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CASE REPORT

Subungual melanoma: a case report of delayed diagnosis despite multiple biopsies

Melanoma subungueal: relato de caso de diagnóstico tardio apesar de múltiplas biópsias

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Abstract

Subungual melanoma is a rare presentation of melanoma, accounting for approximately 3% of all cases of this neoplasm. In this case, the diagnosis was only confirmed after the third biopsy, highlighting the importance of suspecting malignancy based on clinical history and dermatological examination. This report describes the case of a 43-year-old female patient with longitudinal melanonychia on the first and third digits of the right hand. She had undergone two previous biopsies, both showing no evidence of malignancy on histopathological analysis. However, due to high clinical suspicion, a third biopsy was performed, confirming a diagnosis of subungual melanoma *in situ*. In most cases, the prognosis is poor, with frequent bone metastases. The rarity of this melanoma presentation, combined with the diagnostic challenges and the low survival rate, justifies the report of this case.

Keywords: Subungual melanoma. Longitudinal melanonychia. Delayed diagnosis. Nail biopsy.

Resumo

O melanoma subungueal é uma forma rara de apresentação do melanoma, correspondendo a aproximadamente 3% de todos os casos dessa neoplasia. Neste caso, o diagnóstico foi confirmado apenas após a terceira biópsia, ressaltando a importância da suspeita de malignidade com base na história clínica e no exame dermatológico. Este relato descreve o caso de uma paciente do sexo feminino, de 43 anos, com melanoníquia longitudinal no primeiro e terceiro quirodáctilos da mão direita. Ela havia realizado duas biópsias anteriores, ambas sem evidência de malignidade na análise histopatológica. No entanto, diante da alta suspeita clínica, foi realizada uma terceira biópsia, que confirmou o diagnóstico de melanoma subungueal *in situ*. Na maioria dos casos, o prognóstico é reservado, com metástases ósseas frequentes. A raridade dessa apresentação do melanoma, associada aos desafios diagnósticos e à baixa taxa de sobrevida, justifica o relato deste caso.

Palavras-chave: Melanoma subungueal. Melanoníquia longitudinal. Diagnóstico tardio. Biópsia ungueal.

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Introduction

Subungual melanoma has a higher incidence in individuals aged 50-70 years, accounting for 0.7% to 3.5% of all cutaneous melanomas, and is most commonly found on the first and second digits. Its etiology remains unclear, with trauma history, ultraviolet radiation exposure, and heredity being the most discussed contributing factors. The most common clinical manifestation is longitudinal melanonychia.[1-3]

The prognosis is often poor due to late diagnosis, with a 5-year survival rate of 15%. Bone metastases are frequent. Brownish longitudinal melanonychia associated with benign conditions is commonly seen in non-Caucasian patients, which can contribute to diagnostic delays. Evidence suggests that approximately 85% of subungual melanoma cases are initially misdiagnosed.[1,4]

The following case report highlights the need for thorough clinical evaluation and dermatological examination, as well as the importance of performing repeated biopsies in cases of high clinical suspicion of subungual melanoma.

Case report

A 43-year-old female patient, with no comorbidities or history of nail trauma, presented with melanonychia on the 1st and 3rd digits of the right hand and reported prior dermatological follow-up for the lesions. She had previously undergone two nail biopsies, both of which showed no evidence of malignancy on histopathological analysis. However, neither biopsy included the nail matrix for evaluation. She denied any family or personal history of skin cancer or other malignant neoplasms.

Upon examination, dermatological assessment revealed longitudinal melanonychia on the first digit. Dermoscopy showed pigmentation extending to the cuticle, forming a triangular shape with a broader base that progressively tapered toward the nail tip (Figs. 1 and 2).

A new biopsy was performed, this time including the nail matrix (Fig. 3), and histopathological analysis confirmed a diagnosis of subungual melanoma *in situ* (Fig. 4). Immunohistochemical analysis was positive for S100, MELAN A, HMB45, and Ki-67 antigens, further confirming the diagnosis of melanoma *in situ*.

After the lesion was removed, the patient underwent rigorous follow-up. Currently, 4 years after the diagnosis, she is being monitored with medical appointments every 6 months, without any indication of recurrence or new suspicious lesions.

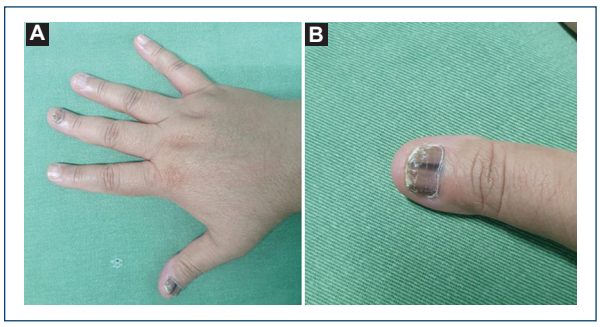


Figure 1. A: melanonychia on the 1st and 3rd digits. **B:** digit where a biopsy was previously performed at another facility.

