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Acral lentiginous melanoma in the Turkish population and a new dermoscopic clue for the diagnosis

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ABSTRACT

Background: The incidence of acral lentiginous melanoma (ALM) in the white population is low. Dermoscopy enhances diagnosis of ALM; however, diagnostic accuracy may sometimes be poor due to the considerable proportion of amelanotic ALM variants.

Objectives: To calculate the proportion of ALM among all melanoma subtypes and to determine the frequency of dermoscopic features of ALM in the Turkish population.

Methods: Out of 612 melanomas, there were 70 cases of ALM, of which 46 showed sufficient image quality for retrospective study of dermoscopic features. Data from patients and their lesions was classified according to clinical features and histopathologic parameters. The dermoscopic variables evaluated were based on pertinent literature on dermoscopy of acral melanocytic neoplasms.

Results: The prevalence of ALM among all melanoma subtypes was 11.4%. Parallel-ridge pattern (PRP) was detected in 60.8% of cases and irregular diffuse pigmentation (IDP) in 28.3%. The ALMs were amelanotic in 24%, showing an atypical vascular pattern in all cases; a new dermoscopic pattern, named "vascularized parallel-ridge pattern" (VPRP), was detected in 13% of ALMs. Irregular lines were observed in 81.8% of subungual melanomas and were often associated with a multicolored background.

Conclusions: ALM has site-specific dermoscopic patterns, with PRP being the most prevalent pattern. The newly described VPRP pattern may be an additional clue for ALM diagnosis, especially in thin amelanotic melanomas.

Background

Acral lentiginous melanoma (ALM) accounts for 2-8% of all melanomas in Caucasians [1-3], 15% to 35% in dark-skinned [4-7], and up to 60% in Asians [8]. The nail unit or subungual melanoma, an anatomical variant of ALM, is even less frequent, accounting for 1-2% of all melanomas in white population [9-12] and 10-20% in Asians [13,14]. "Lentiginous" relates to a histopathologic pattern of proliferation of melanocytes along the dermoepidermal junction (DEJ) as single cells and small nests with areas of confluent growth, although not all acral melanomas display this specific pattern [15]. Of acral melanomas, ALM is the most prevalent histopathologic subtype (40%-80%) [16-18].

Due to the low incidence of ALM, clinical experience is limited to specialized centers. Moreover, the atypical clinical presentation and relatively high frequency of amelanotic variants are seen among ALMs. As a result, delayed diagnosis or misdiagnosis may lead to detection of ALM at a more advanced stage with poor prognosis [15].

Dermoscopy increases the diagnostic accuracy for early ALM diagnosis, helping to differentiate it from acral nevi [19-23]. ALM is typified by pigmentation along the skin ridges, termed "parallel-ridge pattern" (PRP), while acral nevi display mostly the "parallel-furrow pattern" (PFP) [24-28]. Among ALMs, other dermoscopic patterns include the irregular diffuse pigmentation (IDP), defined as structureless, diffuse pigmentation with variable shades of brown to black color and without parallel disposition of pigment [22-24,28]; the multicomponent pattern, defined as exhibiting more than one predominant dermoscopic criteria [29] or a combination of pigmentation patterns [30]; and the polymorphic vascular pattern that is especially seen among amelanotic acral melanomas.

The aim of the present study was to calculate the proportion of ALM among all melanoma subtypes and to determine the frequency of dermoscopic features of ALM in the Turkish population.

Methods

All melanoma cases between 2005 and 2014 were identified retrospectively from the archive of the Dermato-Oncology Unit, Department of Dermatology of Ege University, Izmir, Turkey. Our institution did not require an Ethics Committee approval for this retrospective study of dermoscopic images. For all cases included in the study, the diagnosis of ALM was based on the histopathologic report. Images of all cases of ALM were reviewed; we excluded cases that lacked a dermoscopic image of the primary lesion or when image quality was insufficient for evaluation of pattern.

Dermoscopic pictures were taken prior to biopsy or excision using a polarized light immersion dermoscopic camera (DermLite Foto System, 3Gen, San Juan Capistrano, CA, USA) with oil immersion. In selected cases, we obtained additional images of normal appearing skin around the lesions or at the contralateral acral site.

The clinical and dermoscopic images of all included ALM cases in were analyzed independently by two authors (FO and IK). Clinical data included age, gender, and anatomic distribution. Histopathologic parameters included Breslow tumor thickness and Clark's level of invasion. The dermoscopic variables evaluated were based on pertinent literature on dermoscopy of acral melanocytic neoplasms [22,23,25-28,30,31]. In nail apparatus melanomas, we also analyzed the pattern of involved periungual skin.

Results

There were 612 cases of melanoma in our database. Of these, 70 (11.4%) were diagnosed as ALM. The patients' mean age was 61.2 (range 16-88), and 38 (54.3%) were females. Eighty percent (n=56) of melanomas were located on the feet (50 on plantar surfaces and 6 in toenails) and 20% on hands (5 on palmar surfaces and 9 in fingernails). The mean Breslow thickness was 3.84 mm; 14.3% (n=10) were classified as in situ melanomas, 11.4% (n=8) were <1 mm, while 74.3% were thick melanomas (Breslow thickness 1-2 mm in 7 patients; >2-4 mm in 23 patients; >4 mm in 22 patients). The majority of melanomas (47.1%; n=33) exhibited Clark's level IV.

