Chapter

Subungual Melanoma

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Abstract

Subungual melanoma (SUM) is a subtype of acral melanoma. Its incidence in dark phototypes, Hispanics and Asians, is around 20% and accounts for 50% of acral melanomas. It is an infrequent subtype in Caucasians representing only 3%. Subungual melanoma arises from dormant melanocytes in the nail matrix and exceptionally from melanocytes in the nail bed. In its initial phases of radial growth, it presents as longitudinal melanonychia. The differential diagnoses are melanocytic activation (racial, traumatic), nail matrix nevi, and lentigos. Prognosis depends on Breslow depth at diagnosis. For in situ melanoma, treatment consists of conservative surgical removal of the nail unit with 5 mm margins.

Keywords: subungual melanoma, longitudinal melanonychia, acral melanoma, nail melanoma

1. Introduction

Subungual melanoma (SUM) is a subtype of acral lentiginous melanoma. It is a rare subtype in Caucasians accounting for 3% of all melanomas. In dark phototypes, Hispanics and Asians, it represents 20%, and it is the most frequent malignancy of the nail unit [1].

SUM or nail melanoma arises from dormant melanocytes in the nail unit, mainly in the nail matrix, and exceptionally in the nail bed.

UV radiation is not considered an important risk factor for this subtype of melanoma. Trauma has been a hypothetical etiologic agent. Many patients associate direct trauma to the onset of this malignancy, and it has been hypothesized that inflammation can cause mutations in melanocytes during trauma-induced proliferation; but a direct association has not been proven, and it may only be a coincidence due to increased attention to a longitudinal melanonychia after trauma [2].

SUM has a long radial growth phase that can last for many years; in this stage it presents as longitudinal melanonychia, and the differential diagnosis includes racial and traumatic melanocytic activation, nail matrix nevi, and lentigo of the nail unit [3].

Nail plate pigmentation can also be caused by blood and external pigments such as silver in argyria. Many drugs cause nail pigmentation by drug deposition or by melanocytic activation (minocycline, psoralens, cyclophosphamide, zidovudine). Bacterial or fungal infections (*Proteus mirabilis*, *Aspergillus* sp., *Candida* sp., *Trichophyton rubrum*) can cause nail pigmentation; other subungual tumors such as epidermoid carcinoma and even a subungual wart can present as longitudinal melanonychia [3].

Clues to the diagnosis of melanoma include a single-digit affection, melanonychia wider than 3 mm with a triangular form (this means that the band is growing), rapid widening of a longitudinal melanonychia, onset in adulthood

(melanoma in children is quite rare), and Hutchinson's and micro-Hutchinson's sign [4] (**Figure 1** and **Table 1**).

In more advanced stages, SUM causes nail dystrophy, ridging, partial destruction of the nail plate, ulceration, bleeding, and total destruction of the nail unit (**Figure 2**).

SUM affects women and men equally, although some series report a slight predominance in women. SUM is more common on the dominant hand, and it is more frequently reported on the thumbs and on the first finger on both toes [1].

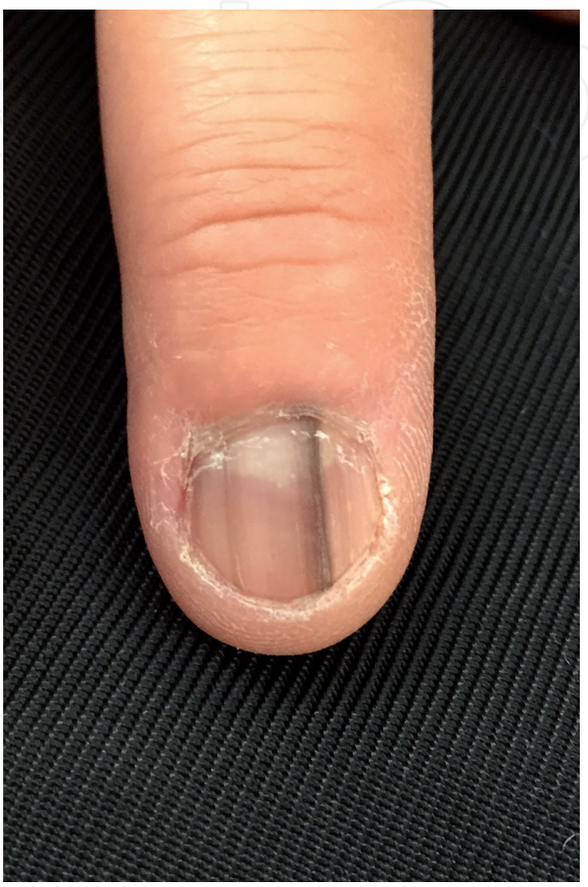

Figure 1.
SUM in situ. Longitudinal irregular melanonychia with nail plate ridging.

