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Misdiagnosed, Mistreated and Delay Diagnosed Acral Melanoma: The Atypical Presentations

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Abstract

Background: Acral skin is the most common site of malignant melanoma in non-Caucasian population. Diagnosis in this anatomic site is often delayed because this area is not routinely examined by patients or primary physicians.

Objective: To perform an earlier diagnosis underlining the importance of dermoscopy helping clinicians to differentiate this disease from the other lesions and biopsies will result in more timely diagnoses and improved survival.

Methods: We present 6 case studies visited in our Department of Dermatology of Naples University between October 2010 and September 2012.

Results: These lesions often mimic other entities like warts, calli, bacterial or fungal infections, foreign bodies, vascular lesions, blisters, melanocytic nevi, subungual hematomas, pyogenic granulomas, onychomycosis, keratoacanthomas, diabetic foot ulcers, traumatic lesions that can lead to misdiagnosis and mistreatment.

Conclusions: Awareness of atypical presentations of acral melanoma may be important to decrease misdiagnosis rates and improve patient outcome.

Keywords: Acral melanoma; Foot; Misdiagnosis; Dermoscopy

Introduction

Acral melanoma (AM) is defined as melanoma affecting the palms, soles and nail apparatus [1]. It is the most prevalent type of malignant melanoma in non-Caucasian populations [2] and accounts for approximately 50% of all melanomas in Japanese and other Asians including Chinese and Korean [3]. In Caucasian melanoma of the foot is the rarest although absolute incidences seem to be almost the same among all races [4].

Prognosis is generally poor because of delayed diagnosis in the advanced stages, especially in melanomas mimicking benign disease or amelanotic lesions. Therefore, accurate diagnosis and adequate treatment of acral melanoma in early curable stages are essentially important to improve the prognosis.

Case Studies: The "Federico II" Experience

Herein are described six case studies of patients visited in our Department of Dermatology of Naples University between October 2010 and September 2012 (Table 1). These patients are reported because of the delayed diagnosis, mistreatment or because they mimicked another disease entity. The first two cases described below were misdiagnosed as verruca. The first case concerns a 68-year-old woman who presented with a verrucous plaque on the sole of her right foot (Figure 1) that had been treated as a plantar wart for 4 months by a podiatrist. A plantar wart was diagnosed, and the patient underwent electrocoagulation therapy without histologic examination. The lesion began to grow, and 6 months later, the patient came to our clinic. Examination of her right foot revealed an erythematous, partially ulcerated, nodular lesion, approximately 2 cm in diameter, covered by a thickened corneal layer. The dermoscopic evaluation revealed the presence of an atypical vascular pattern with residual pigmentation and milky red areas (Figure 2). These dermoscopic structures suggested the diagnosis of melanoma.

The second case concerns a 62-year- old women who presented with an enlarging lesion on the sole of the right foot approximately 5 cm in diameter (Figure 3a), misdiagnosed as a wart and treated for seven months with cryotherapy. The dermoscopic evaluation revealed

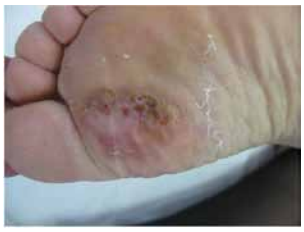

Figure 1: Acral melanoma initially treated as verruca on the sole of the right foot, approximately 2 cm in diameter.

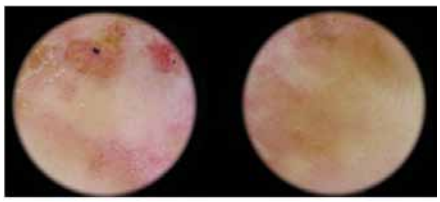

Figure 2: Dermoscopic examination shows an atypical vascular pattern with residual pigmentation and milky red areas.

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Patient No.	Sex	Age (Y)	Race	Tumor Site	Initial Diagnosis	Breslow thickness at diagnosis (mm)
1	F	68	Caucasian	Left sole	Wart	1
2	F	62	Caucasian	Left sole	Wart	1,9
3	M	61	Caucasian	Left foot 4^{th}-5^{th} interdigital space	Intertrigo	1,6
4	F	47	Caucasian	Left foot 3^{th}-4^{th} interdigital space	Pseudomonas infection	7
5	M	43	Caucasian	Left sole	Wart	11,5
6	F	58	Caucasian	Right Sole	Nonhealing Wound	2,1

Table 1: Patient and clinical characteristics.

the presence of an atypical vascular pattern with residual pigmentation (Figure 3b). Lack of response to therapy led to have a punch biopsy in both cases which showed malignant melanoma, acral lentiginous type. Following confirmation with biopsy, definitive surgical intervention in both consisted of resection of the primary malignancy and ipsilateral superficial inguinal lymph node basin resection using a multidisciplinary approach to patient care. Histopathological examination of the first lesion showed an amelanotic malignant melanoma, Breslow's depth of 1 mm; in the second case showed an ulcerated, nodular, amelanotic malignant melanoma, 1.9 mm in Bresolw's thickness. There were no sentinel lymph node metastases.