Of acral melanomas, we analyzed the dermoscopic features in 46 melanomas with sufficient image quality (Table 1). Among global features, PRP was seen in 60.8%, IDP was seen in 28.3%, and multicomponent pattern in 47.8%. Among focal dermoscopic patterns, most frequent were the irregular fibrillar pattern (IFP) in 34.8% and PFP in 30.4%. Among dermoscopic findings described in melanoma on non-glabrous skin, an abrupt edge was seen in 34.8%, irregular streaks in 32.6%, and blue-whitish veil (BWV) in 30.4%. Most lesions (76.1%) showed multiple colors, 52.2% exhibited atypical vessels, and 39.1% showed ulceration.

We observed a new dermoscopic feature in 13.0% (n=6) of the melanomas, termed henceforth as "vascularized parallel-ridge pattern" (VPRP). This new dermoscopic finding is defined as "erythema and dotted vessels filling the ridges and sparing the sulci" (Figures 1-5).

Of ALMs, 24% were amelanotic melanomas, including 4 non-pigmented melanomas and 7 hypopigmented with some remnants of pigmentation under dermoscopy. Atypical vessels were observed in all lesions, with dotted vessels being most common (72.7%, Figure 6). Of amelanotic melanomas, 4/11 (36.4%) showed the VPRP pattern (Figures 1-3).

TABLE 1. Dermoscopic patterns found in our 46 cases of acral lentiginous melanomas (ALM), including involvement of periungual skin in nail apparatus melanoma.

Dermoscopic Patterns	Number of ALM (n, total= 46)	Percentage of ALM (%)
Parallel-ridge pattern (PRP)	28	60.8
Irregular diffuse pigmentation (IDP)	13	28.3
Other patterns:		
Multicomponent	22	47.8
Polymorphic vascular	5	10.9
Starburst	1	2.2
Parallel-furrow (focal)	14	30.4
Irregular fibrillar (focal)	16	34.8
Lattice-like (focal)	1	2.2
Reticular (focal)	2	4.3
Homogeneous (focal)	1	2.2
Non-typical	0	0
Negative fibrillar	5	10.9
Abrupt edge	16	34.8
Irregular dots and globules	13	28.3
Irregular streaks	15	32.6
Homogenous area	11	23.9
Irregular blotch	6	13
Blue-white veil	14	30.4
Scar-like depigmentation	11	23.9
Peppering or grey dots	3	6.5
Ulceration	18	39.1
Atypical vessels	24	52.2
Multiple colors	35	76.1
Vascularized PRP	6	13

Of nail unit melanomas, 11 of 15 cases (73.3%) showed adequate dermoscopic image quality for evaluation. Hutchinson's sign (i.e., pigmentation of the periungual skin) was detected in all cases. The mean Breslow thickness was 1.73 mm and 2 cases were in situ (18.2%). *Melanonychia striata longitudinalis* (MSL), i.e. a pigmented band of the nail plate, was observed in 9 cases (81.8%); however, the bands were comprised of irregular lines with respect to their color, thickness, spacing and parallelism (Figures 7-8). Nail plate dystrophy was seen in 7 cases (64%, Figure 9). The most prevalent dermoscopic feature corresponded to irregular lines (81.8%) and multicolored background (72.7%) (Table 2).

Discussion

In our series, the prevalence of ALM among the melanomas was 11.4%, in contrast to the reported prevalence among Caucasians of 2-8% [1-3]; this slightly higher prevalence may be related to Turkish ethnicity.

The most prevalent dermoscopic pattern in our series was the PRP, seen in 60.8% of ALMs, and in line with previous studies. Saida et al, who first described PRP [25], found this pattern in 86% of cases, with sensitivity and specificity of PRP for ALM diagnosis being 86.4% and 99%, respectively [23]. Likewise, Thomas et al [31] and Argenziano et al [29] have reported that PRP was detectable in 53% and 65.3% of their cases. IDP has been reported as the second most common dermoscopic pattern of ALM; it is more suggestive of invasive melanoma [19,21,23,31]. In our study, IDP was found in 28.3%. The prevalence of IDP reported in the literature is variable: Argenziano et al reported 13.6% [29], Braun et al reported 20.5% [30], Thomas et al 60% [31] and Saida et al 85% [23]. We speculate that IDP is seen in lower frequency in thicker melanomas, as notably 60% of ALMs in our series reached Clark's level IV and V. With regard to other acral patterns, a benign pattern such as PFP can be observed at times [30] but only focally and always together with melanoma-specific criteria. Multicomponent pattern (47.8%) and IFP (34.8%) were the other most prevalent patterns, as expected, in the literature [19]. Additional melanoma-specific criteria, seen in melanomas on non-glabrous skin [32,33]—including abrupt edge, irregular dots and globules (D/G), streaks, and blue-whitish veil (BWV)— were observed in one-third of our series; in addition, the high frequency of ulceration (40%), atypical vessels (>50%), and notably multiple colors (76%) are again attributable to the high proportion of thick melanomas in our series [19].

About one-fifth of cases were nail unit melanomas mainly exhibiting an irregular MSL pattern, with variability in lines, color, thickness, spacing and parallelism, in addition to Hutchinson's sign seen in all cases. Notably, the usual finding of brown background, as previously reported by Thomas et al [31], was replaced by a multicolored background in most of our cases (73%); we find this to be a useful diagnostic clue.