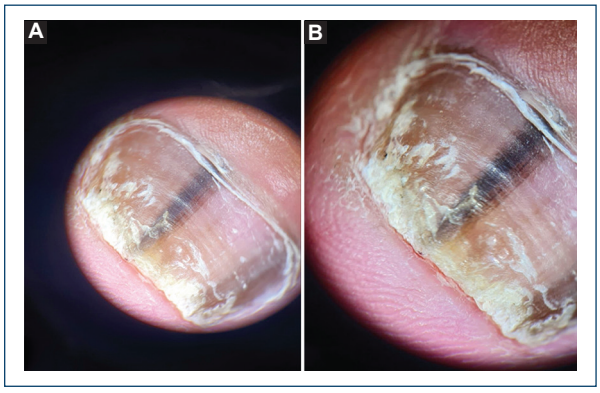


Figure 2. A: dermoscopy of the first finger showing melanonychia extending to the nail fold (Hutchinson's sign) with a triangular shape and progressive narrowing toward the free edge. **B:** higher magnification.

Discussion

Subungual melanoma originates in the nail matrix, with its most common initial manifestation being longitudinal melanonychia. The latter is characterized by a dark brown or black band, which can be caused by hyperplasia or by melanocyte activation. It has various causes, including vitamin deficiencies, bacterial and fungal infections, subungual hematoma, pigmentary disorders, and, more severely, it may be the first sign of melanoma. Longitudinal melanonychia occurs in approximately 70% of cases of subungual melanoma and should be considered a differential diagnosis in all patients with this clinical presentation. Other possible findings are pigmented subungual lesions that may ulcerate, onycholysis, onychomadesis, nail destruction, and bleeding of the nail bed. Hutchinson's sign is a red flag for the diagnosis of melanoma.[1,3]



Figure 3. Nail biopsy, including the nail matrix.

Table 1. ABCDEF mnemonic for suspected subungual melanoma

ABCDEF	
A	Age between 50 and 70 years, African Americans, Native Americans, and Asians
B	Irregular borders, brown-black coloration, and a width of 3 mm or more
C	Change in color or size of the lesion
D	Digits involved (more common in thumbs and index fingers)
E	Extension of pigment onto the nail fold (Hutchinson's sign)
F	Personal or family history of dysplastic nevi or melanoma.

First described by Levit EK et al.[5]

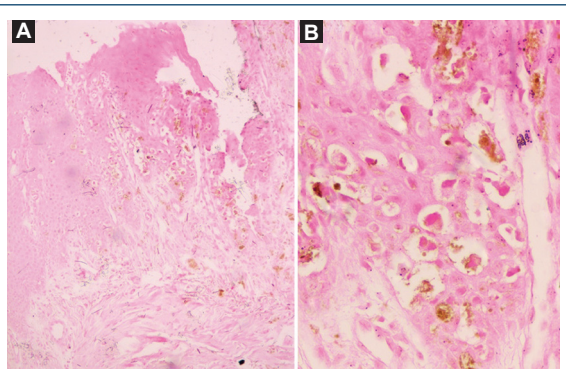


Figure 4. Histopathological slides. **A:** sections show individual proliferation and clustering in small nests of melanocytic cells at the junction of the epithelium and stroma, along with pagetoid extension, with atypical-looking cells with irregular and coarse deposits of melanin pigment in the cytoplasm and large, pleomorphic nuclei. The histological findings favor the diagnosis of subungual melanoma *in situ*. **B:** higher magnification.

The clinical and epidemiological characteristics that should raise suspicion are summarized in the ABCDEF mnemonic (Table 1).[5]

Dermoscopy can be highly useful, facilitating the visualization of irregularities in the borders and coloration of melanonychia, nail dystrophies, and, most importantly, evaluating periungual skin involvement for the presence of Hutchinson's sign.[1]

Diagnosis is confirmed through excisional nail biopsy, which involves removing the entire pigmented area, including the nail fold and affected digit skin. However, the initial biopsy may be inconclusive or yield a false-negative result, highlighting the importance of clinical evaluation for diagnostic suspicion and the need for a repeat biopsy when melanoma is highly suspected.[1]

The surgical approach for treatment should primarily consider oncological safety. However, in non-invasive lesions such as *in situ* melanoma – where the neoplasm does not extend deeply into the nail matrix – functional preservation of the digit can be considered. For invasive lesions, wide surgical excision or amputation of the phalanx proximal to the lesion, and in some cases, even the most distal uninvolved interphalangeal joint, has been recommended. The risk of bone involvement, along with the variability in lesion size and nail apparatus involvement, leads to variability in surgical approaches and a lack of consensus regarding safe margin widths.

Early diagnosis of subungual melanoma is crucial to improving survival rates and reducing the risk of metastasis. A cure is possible in the early stages, emphasizing the need for early detection of this neoplasm.[1,3]

Conclusion

Subungual melanoma remains a diagnostic challenge due to its rarity and its frequent clinical overlap with benign causes of longitudinal melanonychia. This case underscores the importance of maintaining a high index of suspicion and ensuring an adequate biopsy technique, including sampling of the nail matrix. In cases of persistent clinical suspicion, a repeat biopsy is essential to avoid delayed diagnosis. Early recognition is crucial to improving prognosis and reducing the risk of metastasis.

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Conflicts of interest

None.

Ethical disclosures

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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