Presentation, Histopathologic Findings, and Clinical Outcomes in 7 Cases of Melanoma In Situ of the Nail Unit

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Objective: To report on the presentation, histopathologic findings, and clinical outcomes for a case series of MIS of the nail apparatus because melanoma in situ (MIS) of the nail unit has not been well characterized in the literature.

Setting: A division of a tertiary academic center specializing in micrographic excision of cutaneous neoplasms.

Design: Surgical records were searched for cases of MIS of the nail unit for the period of January 1, 1997, to December 31, 2002. The patient demographics and disease presentation, treatment, and clinical course were reviewed.

Results: Seven cases of MIS of the nail unit in white patients were identified. Longitudinal melanonychia was present in all cases, but dyspigmentation of the proximal nail fold and onychodystrophy were uncommon. Histopathologic analysis revealed poorly circumscribed proliferations of single cells over nests with variable pagetoid spread. Atypia was variable. Mitotic activity was low. All cases were treated with micrographic surgery. Amputation was avoided in 3 cases and was limited to partial distal interphalangeal amputation in the remainder. Six cases did not recur locally after initial surgical intervention. With an average of 24 months of follow-up, all patients were free of disease.

Conclusions: Longitudinal melanonychia in a white patient mandates consideration of MIS of the nail unit. Given the nondescript clinical presentation, the threshold for biopsy should be low. The histopathologic findings appear similar to those of MIS in other areas, with asymmetry and poor circumscription predominating. With additional study and further acceptance, micrographically controlled excision has the potential to minimize morbidity. Further investigation is warranted.

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Melanoma of the nail apparatus is a rare entity, comprising only 0.7% to 3.5% of all forms of melanoma.\(^1,3\) Despite its rarity, when melanoma of the nail unit occurs, it may portend a poorer prognosis and lower survival than melanoma of other sites.\(^1,2,4,6\)

The poor prognosis of nail-unit melanoma has been attributed, at least in part, to difficulty establishing an early diagnosis owing to the unique anatomy of the nail. The intervening nail plate can alter light reflectance and make it difficult to discriminate the abnormal pigment deposition of melanoma from that of benign causes. Moreover, a large proportion of nail-unit melanomas (15%-65%) are reported to be amelanotic.\(^4\) If nail-unit pigmentation is noted, patients often attribute such changes to trauma, which leads to delays in formal assessment or decreased participation in diagnostic procedures. Furthermore, there is an overlap of histopathologic features common to acral pigmented lesions such as nail matrix nevi and melanoma including asymmetrically distributed melanocytes, poor dermal maturation, and pagetoid spread.\(^7\)

For all of these reasons, nail-matrix melanoma is generally more advanced at the time of diagnosis than other types of melanoma, and the average depth at diagnosis reported in some series ranges from 3.5 to 4.7 mm.\(^2,8,9\) Consequently, the characteristics of melanoma in situ (MIS) of the nail unit are not well recognized.

In the past, treatment of melanoma of the nail unit has focused largely on amputation. The use of tissue-sparing Mohs micrographic surgery for thin melanomas of the nail unit has potential benefit in avoiding amputation. Herein, we detail 7 cases of MIS of the nail unit that occurred at a single institution and report on the presentation, histopathologic findings, and clinical outcome of each case.
while commenting on the use of Mohs micrographic surgery as a tissue- and digit-sparing intervention.

## METHODS

We reviewed 166 charts of patients with MIS treated by a single academic Mohs micrographic surgeon over the 5-year period from January 1, 1997, to December 31, 2002, for cases involving the nail apparatus. All melanomas had been diagnosed in the Dallas/Fort Worth, Tex, metroplex and had a diagnostic biopsy specimen processed at a single dermatopathology laboratory in the area. All biopsy specimens were signed out by the senior dermatopathologist at that laboratory. Data were gathered retrospectively and included patient age and sex, tumor location, size, and duration prior to biopsy, number of Mohs stages required for excision, repair technique used, and clinical course.

In all cases, a biopsy specimen was obtained from the matrix after reflection of the proximal nail fold, and the tissue was fixed in 10% neutral buffered formalin. For surgical specimens, standard fresh tissue Mohs technique was used in all cases. Frozen sections were evaluated for margin status by the Mohs micrographic surgeon at the time of surgery and retrospectively confirmed by a board-certified dermatopathologist. In some cases, MART-1 immunohistochemical staining was performed on frozen sections using standard techniques (MART indicates melanoma antigen recognized by T cells).

Institutional review board approval was obtained prior to initiation of this project.

## RESULTS

Seven patients with biopsy-proven MIS of the nail unit were discovered. Four women and 1 man had lesions of the fingernails, while 1 man and 1 woman had lesions of the toenails. Five cases occurred on the left side of the body, while 2 cases occurred on the right. The most common digit involved was the index finger, present in 3 of 5 cases on the upper extremity. Both cases of the lower extremity occurred on the great toe. The age at diagnosis ranged from 34 to 87 years. All patients were white.

