

# Verrucous melanoma: differences and similarities between primary and secondary varieties

Daniel Feinsilber<sup>1</sup>, Nora Kogan<sup>2</sup>, Olga Matilde Rosati<sup>3</sup>, Cristina Corbella<sup>4</sup>, Roberto Schröh<sup>5</sup>, Ignacio Calb<sup>6</sup>

## Abstract

Verrucous melanoma (VM) is an extremely rare variety that may develop on any clinical type of melanoma (secondary VM), or be a primary type. This implies differences and similarities. From January 1991 to September 2007 we studied 526 patients who developed 545 melanomas, and found 4 (0.7 percent) primary VM and 6 (0.9 percent) secondary VM. Both affect men and women equally. Mean age of patients of primary type was 37.7 years, with the head as main site of location. Mean age of patients of secondary type was 40.1 years, most often located on limbs. Primary VM is an exophytic tumor that has a better prognosis if detected in *in situ* or microinvasion stage, and requires less aggressive treatment. Diagnosis is difficult because it mimics seborrheic keratosis or pigmented verrucous nevi (Dermatol Argent 2009; 15(2):106-110).

**Key words:** primary and secondary verrucous melanoma.

## Introduction

Verrucous melanoma (VM) is an extremely rare variety that may develop on any conventional clinical type of melanoma (lentigo maligna melanoma, LMM; superficial spreading melanoma, SSM; nodular melanoma, NM; acral lentiginous melanoma, ALM) or be a primary type, that is, totally *de novo*. This implies differences and similarities in clinical, pathological, evolutive, and therapeutic aspects, because when appearing on a part of any of the various clinical forms of melanoma (secondary VM) it has no incidence on prognosis, which is essentially related to the Clark level and the Breslow thickness detected in the exo-endophytic invasion. In contrast, in the *de novo* variety it is generally an exophytic tumor diagnosed in *in situ* or at microinvasion stages, with a more favorable prognosis and a less aggressive therapeutic. In the latter case, difficulties arise with diagnosis, since they mimic seborrheic keratosis and pigmented verrucous nevi, mainly located on legs and cheeks; this location is typical in young women with phototypes IV or V. Therefore, early diagnosis is of utmost importance, with a 95 to 100 percent healing probability. The purpose of this work is to establish differences and similarities between primary and secondary verrucous MM on the above mentioned aspects.

## Material and methods

In the Dermatology Department Oncology Section of Hospital Ramos Mejía we conducted a retrospective study of all malignant melanoma (MM) cases studied between January 1991 and September 2007. Included were 526 patients who

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1. Staff Physician. Head of Oncodermatology and Dermatology Surgery Section of the Dermatology Department, Hospital "J. M. Ramos Mejía". Authorized Teacher UBA.
2. Staff Physician. Adjunct Teacher UBA.
3. Attending Physician.
4. Staff Physician, Pathology Department.
5. Staff Physician. Head of Dermopathology Section. Authorized Teacher UBA.
6. Head of Pathology Department, Hospital Piñeiro.

## Correspondence

Daniel Feinsilber: Av. Entre Ríos 655 2º B, (1080) Autonomous City of Buenos Aires, Argentine | Republic. Ph. 4381-9159 | dafeinsilber@gmail.com

developed 545 melanomas, whereof 4 (0.7 percent) were primary or *de novo* VM (Table 1), and 6 (0.9 percent) were secondary VM (Table 2). These patients with histopathological diagnosis of VM were evaluated according to gender, age, lesion location, clinical aspects, histoprognosis factors, therapeutic behavior, and evolution.

## Results

In this case-control study we observed that both *de novo* and secondary VM equally affect male and female. In the former, age range was 17 to 58 years, with a mean of 37.7 years, while in the latter, age range was 16 to 72 years with a mean of 40.1 years. *De novo* VM was located on the head, cheek and ear in two cases, and the other two appeared one on the back and the other on an upper limb (arm). Secondary VM was distinctive for the limb location in the four cases.

Evolution time at consultation was from 3 months to 3 years (mean 17.7 months) in *de novo* VM, and from 6 months to 2 years (meand 14.3 months) in secondary VM.