About one-quarter were amelanotic melanomas, in line with the previous reported frequencies by Thomas et al (28%-34%) [31], and Kato and coworkers (19.6%) in the Japanese population [34]. Furthermore, all melanomas exhibited atypical vessels, and in fact, the lack or scarcity of pigmentation allowed a clear visualization of the dermoscopic vascular pattern. Argenziano et al found that dotted vessels were detectable in 22.7% of melanomas, while erythema (defined as pinkish color within areas of regression or at the border of the lesion) was combined with different types of vessels in 43/159 melanomas [35]. Erythema was also slightly more prevalent among in situ melanomas, compared with invasive

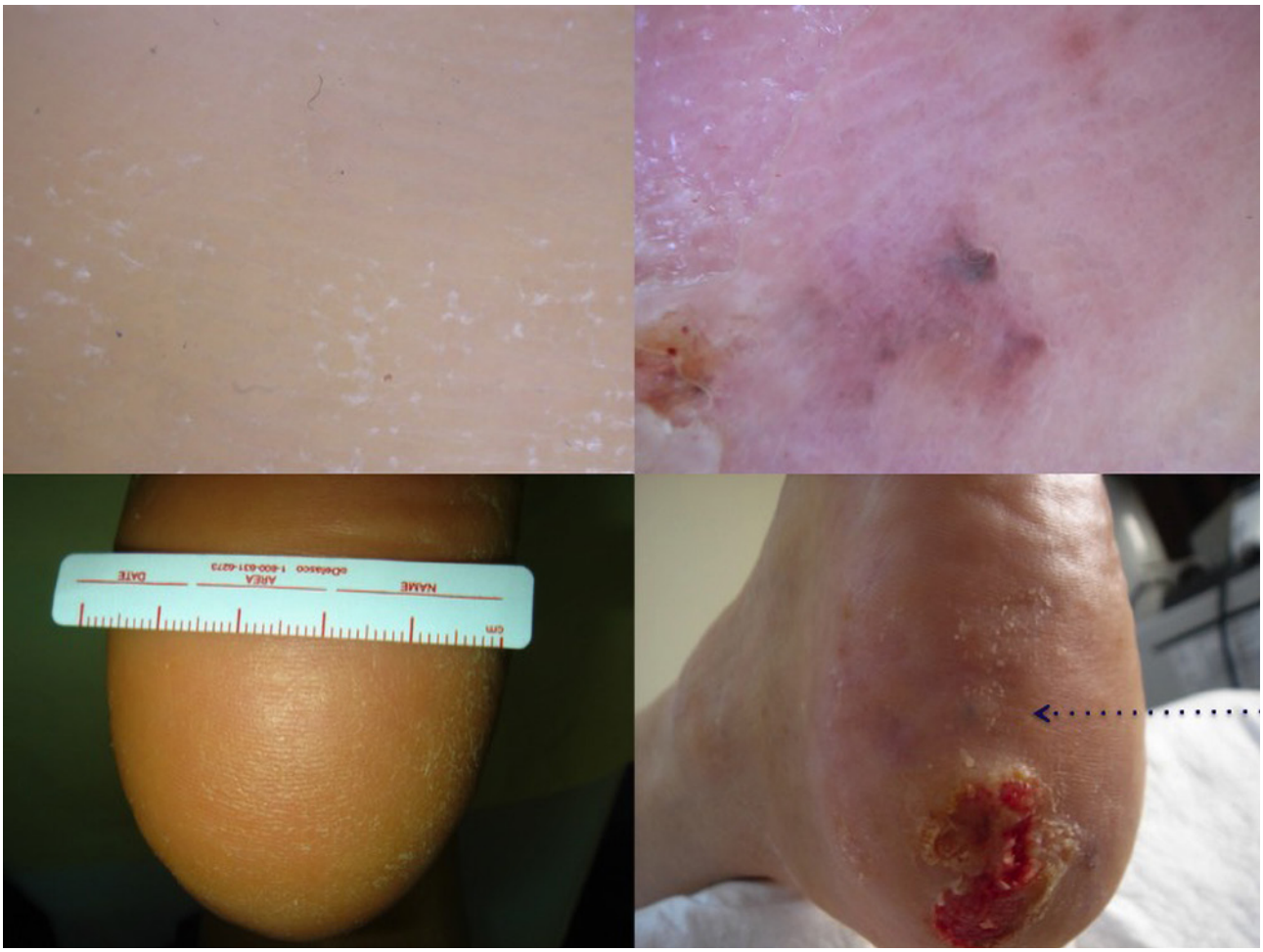

Figure 1. Vascularized parallel-ridge pattern (VPRP). Acral lentiginous melanoma, Breslow 3.3 mm, Clark III. At dermoscopic evaluation, presence of erythema and some dotted vessels on the ridges, sparing the sulci (right). No erythema is detectable on the other healthy sole (left). [Copyright: ©2018 Ozdemir et al.]

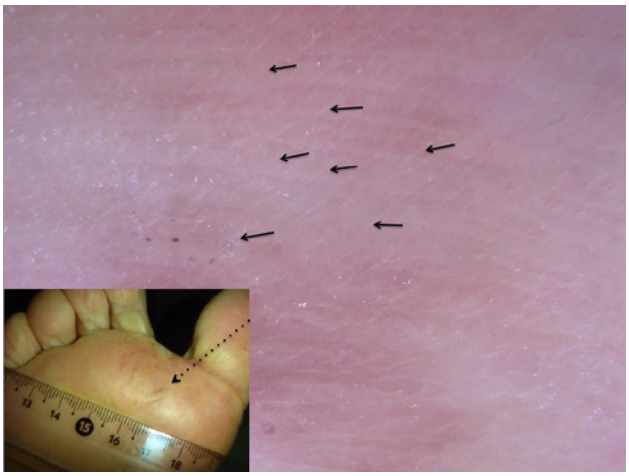

Figure 2. Vascularized parallel-ridge pattern (VPRP). Acral lentiginous melanoma, Breslow 0.8 mm, Clark II. Evidence of erythema and few dotted vessels on the ridges, together with negative fibrillary pattern; white lines corresponding to eccrine ducts in the horny layer are seen throughout the lesion (arrows). [Copyright: ©2018 Ozdemir et al.]