Melanonychia represented the primary indication for biopsy in all cases. In some cases, the entire nail was pigmented, while in other cases, one or multiple pigmented bands of various widths (2-9 mm) were present. Accompanying onychodystrophy was present in only 2 of 7 cases. The duration of pigmentation ranged from 7 months to 6 years. Pigmentation of the proximal nail fold, described as Hutchinson sign, was positive in 3 of

<table>
<thead>
<tr>
<th>Patient No./Sex/ Age at Diagnosis, y</th>
<th>Location</th>
<th>Hutchinson Sign</th>
<th>Duration of Lesion Prior to Biopsy, mo</th>
<th>Mohs Stages Performed</th>
<th>Immunostains on Frozen Sections</th>
<th>Repair Type</th>
<th>Follow-up, mo</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/34 Right second finger</td>
<td>Negative</td>
<td>2 y</td>
<td>1</td>
<td>MART-1</td>
<td>Cross-finger flap</td>
<td>10</td>
<td>Yes*</td>
<td></td>
</tr>
<tr>
<td>2/F/64 Left third finger</td>
<td>Positive</td>
<td>4 y</td>
<td>2</td>
<td>None</td>
<td>Partial DIP amputation</td>
<td>25</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>3/F/53 Left fifth finger</td>
<td>Negative</td>
<td>6½ y</td>
<td>1</td>
<td>None</td>
<td>FTSG</td>
<td>35</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>4/M/67 Left great toe</td>
<td>Negative</td>
<td>1 y</td>
<td>3</td>
<td>None</td>
<td>Partial DIP amputation</td>
<td>38</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>5/F/54 Left second finger</td>
<td>Negative</td>
<td>7 mo</td>
<td>2</td>
<td>None</td>
<td>FTSG</td>
<td>29</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>6/F/43 Right great toe</td>
<td>Positive</td>
<td>3 y</td>
<td>1</td>
<td>None</td>
<td>FTSG</td>
<td>23</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>7/M/58 Left second finger</td>
<td>Positive</td>
<td>6 y</td>
<td>1</td>
<td>MART-1</td>
<td>Partial DIP amputation</td>
<td>10</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: DIP, distal interphalangeal; FTSG, full-thickness skin graft; MART, melanoma antigen recognized by T cells.

*“Atypical melanocytic hyperproliferation” recurred at the site per outside pathology laboratory report 5 months after the initial Mohs procedure.

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**Figure 1.** Representative images of longitudinal melanonychia prior to biopsy. Note the positive Hutchinson sign in panel B. Scales indicate millimeters.
demonstrated marked nuclear enlargement and a coarse distribution of chromatin. Increased mitotic activity was not a prominent feature. Representative photomicrographs are provided in Figure 2.

At the time of excision, all patients were without lymphadenopathy or signs of systemic disease. Histologically tumor-free margins were obtained in all patients per the surgeon’s examination of frozen sections at the time of surgery. Representative intraoperative photographs are provided in Figure 3A and B. Four tumors (37%) were cleared in a single stage; 2 (29%) required 2 stages; and 1 required 3 stages. In 2 cases, MART-1 immunohistochemical staining was performed on frozen sections. It is the policy of the microscopic surgeon (R.S.T.) to use immunohistochemical staining only if, on examination of initial frozen sections, difficulty is encountered discriminating between melanocytes and surrounding keratinocytes.

Frozen sections were retrospectively reviewed by a board-certified dermatopathologist, who agreed in all cases but one that either a tumor-free plane had been rendered at the time of surgery or that additional stages were needed. In case 4 (Table), the single case of disagreement, the dermatopathologist noted an intraepithelial proliferation of atypical melanocytes and believed it represented a focus of residual MIS on the final stage.

Representative frozen sections, 1 positive and 1 negative, are shown in Figure 4.

Repairs were performed via referral to a plastic surgeon. Full-thickness skin grafts were performed in 3 patients. Partial distal interphalangeal (DIP) amputations were performed in 3 patients. A cross-finger flap was performed in 1 patient. Representative images of the repaired digits are shown in Figure 3C and D.

Follow-up time for all patients ranged from 10 to 38 months (mean, 24 months). One patient experienced a recurrence of pigmentation at the operative site 5 months after surgery and underwent another biopsy. After a finding of “atypical melanocytic hyperplasia,” the patient elected to have a partial amputation performed at an outside institution. In a telephone follow-up 10 months after her original diagnosis, she reported that she was without recurrence or complications. To date, no other patient has demonstrated a local recurrence or metastatic disease.

COMMENT

Melanoma of the nail unit is typically more advanced than other melanomas at the time of diagnosis. Consequently, traditional surgical intervention for this type of malignancy has focused predominantly on amputation.2,3,10 Nonamputative excision has been rarely advocated in the surgical literature.1,11 Moreover, less is known regarding the presentation, histopathologic findings, and clinical course of MIS of the nail apparatus than of other forms of MIS.