Follow-up time after surgical treatment was from 3 to 16 years in *de novo* VM, with 75 percent survival, while in secondary VM it was from 2 to 8 years with 100 percent survival. In the first group, the patient with late diagnosis of the lesion (>3 years of evolution) (case 2) died with 3 years survival after surgical treatment. In the secondary VM group, follow-up could not be performed in one patient, because he returned to his country of origin (case 8).

Of the verrucous melanomas, both *de novo* and secondary, 50 percent developed on a congenital me-



**Figure 1.** Female, aged 43, cheek, 2 years' evolution. Clinical diagnosis: seborrheic keratosis. Histopathological diagnosis: verrucous MM, level I.

lanocytic nevus as verified by reference of the patient and/or third parties, previous photos, or histologically.

## Comments

In 1967, Clark<sup>1</sup> mentions four clinical forms of melanoma, that is: superficial spreading melanoma (SSM), lentigo maligna melanoma (LMM), verrucous melanoma (VM) and nodular melanoma (NM). In this revision, he identifies the difficulties of histologic diagnosis of VM, and refers a higher frequency of VM developing on SSM, without differences of gender, and with a mean age of 55 years. Two years later, Clark points out that

**TABLE 1.** DE NOVO VERRUCOUS MELANOMA.

Case	Sex	Age	Location	Presumptive diagnosis	Histopatologic diagnosis - level - thickness	Evolution time	Follow-up
1	M	17	Ear	CMN	VM - II - 2.6 mm (Figures 2 and 3)	8 months	4 years
2	M	58	Back	SSM	VM - III - 1.5 mm	> 3 years	† 3 years
3	F	43	Cheek (Figure 1)	SK	VM - I - in situ	2 years	3 years
4	F	33	Arm	CMN	VM - I - in situ	3 month	16 years

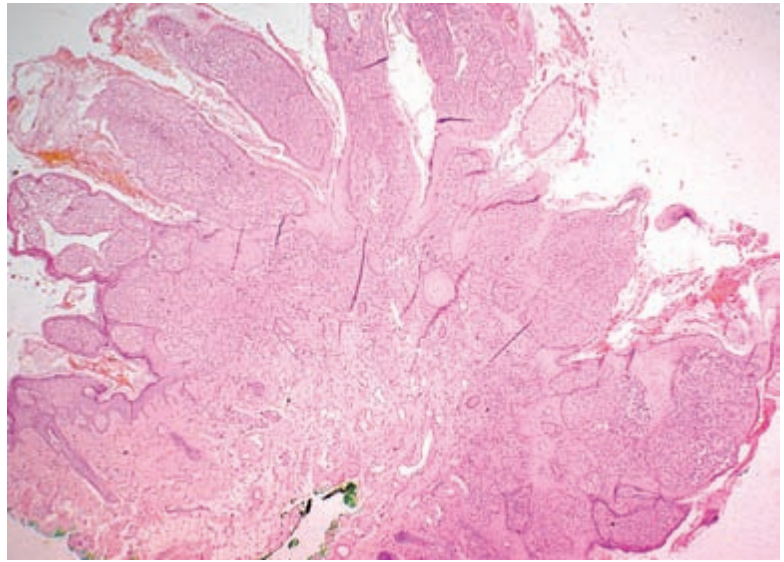
CMN: congenital melanocytic nevus. SSM: superficial spreading melanoma. SK: seborrheic keratosis. VM: verrucous melanoma.