A	Age: 40–60 years. Does not rule out in children African, American, Asian, Hispanics
B	Band: brown-black irregular Blurred borders >4 mm
C	Change: rapid increase in size No change: failure to improve
D	Single digit: Thumb-hallux-index finger Dominant hand Nail dystrophy: ridging ulceration
E	Extension—Hutchinson's sign: pigment on nail folds Micro-Hutchinson: cuticle pigmentation visible with dermoscopy
F	Family or personal history of melanoma

Adapted from [4].

Table 1. *ABC rule to suspect SUM.*

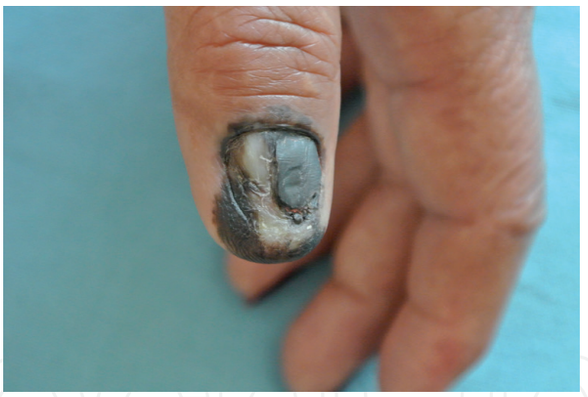

Figure 2.
Invasive SUM with Hutchinson's sign and partial destruction of the nail plate.

SUM is frequently diagnosed in advanced stages, due to a delay in diagnosis by healthcare providers not aware of its existence and clinical presentation or due to lack of access to medical services. The median Breslow at diagnosis is between 4 and 6 mm [1].

2. Dermoscopy

Dermoscopy of the nail unit is a noninvasive method that can help identify high-risk features.

Dermoscopy is useful to distinguish blood; subungual hemorrhage has a distinctive pattern of globules with distal streaks, a filamentous end, and red to brown or deep purple color. It is important to consider a bleeding tumor and rule out that possibility [5].

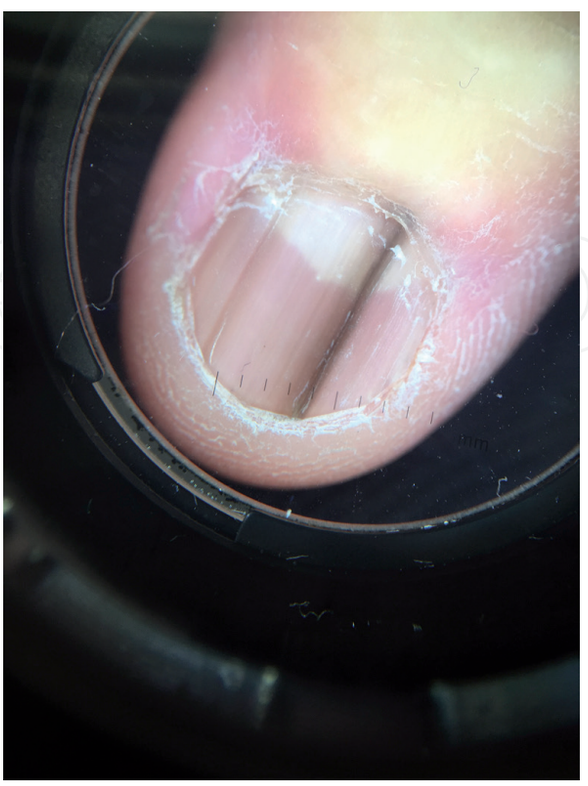

Figure 3.
Dermoscopy of SUM in situ. Irregular multiple heterogenous brown bands with blurred edges and microhutchinson's sign.

Subungual melanoma should be suspected and ruled out in heterogeneous longitudinal brown or black melanonychias, when bands are irregular in color, thickness, and spacing. SUM can also present as a diffuse dark background with barely visible lines (**Figure 3**). When a brown coloration in the background is overlaid by regular, parallel, and pigmented lines, the most probable diagnosis is a nevus.

Edge blurring is another sign associated with SUM. Hutchinson's sign is considered an indicator of SUM; however, it can also be found in benign nevi. Atypical Hutchinson's sign in SUM is asymmetric and polychromatic, and the pigment is distributed in a disorderly fashion. Micro-Hutchinson's sign is periungual pigmentation invisible to the naked eye and only observed with dermoscopy; it has only been described in SUM. Triangular shape of the longitudinal band (wider proximally than distally) indicates rapid growth [5, 6].