The initial misdiagnosis obviously results in delayed appropriate care. Two exemplary cases below exemplify this scenario.

A 61-year-old white man had an ulcerative lesion of the interdigital site of his foot (Figure 4a). As a result of maceration of the surrounding skin, it had been misdiagnosed as intertrigo and treated with systemic and topical fungal medications without a direct microscopic examination of fungal elements confirming diagnosis. After 6 months of treatment the patient was referred to our Department because the lesion continued to persist and spread. The past medical history was unremarkable. On the examination there was an ulcer located on the medial aspect of his fifth toe measuring 3.5 x 1.5 cm. Skin scraping taken from the lesion was examined with KOH, and fungal elements were not detected. Also there was no growth on Sabouraud's dextrose agar. The lesion was examined dermoscopically and revealed the presence of an atypical vascular pattern with residual pigmentation focally detectable at the periphery (Figure 4b). These dermoscopic structures suggested the diagnosis of melanoma.

The lesion was biopsied by incision and the diagnosis of an acral melanoma was made. The patient was sent for complete excision with the amputation of his fifth toe by the plastic surgery department. Histopathologic examination revealed a Breslow's depth of 1.6 mm. There were no sentinel lymph node metastases.

Likewise, a 47 years old woman was treated as a Pseudomonas interdigital infection for 11 months (Figure 5a) until she came to our Department where the clinical and dermoscopic examination (Figure 5b), similar to the previous case, led us to make a biopsy that confirmed the suspicion of melanoma. In the Department of plastic surgery a wide excision was performed that resulted in the amputation of the third and fourth toes with a thickness of the tumor more than 7 mm. Given the positiveness for metastases of the lymph node, an inguinal emptying was done. The patient died at 18 months after surgery.

In the following case study, the delay of the patient initial care was the primary reason for the significant depth of the melanoma. A 41-year-old Caucasian man was admitted to our Department due to a nodular lesion on his plantar left foot (Figure 6). He referred a cryotherapy for a verruca in that site 15 years before. Since 4 years he noted the advent of a nodular lesion careless to be inspected by a physician until the spontaneous bleeding and his walking difficulties. In the last 6 years he was also submitted to annual nevi follow-up, however without any examination of the foot.

The lesion seemed to be composed by three palpable coalescing nodules and measured approximately 4x2 cm.

A careful dermoscopic examination was performed, which revealed an atypical vascular pattern with residual pigmentation and ulceration in the medial part of the lesion (Figure 7). Due to a very strong suspect of melanoma, 2 punch biopsies were performed, one near the ulceration, the second in the lateral part of the lesion. The histopathologic examination stated an amelanotic melanoma. The patient was subdued to a complete excision at the Department of plastic surgery. The tumor metastases; He is nearing 1-year survival mark without any new lesion, recurrences or metastases.

AMs can also mimic lesion like ulcer, in patients with diabetes this can further complicate the diagnosis. After 6 months of incorrect treatments, a 58-year-old diabetic man came to our Department with an acral lesion resembling a nonhealing wound (Figure 8a). The resistance to the various treatments and the atypical vascular pattern at the dermoscopy (Figure 8b) led us to make a biopsy that confirmed a melanoma with a Breslow's depth of 2.1 mm.

Discussion

At Department of Dermatology and Plastic Surgery of Naples University "Federico II" 901 melanomas between January 2004 and September 2012 were diagnosed and excised. Of these, 2.8% (25 cases) were acral with a 24% (6 cases) with an atypical presentation. These data are in agreement with the literature, where the acral melanoma accounts about 3% to 15% of all cutaneous melanoma [5].

Main risk factors identified in formers studies are previous trauma, a high total number of naevi on the whole body, a high body mass index, naevi on the soles/toes, an older age, professional exposure to agricultural chemicals, a history of skin cancer and consumption of alcohol [6-8].

Misdiagnosis and delay in diagnosis are important argument in the discussion of a cancer that is curable by conservative operations in its early stages but has an extremely poor outcome in advanced states. A population-based study of 166 cases of acral melanoma demonstrated that misdiagnosis was associated with increased Breslow thickness (3.8 vs 2.2 mm) and lymph node metastasis (45% vs 23%) relative to correctly diagnosed lesion [9].