**TABLE 2.** SECONDARY VERRUCOUS MELANOMA.

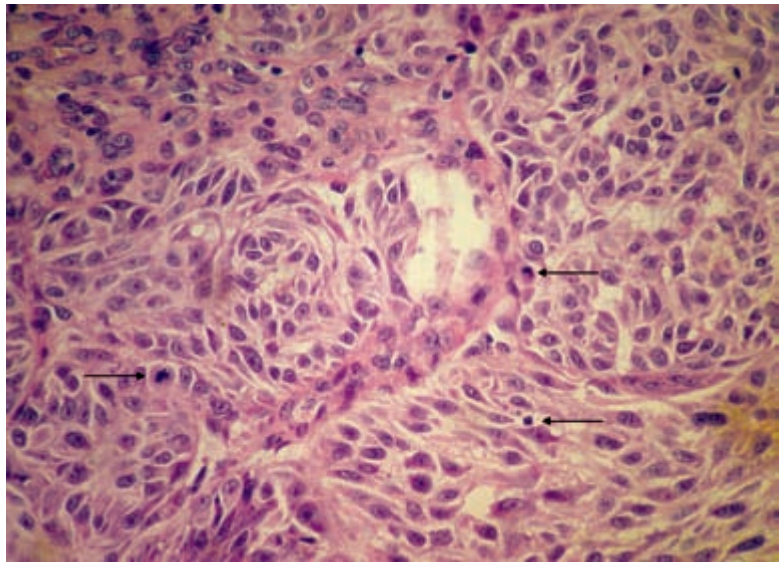
Case	Sex	Age	Location	Presumptive diagnosis	Histopatologic diagnosis - level - thickness	Evolution time	Follow-up
5	M	53	Leg	SSM	SSM - III - 1.47 mm	6 months	3 years
6	F	35	Leg	SSM	SSM - III - 1.31 mm	2 years	4 years
7	F	16	Foot	ALM	ALM - V - 8 mm Neurotropism	2 years	4 years
8	M	72	Foot	ALM (Figure 4)	ALM - IV - 2.6 mm (Figure 5)	8 months	-
9	F	38	Back	MN	NM-IV - 5.5 mm	1 years	2 years
10	M	27	Neck (Figure 6)	SSM CMN	SSM-II - 0.73 mm (Figure 7)	1 years	8 years

SSM: superficial spreading melanoma. ALM: acrolentiginous melanoma. NM: nodular melanoma. CMN: congenital melanocytic nevus.

any melanoma, except nodular, may develop verrucous parts, thus deleting VM from the classification, and including acral lentiginous melanoma (ALM). In 1968 Abulafia and Grinspan<sup>2</sup> report as “atypical melanoacanthoma” what later should be known as verrucous melanoma. These authors mention the verrucous and pigmented feature of lesions, which appear mainly on the head (face and scalp) of both sexes and may be diagnosed as pigmented seborrheic keratosis, pigmented basal cell carcinoma, or pigmented nevus. They report two female cases aged 60 and 69 with lesions of verrucous aspect located on the skin of upper lip and cheek measuring 15 and 10 mm in diameter, respectively, and clinically diagnosed the first as seborrheic keratosis and the second with differential diagnosis of melanoma, seborrheic keratosis, and basal cell carcinoma. Histologically, both lesions were characterized by being acanthomatous, hyperkeratotic, and papillomatous circumscribed hyperplasia, with the presence of atypical melanocytes, which in the first case only involved epidermis, thus being an *in situ* VM. The second case the lesion invaded the papillar dermis, thus referring to a Clark level II microinvasive VM. In 1980, Schwartz et al.<sup>3</sup> published two cases of SSM with verrucous areas, and insisted on providing identity to this clinical variant; they referred that the Breslow thickness of VM depends in part on the extent of epidermal acanthosis and papillomatosis. In 1982, Kuehl-Petzoldt et al.<sup>4</sup> differentiated for the first time the clinical forms of melanomas with verrucous areas from *de novo* verrucous melanoma, which they called *in sensu strictu* (ISSVM). These authors examined 1108 melanomas, whereof 101 were verrucous. Of these, 35 percent were SSM, 28 percent were ISSVM, 25 percent were NM, 6 percent were LMM, 3 percent were non-classified, 2 percent were ALM, and 1 percent was *in situ*. *In sensu strictu* VM is clinically described as uniformly brown or black lesions, generally on limbs and not ulcerated, which histologically do not show Pagetoid pattern of neoplastic cells in epidermis, with dermoepidermal nests and solitary atypical melanocyte hyperplasia in the basal layer of epidermis. They found a slightly better prognosis for verrucous melanomas in general, but deemed such difference as non-significant. In 1988, Steiner et al.<sup>5</sup> reported five cases of MM (4 SSM and 1 LMM) with verrucous areas, stressing the importance of differential diagnosis with verrucous pigmentary lesions such as seborrheic keratosis. These authors stated that VM is clinically characterized by having a hyperkeratotic verrucous surface with horny plugs, dark and relatively uniform



**Figure 2.** Hyperkeratosis, papillomatosis, junctional activity, hypertrophy of hair follicular infundibulum (H-E 40×).