The 7 cases detailed in our report occurred in men and women of various ages. Fingernails and toenails were involved, with the index finger and great toenail most commonly implicated. All patients in this study demonstrated longitudinal melanonychia, but the appearance of this finding was variable. The affected area ranged from 2 to 9 mm in width and was described in some cases as uniform and in others as multicolored. Accompanying onychodystrophy was found in just 2 cases.

Only 3 of 7 patients demonstrated Hutchinson sign, or periungual extension of pigment into the proximal nail fold. While some researchers have regarded this as an important indicator of melanoma,12 other experts have cautioned against relying on this sign because it is not sensitive and is only somewhat specific.4 The present patients reported having nail pigmentation from 7 months to 6 1/4 years prior to diagnosis of MIS. Similar delays have been reported in another series of invasive melanomas of the nail unit in which an average of 5.12 years elapsed prior to diagnosis.1

Some investigators have detailed case series demonstrating that benign lesions predominate as the cause of longitudinal melanonychia.13 The highly varied physical findings in our series lead us to agree with others who recommend a thorough evaluation for nail-unit melanoma for white patients with longitudinal melanonychia.4,14

The most common histologic diagnosis of longitudinal melanonychia in adults is a benign melanotic macule.15 In the present series of MIS of the nail unit, lesions commonly demonstrated a poorly circumscribed...
proliferation of melanocytes with varying degrees of pagetoid spread. Single melanocytes predominated over small nests in most fields. Atypia was variable, and mitotic activity was low.

Amputation as a definitive therapy for nail-unit melanoma has traditionally been justified by the later diagnosis and increased thickness of this form of melanoma compared with other forms. Given the trend toward narrower margins for all melanomas, it is appropriate that Mohs surgery be explored as a tissue- and digit-sparing procedure in the treatment of MIS of the nail unit.

In our series of 7 patients, 3 patients were able to preserve the digit in its entirety, while 3 patients needed only partial DIP amputation (amputation above the DIP joint) with minimal morbidity. In case 2, a partial DIP amputation was performed, despite a planned full-thickness skin graft, after unanticipated damage was noted to the extensor retinaculum (Figure 3B).

Because minimal morbidity was desired in all cases, an open-forum multidisciplinary conference was held to discuss with our surgical colleagues the various indications for full-thickness skin graft vs partial DIP amputation. Nondermatologists present at the forum expressed uncertainty and unfamiliarity regarding the adequacy of micrographic techniques for removal of MIS of the nail unit. It was to alleviate their uncertainty and with their encouragement that we conducted the present study.

Six of our 7 patients were free of disease after primary surgical intervention at an average of 24 months of follow-up. Of concern was a single case of recurrent “atypical melanocytic hyperplasia,” which prompted our patient to pursue a revision partial amputation. Brodland,1 in a study of Mohs surgery as treatment for 14 nail-unit melanomas of various depths, included 4 MIS lesions and reported a total of 3 local recurrences, 2 of which occurred in MIS tumors.

Indeed the use of frozen sections for the evaluation of margins in melanoma is not without controversy. Studies of long-term survival in patients with melanoma support the conclusion that physicians trained in examining frozen sections can accurately identify subclinical extension of melanoma.16,17 However, other paired comparisons of frozen sections vs paraffin embedding have demonstrated increased diagnostic accuracy with permanent techniques.18-20

Currently, our dermatologic surgery division uses frozen sections, occasionally with immunohistochemi-

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**Figure 3.** Intraoperative (A and B) and 1-month postoperative (C and D) images from case 6 (A and C) and case 2 (B and D) as detailed in the Table. Scale is in millimeters.
cal staining, for evaluation of surgical margins of MIS resection regardless of location. Our dermatopathologist and micrographic surgeon agreed in the interpretation of all surgical margins, with the sole exception of a possible small focus of MIS present on the final stage of case 4. However, the significance of this finding is unclear since the patient has maintained the longest disease-free survival of any in our series. Further investigation into the efficacy of frozen sections vs paraffin techniques for margin evaluation in MIS may be justified, particularly when the challenging topography of the nail unit is involved.

In conclusion, the diagnosis of MIS of the nail unit can be difficult to establish for multiple reasons. Clinically, the presence of longitudinal melanonychia in a white patient mandates further evaluation, regardless of the presence of a Hutchinson sign or the absence of onychodystrophy. Histopathologic diagnosis of MIS of the nail unit can be characterized by an asymmetric proliferation of melanocytes with a predominance of single cells over small nests and variable degrees of atypia. Further multidisciplinary study and education regarding the use of micrographic surgery for MIS of the nail unit is justified because of the tremendous potential for tissue conservation and reduced morbidity.

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REFERENCES