In this context, the awareness of atypical presentations of AM that may result in a diagnostic delay acquires particular importance. The diagnostic delay was reduced significantly over the years thanks to skin cancer prevention campaigns that led patients to skin self-exam every 3 months and an annual visit to the dermatologist. However, as our cases report, the delay in diagnosis can also arrive to be on the order of several months especially in patients with a low socio-economic class whose compliance tends to be lower and in these locations where the inspection, even self-made, is more difficult.

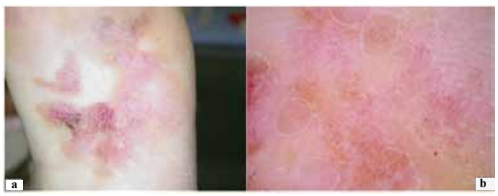

Figure 3: Acral melanoma of the sole with a verrucoid aspect (a). The dermoscopic evaluation revealed the presence of an atypical vascular pattern with residual pigmentation (b).

Figure 4: Amelanotic melanoma of the interdigital site of the foot (a). The dermoscopic evaluation revealed the presence of an atypical vascular pattern with residual pigmentation focally detectable at the periphery (b).

Figure 5: Melanoma of the third and fourth toe treated as a Pseudomonas infection for more than 11 months. Dermoscopic examination reveal an aspecific pattern. (a, clinical presentation; b, dermoscopy).

These patients were reported because of the uniqueness of the presenting symptoms, delayed diagnosis, or because they mimicked another disease entity. The most common misdiagnosed AM cases included wart, callous, bacterial or fungal infection, foreign body, vascular lesion, blister, melanocytic nevus, subungual hematoma, pyogenic granuloma, onychomycosis, keratoacanthoma, diabetic foot ulcer, traumatic lesion. Misdiagnosis and delay in diagnosis are particularly like in cases of amelanotic and hypomelanotic melanoma [10]. The initial misdiagnosis results in delayed appropriate care like cryotherapy or topical fungal medications. In these case reports, the delay of a patient to go to be visited by a physician and the inappropriate diagnosis at first time is important reasons for the significant depth of the melanoma. Other factors that can contribute to this poor prognosis are the particular aggressiveness of AM [11] and the particular anatomic site, not routinely examined by patients or primary care physicians.

The classic ABCD visual signs of melanomas can be difficult to ascertain, however, especially in these cases when acral and nail units are involved. To improve prognosis, early detection is essential. Introduction of dermoscopy was a great epoch in this field. The most important feature detected in the acral melanoma is the parallel ridge pattern (Figure 9a) [2]. This dermoscopic pattern is completely opposite from pigmentation on the furrows seen in acral nevus (Figure 9b) [12]. In early acral melanoma, this pattern covers almost the whole lesion in most cases while in the more advanced tumor the parallel ridge pattern is detected focally within the lesion.

Another dermoscopic pattern seen in acral melanoma is irregular diffuse pigmentation, showing rather structureless, diffuse, brownish-black pigmentation with variable shades, occasionally also associated with grayish tone [13]. This pattern is more frequent in advanced lesion compared with parallel ridge pattern [14].

In much more advanced lesions of acral melanoma, other dermoscopic features seen in advanced melanoma on other anatomical sites are detected, such as irregular dots /globules, irregular streaks, blue-white veil, ulceration and polymorphous vessels. Moreover, the atypical parallel furrow pattern, the atypical lattice-like pattern, and the irregular fibrillar pattern could be focally detected within the lesions of advanced acral melanoma [2].

In 2007, Saida and Koga proposed the three-step algorithm for the management of acquired acral melanocytic lesions [15], introducing a new category with no need of further follow up in 2011 (Table 2) [16]. According to this algorithm, if a lesion presents the parallel ridge pattern, a biopsy is strong recommended. If the lesion does not show this pattern but exhibit a typical benign pattern (typical parallel-furrow, typical lattice-like or regular fibrillar pattern –Figure 9b,c,d) there is no need of further follow up. If the lesion does not show these dermoscopic patterns instead, we consider the maximum diameter: if the lesion is more than 7 mm, we biopsy it, while if it is 7 mm or less, we recommend a periodic follow up. A category with no need of

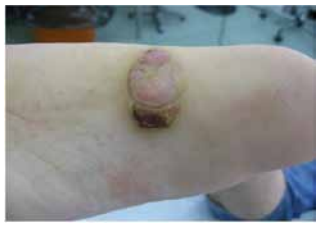

Figure 6: Acral melanoma involving the central and lateral mid arch.

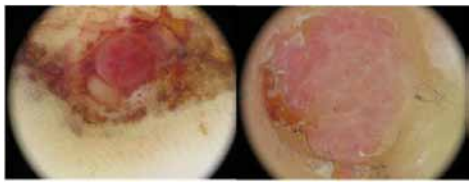

Figure 7: Dermoscopic examination revealed an atypical pattern with residual pigmentation and ulceration in the medial part of the lesion.