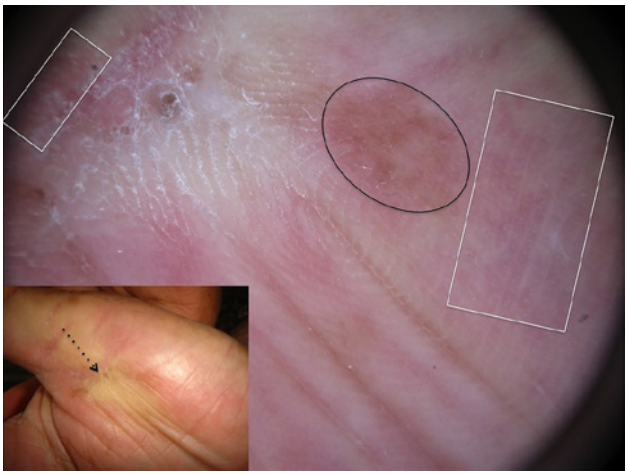

Figure 3. Parallel-ridge pattern (PRP) and vascularized PRP (VPRP). Recurrent, in situ, acral lentiginous melanoma (original lesion was ALM, Breslow 2.5 mm, Clark IV). Both patterns are detectable side-by-side (PRP in circle, VPRP in rectangles). [Copyright: ©2018 Ozdemir et al.]

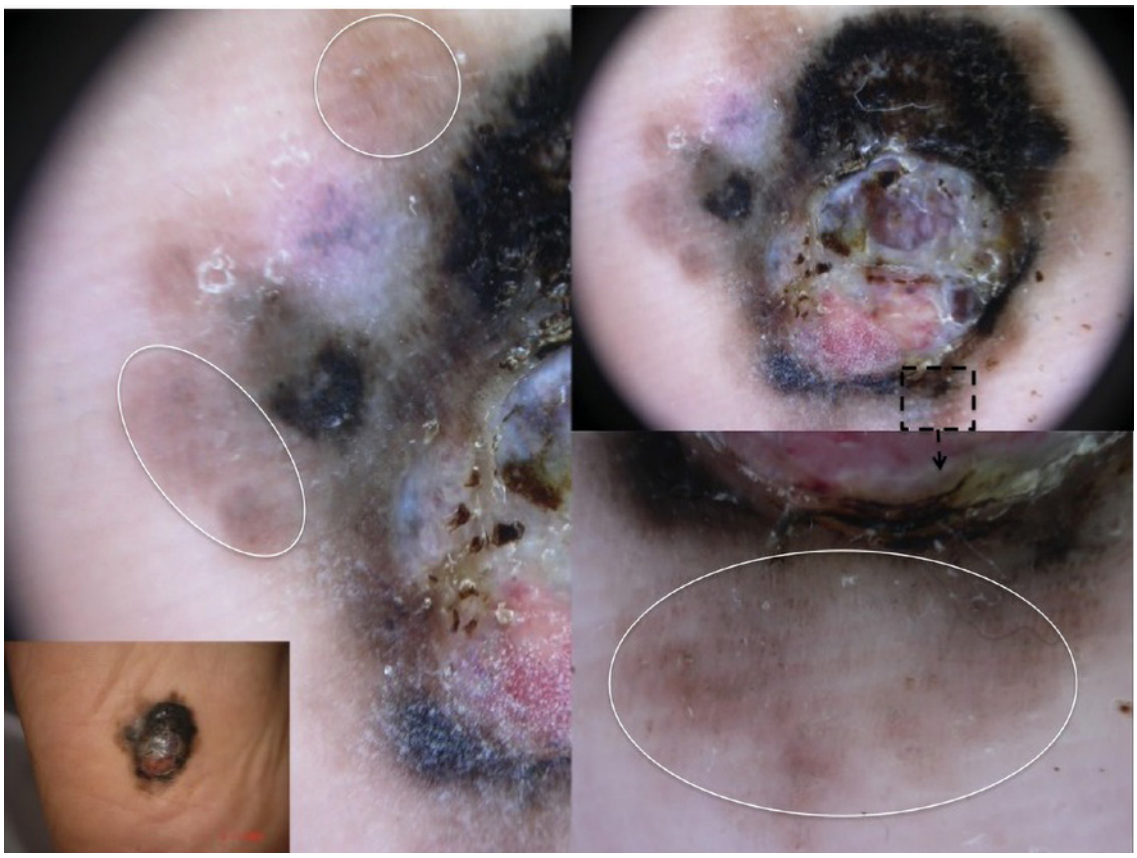

Figure 4. Vascularized PRP (VPRP). Acral lentiginous melanoma, Breslow 4.39 mm, Clark IV. VPRP (in circles) is detectable along with remnants of pigmentation and gray dots. [Copyright: ©2018 Ozdemir et al.]