**Figure 3.** Spitzoid atypical melanocytes with prominent nucleoli and mitosis in the deep area of the lesion. VM, level II, thickness 2.6 mm (H-E 400×).

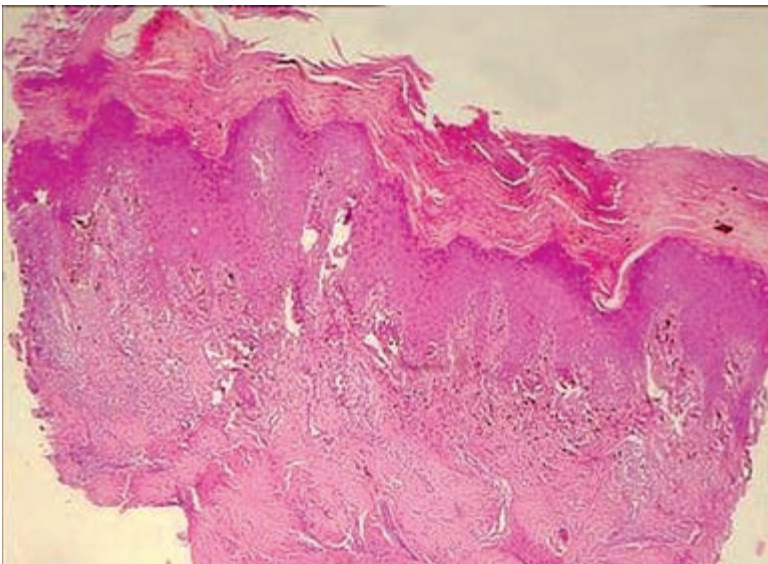
pigmentation, sharp demarcation with moderately irregular borders, and firm and fleshy consistence. They established that the histopathological features are: epidermal hyperplasia with crest extension and telangiectasias in the extended dermal papillae, orthohyperkeratosis with irregular parakeratosis, abundant melanic pigment and atypical fragmented melanocytes in the stratum corneum, focal hypergranulosis, atypical melanocytes proliferating in the basal layer and through the epidermis, fusiform or epithelioid cells and inflammatory infiltrate in bands with numerous melanophages. These authors suggest that the discrepancy between Breslow thickness and Clark level is caused by the marked epidermal hyperplasia and the hyperkeratosis; therefore, tumors that appear clinically advanced show moderate thickness.

In 1991 Abulafia et al.<sup>6</sup> refer again to atypical melanoacanthoma as a fifth MM variety with clinical aspect similar to seborrheic keratosis





**Figure 4.** Male, 72 years old. Pigmented tumor, exophytic, verrucous, black, with vegetating 4 × 4 cm surface, of 8 months evolution, on lateral-medial aspect of left foot.



**Figure 5.** ALM with verrucous parts, Clark level IV, 2.6 mm thick; dominant cell type: epithelioid; moderate TIL, low mitotic index, nuclear degree II. Free surgical margins. Sentinel node: negative (H-E 100x).

or melanocytic verrucous nevus, and with acanthomatous hypertrophy histopathology of pilosebaceous infundibulum associated with atypical melanocyte proliferation. These authors report that this atypical melanoacanthoma is what Kuehnl-Petzoldt called “in sensu stricto” VM, and must be considered a primitive verrucous melanoma. They studied 37 cases of atypical melanoacanthoma or VM, whereof 29 (78.4 percent) were *de novo* and 8 (21.6 percent) showed development of this verrucous aspect in the other clinical forms of MM. They stated that the former have an incidence of 2 to 3 percent, and the prognosis should be less severe than the rest of MM varieties, due to the extended intraepithelial growth. They observed that *de novo* VM dominates in females and appears most frequently in lower limbs.