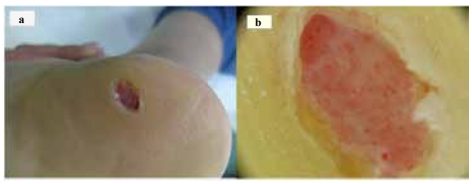

Figure 8: Amelanotic melanoma of the foot resembling an ulcer (a). The resistance to the various treatments and the atypical vascular pattern at the dermoscopy together with a total absence of pigment led us to make a biopsy that confirmed a tumor with a Breslow's depth of 2,1 mm.

further follow up is based on the concept of de novo histogenesis of acral melanoma [12-18].

Anyway in presence of a doubtful acquired acral lesion presenting neither a parallel ridge pattern nor a typical benign dermoscopic pattern that may mimic another disease, we recommend a biopsy independently of its maximum diameter. Mycotic infections may easily exclude in an ambiguous acral lesion with a simple direct microscopic examination of fungal elements. Diagnostic workup of plantar warts and nail-deforming lesions in older patiens, as exemplified in our cases, should include biopsy to exclude a melanoma of the foot [9].

Shave biopsies should be avoided as the thick stratum corneum of acral skin, coupled with the thickened stratum corneum and acanthosis characteristic of acral lentiginous melanoma [19], may result in failure to sample deeper, diagnostic pathology. We warmly suggest excisional or carefully planned incisional biopsies, instead. In the context of a large lesion, we may perform more than a single punch biopsy in those areas, more suspicious of malignancy after a diligent clinical and dermoscopic examination, whose histologic result would be conclusive.

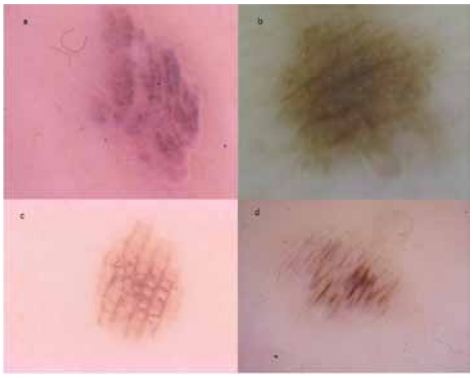

Figure 9: Most common dermoscopic patterns in early acral melanoma and acquired acral nevus. Major dermoscopic pattern of early acral melanoma is the parallel ridge pattern (a). The parallel furrow pattern (b), in which parallel pigmented lines are seen along the furrows of the skin markings, the lattice-like pattern (c), composed of the parallel lines on the furrows as well as of the lines bridging the parallel lines, resulting in a lattice-like pigmentation, and the fibrillar pattern (d), formed by densely packed fine fibrillar pigmentation arranged in the direction crossing the parallel skin markings, are typical of acral nevi.

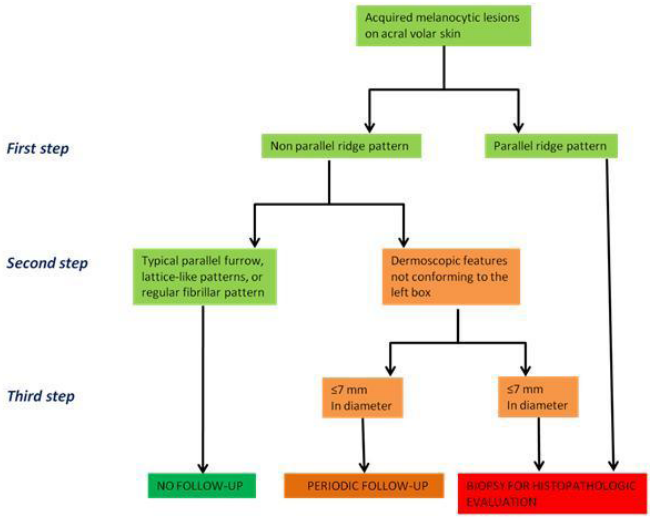

Table 2: Saida's three-step algorithm for the management of acquired acral melanocytic lesions 16.

Associated diseases often found in the ederly patient, such as diabetes, arterial disease, and venous insufficiency, can complicate the biopsy. Elderly patiens can also have a difficult time performing postoperative care to a biopsy site on the foot, increasing the risk of infection. Moreover nail unit biopsies can result in permanent structural changes, matrix involvement can result in absence or splitting of the nail plate, and nail bed excisions can result in onycholysis leading to fungal infections and partial tears of the nail plate.

Obviously, patient education expecially in men older than 50 years about the existence of acral melanoma and regular skin surveillance remain headstones of secondary prevention [20,21]. Awareness that atypical presentations of acral melanoma may thus increase the rate of correct diagnosis and improve patient outcome for this potentially curable disease at its early stages.

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