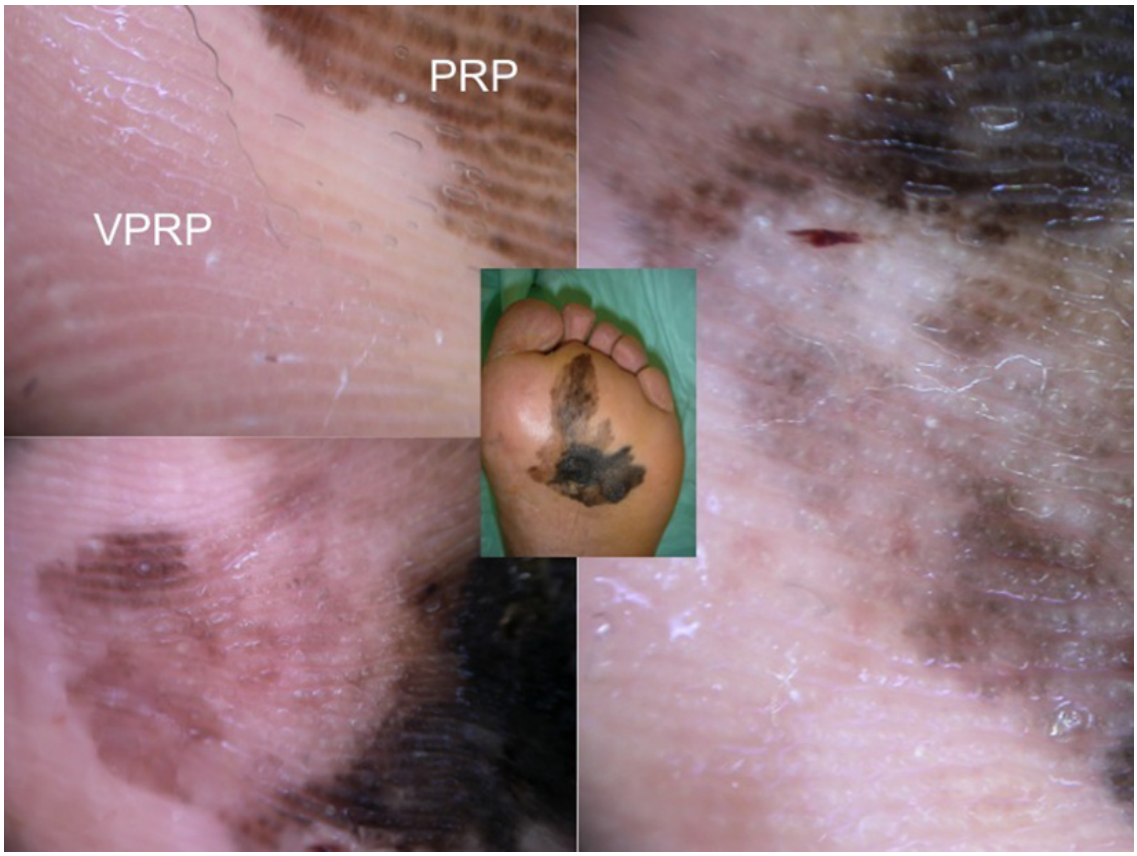

Figure 5. Parallel-ridge pattern (PRP) and vascularized PRP (VPRP). Acral lentiginous melanoma, Breslow 2.26 mm, Clark IV. Both patterns are seen side-by-side (top left) and intermingled with each other (bottom left and right). [Copyright: ©2018 Ozdemir et al.]

