomegaly. Except for the slightly increased blood sedimentation rate (29mm/h), other laboratory examinations including serum lactate dehydrogenase, serum alkaline phosphatase, cancer markers, and, chest X-ray and abdominal ultrasonography were negative or within the normal limits. The lesion was totally excised with a 2 cm safety margin because the lesion could have

been an MM, while a punch biopsy was taken from one adjacent yellowish-brown papule to compare. The histopathological examination of the melanocytic papule revealed only a few atypical melanocytes in the epidermis, as well as numerous, multinucleated and hyperchromatic atypical melanocyte nests, which were scattered in an irregular manner throughout papillary dermis, with a radial growth pattern.

The nest sizes and counts increased toward the reticular dermis, but did not invade papillary-reticular dermal interface. Thus, Clark level was determined as II (Fig. 2a,b). The Breslow thickness was 3 mm. In the lesion, microsatellite, perineural or lymphatic invasion, and tumor regression were not seen. Mitotic index was 1/10. Immunohistochemically, the tumor showed mild immunopositivity with Human Melanoma Black (HMB45) (Fig. 2c), and strong positivity with Melan-A (MART-1) (Fig. 2d), and S100 (Fig.2e). Ki67 proliferation index was 20% (Fig. 2f).

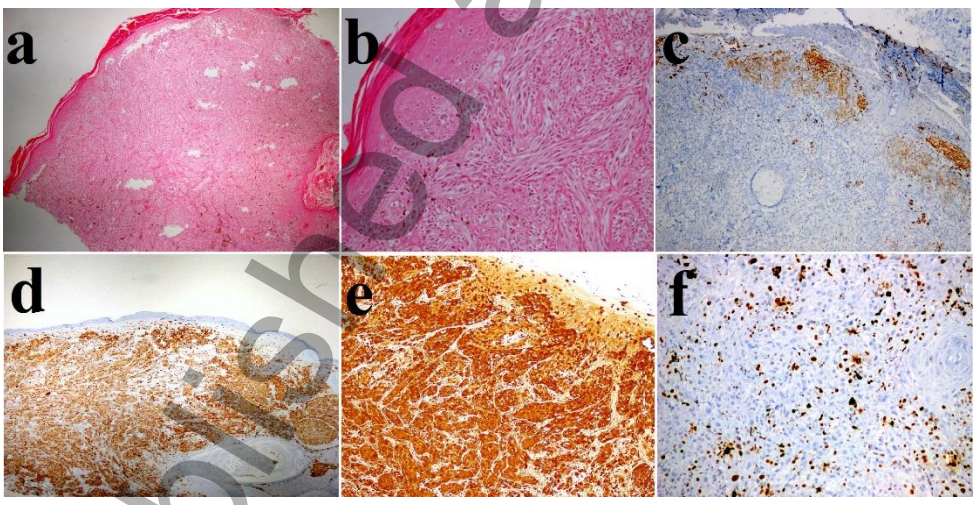

Fig. 2: On cross sections, focal parakeratosis, mild thinning, scattered atypical melanocytes in the epidermis, numerous melanocytic nests in the papillary dermis (a. HEX40, b.HEX200), and positive immunohistochemical stainings (c. HMB45X100), d. MART-1 X40, e. S-100X100, and f. Ki67X200) of the lesion being monitored.

With the histopathological and immunohistochemical findings, the diagnosis of SSM was confirmed. Histopathological examination of the adjacent lesion was consistent with a SK (Fig.3).

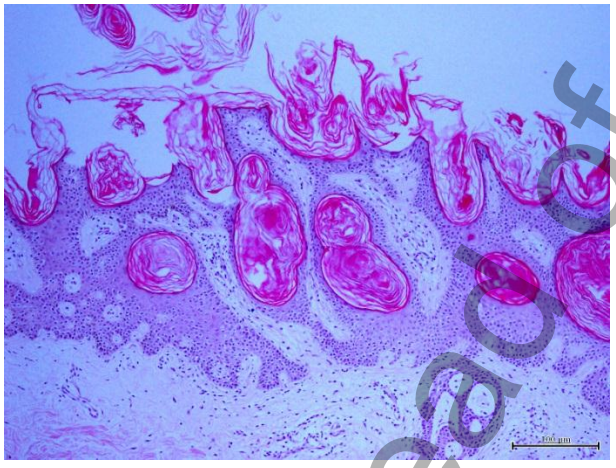

Fig. 3: In the histopathology of adjacent seborrheic keratosis, an exophytic expansion of acanthotic epidermis associated with papillomatosis, which was composed of broad interconnecting bands of cells containing the multiple horn cysts, was seen (HEX100).

After the diagnosis, a sentinel node biopsy was considered because clinically palpable nodes were absent. To mark regional lymph nodes, methylene blue dye was injected to the site of the primary melanoma. After identifying first-echelon lymph node by injection methylene blue dye, the sentinal node was excised from the right axilla. Its histopathology did not show any atypical melanocytes, and previously mentioned immunohistochemical stainings for MM were negative. No regional or systemic metastases were detected on chest and abdominal computed tomography scans. Based on this evidence, clinical stage of the lesion was identified as Stage-IIB (pT3bN0M0) according to the 7th edition of the American Joint Committee on Cancer (AJCC) staging system. Because the lesion was considered as limited to the skin, no additional therapy was implemented. The patient still continues to be checked in six-month intervals. No recurrence has been observed during 18-month follow-up period.