A grayish longitudinal background either alone or overlaid by thin homogenous gray lines is suggestive of melanocytic hyperplasia as in lentigo or lentiginoses (Laugier-Hunziker syndrome, Leopard syndrome, Peutz-Jeghers-Touraine disease), in drug-induced, ethnic, and traumatic nail pigmentation.

Amelanotic SUM is a very difficult diagnosis; in this rare case, the nail plate is often partially destroyed by a bleeding, erythematous vegetating tumor. Dermoscopy can show areas of remanant pigmentation and vascular disorder: irregular vessels and milky-red areas [5].

3. Nail matrix biopsy

Nail matrix biopsy remains essential for diagnosis. Most melanomas arise from the distal matrix; by performing dermoscopy of the free edge of the nail plate, it is sometimes possible to determine the origin of melanonychia. If the distal matrix is the origin of melanonychia, the ventral aspect of the nail plate will be affected, and if the proximal nail matrix is the origin, the dorsal aspect of the nail plate will be pigmented.

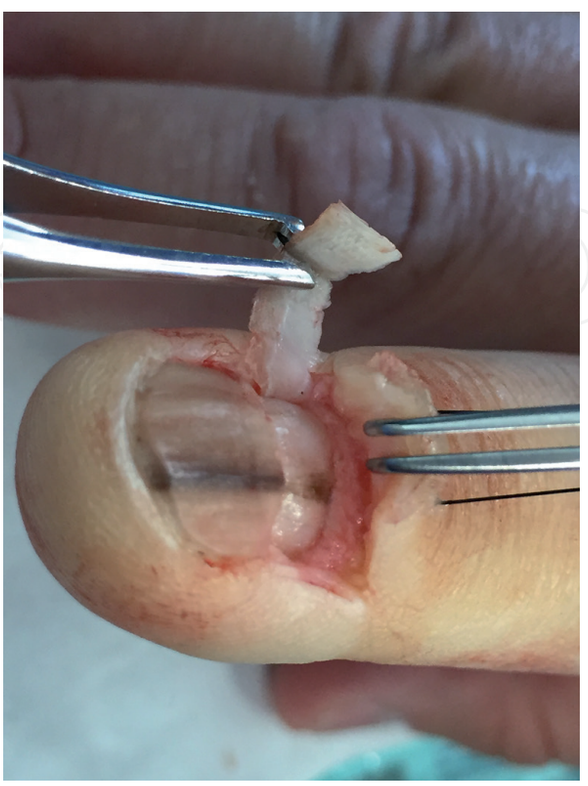

Figure 4.
Nail matrix biopsy technique: proximal nail fold flap and exposure of the nail matrix.

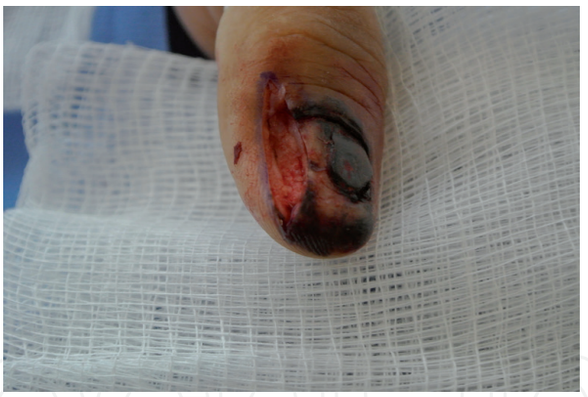

Figure 5.
Lateral longitudinal nail biopsy.

The surgical technique consists in exposing the nail matrix, identifying the origin of melanonychia, and taking a representative sample of the nail matrix without leaving permanent nail dystrophy. This technique is performed under digital block anesthesia. First, the nail plate has to be removed, and a flap of the proximal nail fold elevated so that the proximal and distal nail matrix is exposed (**Figure 4**).

Intraoperative dermoscopy of the nail matrix is an effective tool to precisely identify the origin of the pigment. A longitudinal matrix biopsy, no more than 3-mm-wide or a 3-mm-punch biopsy, can be done without risk of dystrophy; a shave biopsy of the matrix 1 mm deep is enough to make the diagnosis and lessens the risk of permanent dystrophy. There is no need to suture the nail matrix; the nail plate and the proximal nail fold are relocated and sutured with a 4-0 nonabsorbable suture.