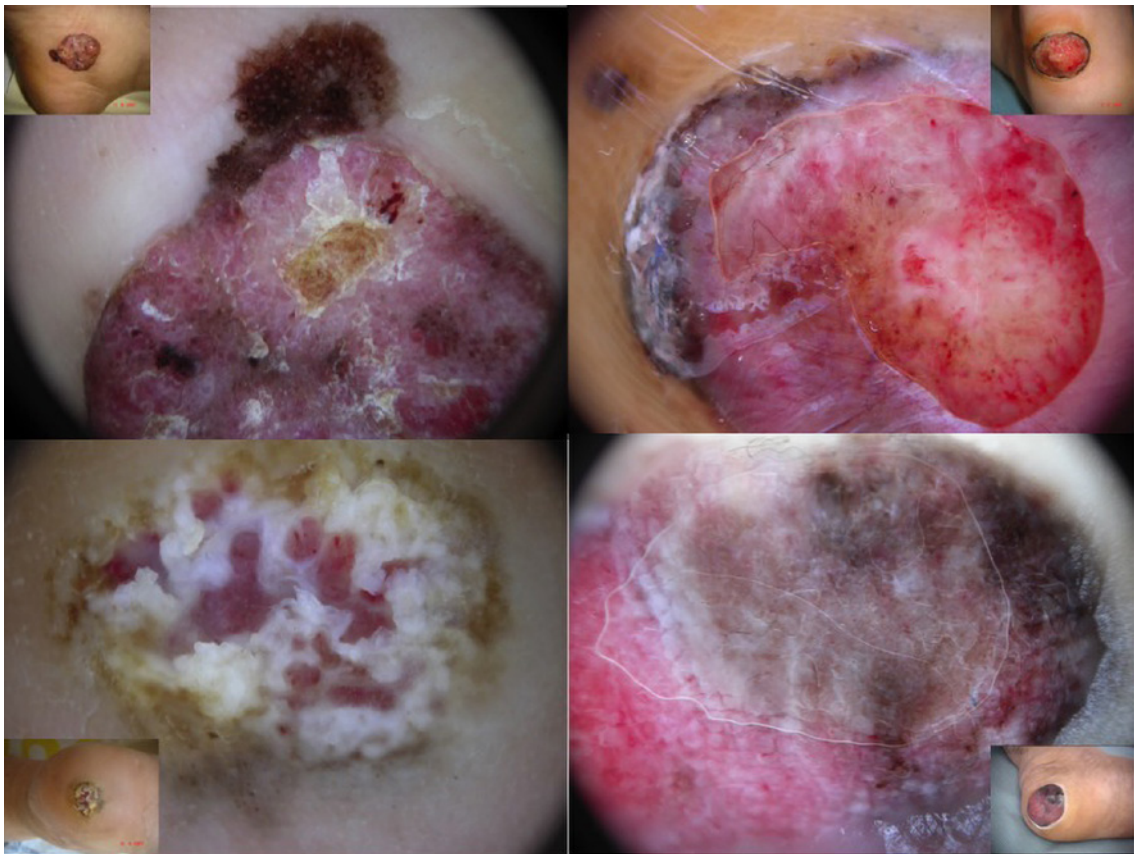

Figure 6. Examples of amelanotic melanomas showing remnants of pigmentation and atypical vessels on dermoscopy. [Copyright: ©2018 Ozdemir et al.]

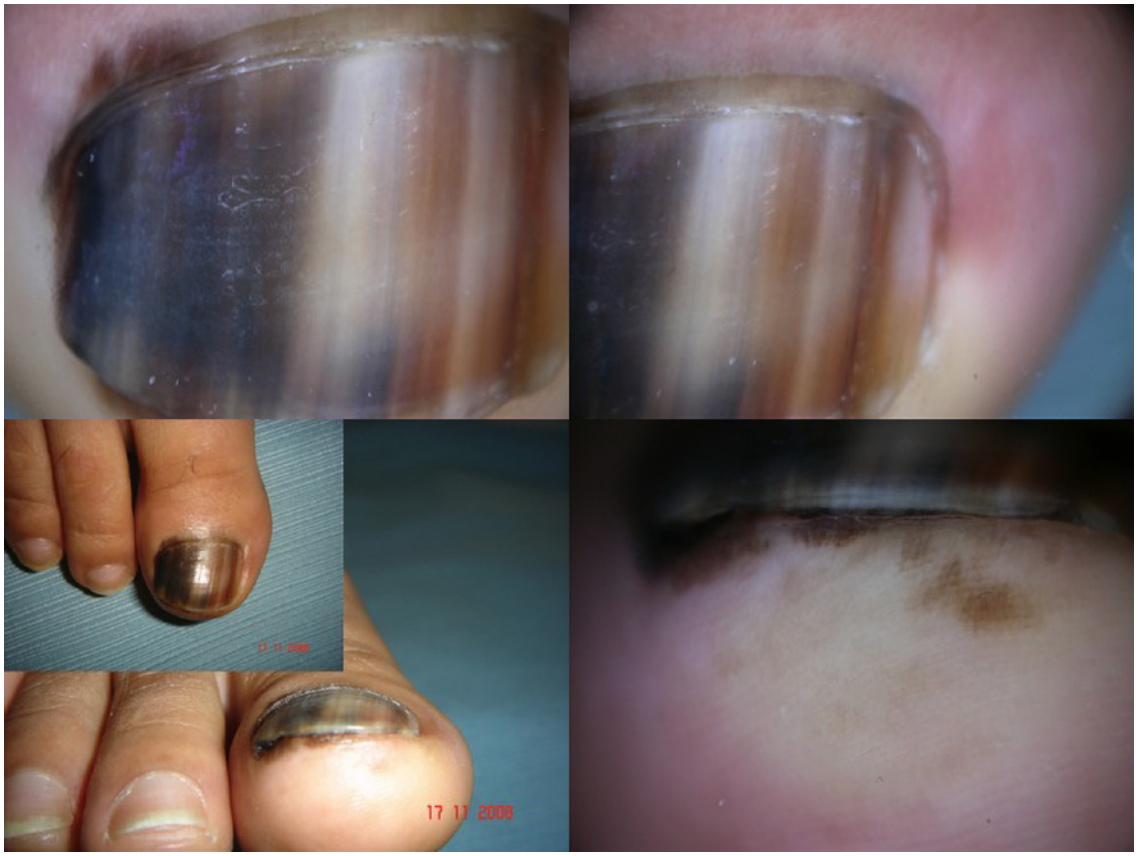

Figure 7. Nail unit melanoma dermoscopic features. Breslow 0.9 mm, Clark III. The longitudinal bands show irregular colors and lack of parallelism. Hutchinson's sign is detectable at clinical inspection. [Copyright: ©2018 Ozdemir et al.]