DISCUSSION

Although the diagnosis of MM can be straightforward in typical cases, sometimes distinguishing especially early MMs from surrounding lesions such as benign nevi, lentigines and SKs with atypical clinical presentation can be difficult, and may lead to overlooking a MM or cause unnecessary excision of benign lesions (3). To aid early diagnosis and also decrease false diagnosis rates of MM cases, some guidelines have been described such as ABCD mynemonic (1985) or its updated form ABCDE rule (2004) (1,2,4). In order to facilitate the rates of correct diagnosis, Jensenn et al. also proposed a modification to the ABCDE rule (2015). It is the ABCDEF rule by the addition of the letter "F" which stands for "Funny looking" (1).

These rules aim to facilitate in the diagnosis of MM and determine some distinctive tips including asymmetry, border irregularity, color variation, diameter greater than 6mm, and evolving (1, 5). However, because none of the rules are exactly diagnostic, and choosing which one will be used in the examination usually depends on individual preference of physicians, having some practical and wayshower knowledge by the patients is very important. On the other hand, the "ugly duckling" concept was introduced to the literature by Grob et al. in 1998 as " an outliner nevus that is differentiated from the surrounding moles by its unusual and suspicious features for malignancy" (1, 4). The latter rule aim to primarily identify an outliner or possibly malignant melanocytic lesion from other surrounding melanoctic lesions, but do not help to distinguish MM from non-melanoctic benign lesions such as basal cell carcinomas, hyperpigmented scars, pigmented fibrohistiocytic lesions like dermatofibroma, or pigmented keratinocytic lesions such as pigmented actinic or SKs which can appear in atypical presentations (6), as in our patient's lesion. On the other hand, SKs are the most common benign cutaneous skin tumors which can have a variety of clinical appearances.

They develop from the proliferation of epidermal cells and occur especially in older individuals. They are usually asymptomatic but can cause icthness, bleeding, oozing and are usually unatractive. Sometimes they become inflamed when they rub under clothing (7,8). SKs typically have an appearance of being stuck on the cutaneous surface, and colors of the lesions may vary from pale-brown to dark-brown or black. The lesions can grow many centimeters. They multiply in about half of the patients, in which a familial and autosomal dominant mode of inheritance exist (8, 9). Our patient did not have any familial history. Peoples are sometimes concerned that these growing lesions are malignant. However, others can not notice a dysplastic nevus or MM that develops among SKs due to their similar appearances. In this case, a significant danger will arise because MM cannot be diagnosed at an early stage.

The association of multiple eruptive seborrheic keratoses with internal malignancies is described as the "sign of Lesser-Trélat". This phenomenon is frequently observed especially with gastrointestinal adenocarcinomas. However, an eruption of SKs can develop after an inflammatory dermatosis such as eczema or severe sunburn, in which no associated malignancy is expected (9–11). Our patient has had numerous non-pigmented and pigmented SKs on his back, but we did not detect any findings to support any internal malignancy. Due to his job needs to work under the sun for long years, we thought that the reason for development of their numerous SKs was continious ultraviolet exposure. The clinical differential diagnosis of SKs include melanocytic nevus, verruca vulgaris, condyloma acuminatum, fibroepithelial polyp, epidermal nevus, MM, actinic keratoses, pigmented basal cell carcinomas, and squamous cell carcinomas (7, 8, 12). Indeed, distinguishing superficial SKs from LM may be difficult, as well as an inflamed SKs may be confused with MM. Izikson et al. reported a retrospective review of 9204 consecutive pathology reports, which contained clinical diagnoses of SK, revealed that 61 of these specimens (0.66%) were MM. They also stated that MM was in their clinical differential diagnosis of 31 cases (51%).

Additionally, the pigmented and dome-shaped acanthotic SKs may closely resemble a melanocytic nevus, but the surface is less lustrous and the follicular orifices are plugged (12). In our patient, beyond the typical clinicopathological appearances of both MM and SK, especially the transition zone between the two tumors which included irregular pigment network, pigment regression areas and plenty of vascularized pinkish macular area, enabled us to diagnose, dermatoscopically. However, sometimes SKs can show some unusual dermatoscopic patterns such as irregular pigment network, bowenoid, hairpin, keratoacanthoma-like, blue-nevus-like, lichenoid, clonal or spitzoid, which cannot be clearly differentiated from common skin malignancies (13).

Follow-up for patients with multiple SKs is important because malignant transformation can rarely develop within a SK (14,15). In our patient, due to the fact that both lesions had typical and individual histological features, and they did not have any overlapping findings, we thought that development of this MM was independent of the adjacent SK. Because the new SKs are usually continue to develop over time, patients may not pay attention to newly appearing lesions. However, one of the newly occuring lesions may not be a SK but, in fact, MM. In conclusion, our patient noticed his MM, due to its different appearances from the surrounding SKs. However, we think that "ugly duckling" concept cannot be used to describe this condition, because of the non-melanocytic nature of the surrounding lesions. Therefore, based on the interesting expression of our patients, and as a non-nevoid alternative to "ugly duckling" sign, we propose a new term to describe this phenomenon (MM hidden among non-melanoctic skin lesions such as SK) which is "hidden- wolf among the lambs". We believe that this term will be useful for both physicians and patients, and teaching it to patients with multiple non-melanocytic skin lesions can increase their awareness about possible malignant development among their lesions, as well as lead to early identification of MM.

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