In 1993, Blessing et al.<sup>7</sup> reported 20 cases of VM representing 3.2 percent of the total of melanomas seen between 1970 and 1991. But in contrast to the above authors, they were found more frequently in males, with an average age of 57 years and located mainly on the back and the thighs. In over 50 percent, prior clinical diagnosis was benign lesions such as verrucous nevus, papilloma and seborrheic keratosis.

In 1994, Buezo et al.<sup>8</sup> reported two cases of LMM with verrucous areas, emphasizing that clinical similarities with verrucous benign lesions make early diagnosis of MM difficult.

In 1997, Herrera Sánchez et al.<sup>9</sup> reported a female case with leg VM of several years evolution and clinically not suggesting a melanoma diagnosis. They reviewed 207 MM and found only one case of VM (0.4 percent).

VM is deemed a MM variety and not a clinical form in the 2000 Australian Guidelines,<sup>10</sup> and in Argentina it was defined in the Melanoma Consensus of the Argentine Dermatology Society [*Consenso sobre Melanoma de la Sociedad Argentina de Dermatología*] in 1998 (updated in 2003).<sup>11</sup>

## Conclusion

VM is a MM variant, whose development in a part of a previous melanoma does not affect the prognosis. We believe that the *de novo* VM shows a noninvasive growth,<sup>4</sup> which is slower than secondary VM. *De novo* VM is an exophytic tumor, generally with more favorable prognosis when diagnosed in the *in situ* or microinvasion stages; the most important histoprognosis factor is the Clark level, thus requiring a less aggressive surgical therapeutic.

It is found in young adults; in our cases, the mean age (37.7 years) was lower than the one found in the literature.<sup>1-3,7</sup> It is located mainly on the head and the limbs.

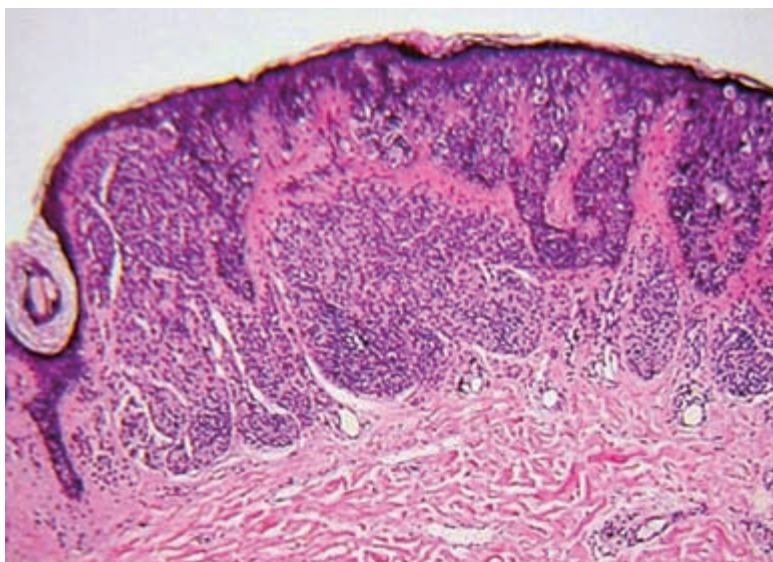
Diagnosis is difficult because they mimic seborrheic keratosis and pigmented verrucous nevi; biopsy and histopathological control must be done of seborrheic keratosis with an unusual aspect, fast growth, and in young females with phototypes IV and V.

Early diagnosis is important, and cure probability ranges between 95 and 100 percent.

The treatment of choice is surgical, with lateral 5 to 10 mm resection margins, while it is the *in situ* or microinvasive stage, including superior or the whole hypodermis; the treatment shall be adjusted to the invasive vertical growth according to conventional guidelines provided for melanoma.



**Figure 6.** Male, aged 27, neck with surface congenital nevus from birth.



**Figure 7.** SSM with verrucous areas developed on small superficial congenital nevus (Zitelli's nevus), level II, thickness 0.73 mm. Dominant cell type: epithelioid; moderate TIL, low IM, GN II (H-E 100x).

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