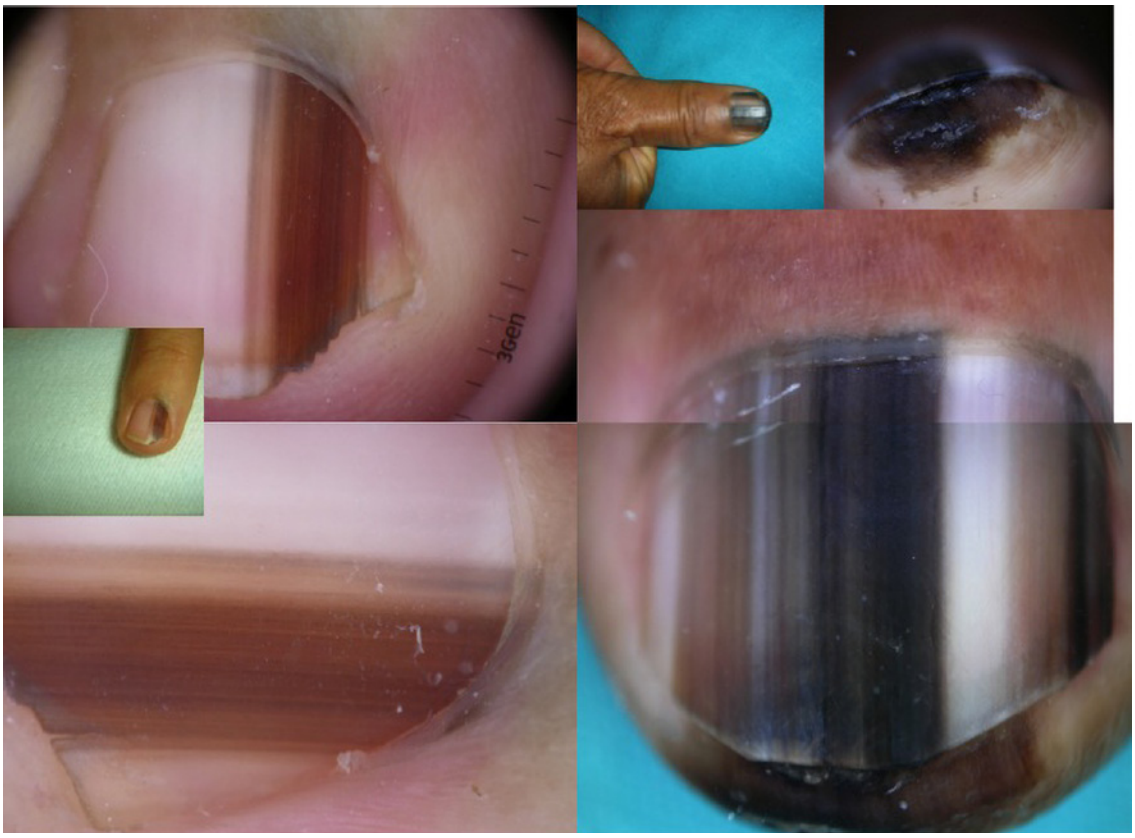

Figure 8. Nail unit melanoma dermoscopic features. Two in situ melanomas. The lines are irregular in thickness and spacing. [Copyright: ©2018 Ozdemir et al.]

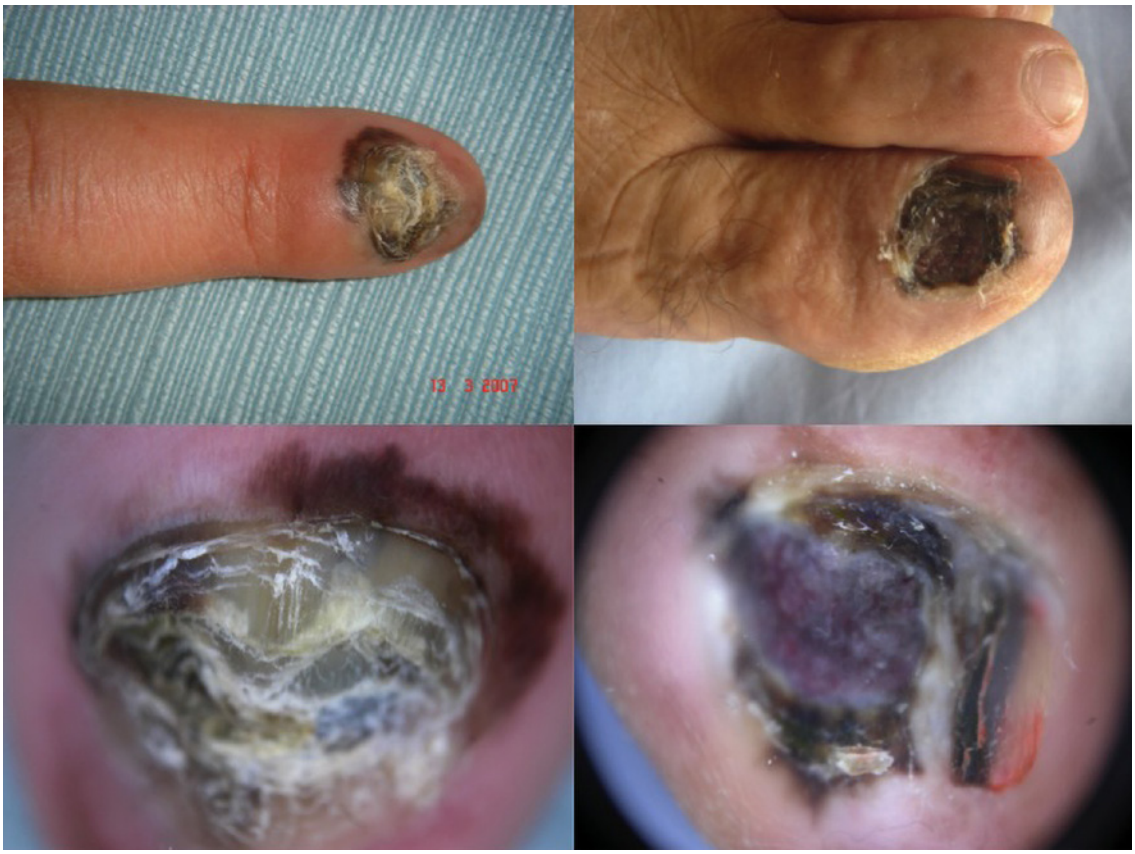

Figure 9. Nail unit melanoma dermoscopic features. (On the left) Breslow 2.7 mm, Clark III. (On the right) Breslow 3.2 mm, Clark IV. Both show nail plate dystrophy. Triangular shape of the band and microhemorrhage are detectable on the right. [Copyright: ©2018 Ozdemir et al.]