In cases of invasive SUM, a lateral longitudinal nail biopsy that includes the proximal fold, the matrix lateral horn, the nail bed, the plate, and the distal nail fold is easier to perform and gives the pathologist enough tissue to make the diagnosis and report Breslow depth (**Figure 5**).

4. Histology

Nail matrix biopsy is still essential for SUM diagnosis. Normal nail matrix has between 4 and 14 melanocytes per mm (mean 6.86 cells/mm per mm stretch of nail matrix epithelium) [7].

The presence of nests without atypia is distinctive of nevi, especially in a child with a well-demarcated, uniformly pigmented, single, longitudinal band [8].

The histologic distinction between a benign subungual pigmented macule (lentigo or lentigo-like hyperpigmentation) and an early lesion of SUM can be difficult.

This benign lentigos may histologically only show an increase in melanin deposition in keratinocytes, melanocytes, and/or macrophages without proliferation of melanocytes (melanocytic activation). However, these benign lesions may show proliferation of melanocytes as well. The mean density of melanocytes in lentigos is around 15.3 cells per 1-mm-stretch nail matrix. There is no confluence of melanocytes. Cytologic atypia has to be absent or mild. There is no inflammation associated. Pagetoid spread may be present but only focally.

SUM in situ shows a much greater proliferation of melanocytes (mean 58.9 cells per 1 mm of stretched nail matrix) that ranges from 39 to 136 melanocytes per 1 mm of stretched nail matrix. There is at least focal confluence of cells with various grades of cytologic atypia: nuclear enlargement, hyperchromatism, irregular nuclear contours, and prominent nucleolus. Dendrites are thicker and larger. Pagetoid spread is found in almost all lesions of SUM, and inflammation in the

epithelial stromal interface is frequent [6, 7]. In some cases of SUM with lentiginous growth of single atypical melanocytes, immunohistochemical stains with MELAN-A and HMB-45 may ease the diagnosis.

Invasive SUM has denser proliferation of atypical melanocytes arranged in aggregates and sheaths and may lead to nail dystrophy, nail destruction, and ulceration.

It can be difficult to measure Clark level and Breslow thickness, because the distinction of the onychodermis is not always clear and the underlying phalanx is separated by only a thin dermal collagen layer [6].

5. Treatment

SUM in situ must be surgically removed with wide resection of the entire nail unit with a 5-mm-wide margin and periosteum depth (**Figure 6**).

Reconstruction can be performed with the next finger banner flap and a full thickness graft, or it heals by the second intention with good functional results [1].

Treatment for invasive SUM is amputation of the phalanx.

Sentinel lymph node biopsy should be performed in SUM with Breslow depth >1 mm and in SUM >0.8 mm with ulceration [1, 9–11].

The most important factors for prognosis and survival are Breslow depth, ulceration, and nodal status at diagnosis [10, 11].

SUM has the same prognostic factors as other subtypes of melanoma. The adverse outcomes associated with SUM are due to delay in diagnosis because of a lack in recognition by health professionals and advanced stages at diagnosis.

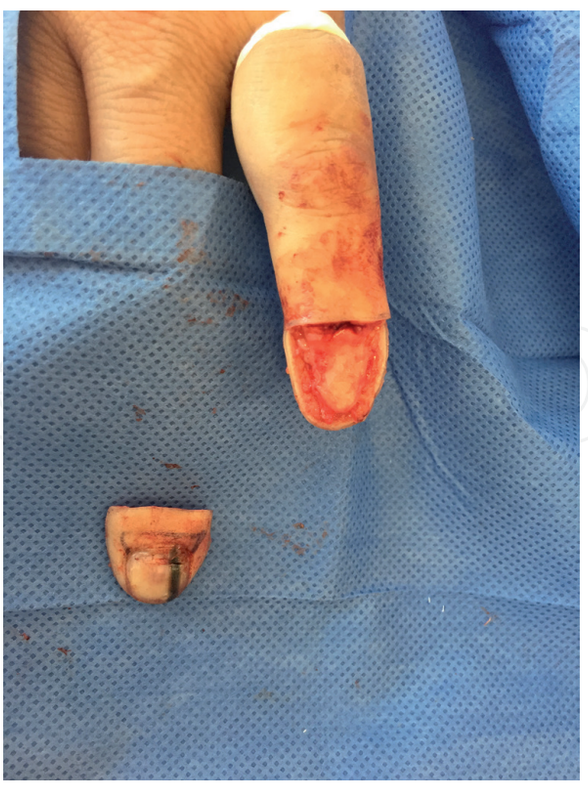

Figure 6.
Resection of the nail unit with 5 mm wide margins and periosteum depth.

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