TABLE 2. Dermoscopic patterns of nail unit melanomas.

Dermoscopic Patterns	Number of Subungual Melanomas (n, total = 11)	Percentage of Subungual Melanomas (%)
Multicolored background	8	72.7
Brown background	3	27.3
Irregular lines	9	81.8
Blood spots	6	54.5
Linear microhemorrhages	2	18.2
Triangular shape of the band	1	9
Micro-Hutchinson's sign	0	0

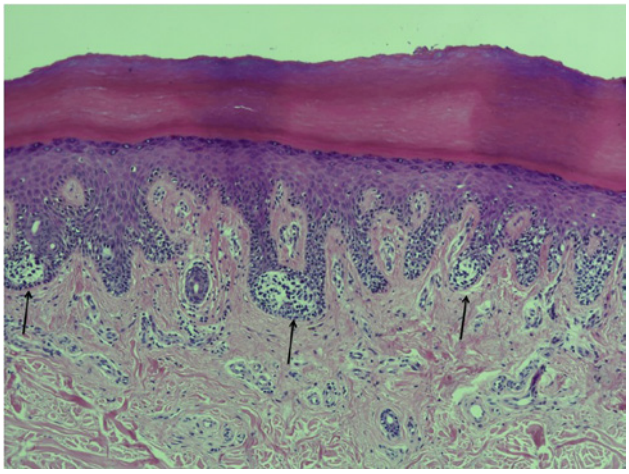

Figure 10. Histopathologic section of periphery of acral melanoma shown in Figure 2. Breslow 0.8 mm, Clark II. Proliferation of non-pigmented cells may be identified around crista intermedia (arrows). Hematoxylin and eosin (H&E) staining (original magnification x100). [Copyright: ©2018 Ozdemir et al.]

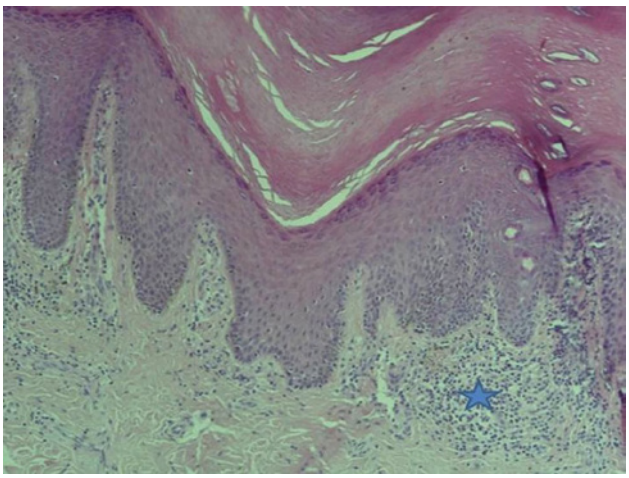

Figure 11. Histopathological section of periphery of acral melanoma shown in Figure 5. Breslow 2.26 mm, Clark IV. Prominent vascular proliferation (asterisk) is detectable around crista intermedia/eccrine ducts, compared to other parts. H&E staining (original magnification x100). [Copyright: ©2018 Ozdemir et al.]

melanomas [35]. Steglich et al stated that melanoma initially shows dotted vessels and that with greater thickness, vascular polymorphism increases, with hairpin and linear-irregular vessels associated with milky-red areas. Dotted vessels may be the only clue to suspect non-pigmented melanoma [36]. Similar to thin amelanotic melanomas on non-glabrous skin showing only dotted vessels under dermoscopy, VPRP may be an important alerting sign for early diagnosis of ALM.

Melanoma cells, mostly among in situ melanomas, tend to cluster around the crista intermedia, leading to pigmentation on the ridges, seen as PRP on dermoscopy [22]. This may be due to the tendency, shown by melanocytic stem cells generating melanoma, to reside, at the beginning, near the crista intermedia or the eccrine ducts. On the other hand, in deeply invasive melanomas, tumor cells tend to diffusely proliferate with a similar intensity in both crista intermedia and crista limitans [22]. Since vascularization and inflammation is likely to be greater where the neoplastic melanocytes proliferate, we reason that in amelanotic cases, the increased vasculature will be most prominent along the same region, namely, the crista intermedia (Figure 10). This will manifest under dermoscopy as erythema and dotted vessels on the ridges, along the crista intermedia areas, accounting for the dermoscopic feature described herein as VPRP (Figure 11). In pigmented ALM, melanin obscures the increased vascularization leading to the PRP pattern. This is best seen in hypopigmented melanomas, whereby PRP in the lightly pigmented and VPRP in the amelanotic areas can both be seen.

Conclusion

In conclusion, we found that ALMs in Turkish patients display similar dermoscopic patterns as reported in other populations, with PRP being the most frequent. A lower incidence of IDP pattern may be related to the higher mean thickness of melanomas in our series. A newly described dermoscopic pattern, VPRP, may be important for the diagnosis of thin amelanotic ALMs. However, the significance of this dermoscopic feature needs to be validated in larger series.

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