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# A non-healing ulcerated fingertip following injury

A man went to his primary care physician 3 months after slamming his right thumb in a car door. The nail had turned black and sloughed off several weeks later, leaving a red, draining wound on the tip of his thumb. The wound drained continuously for the next 2 months and showed little progress in healing.

His physician started him on antibiotics, but the wound still showed no progress in healing over the next 6 weeks. Cultures were obtained that grew out *Staphylococcus* and *Streptococcus* spp. Another course of antibiotics was given, but the patient's condition failed to improve.

At this point the patient was referred to a surgeon. He missed several appointments before finally presenting to the

surgery clinic nearly 6 months after his original office visit. He was diagnosed clinically as having a giant pyogenic granuloma and was given antibiotics as well as silver nitrate sticks to cauterize the wound daily. After missing several more follow-up appointments, the patient returned with a spongy, weeping soft-tissue wound over the dorsum of his right thumb [that] doubled in size over the past 3 months (**FIGURE**). Radiographs obtained at that time were normal, but a bone scan revealed late uptake, cause for concern that this was osteomyelitis.

■ **What is the differential diagnosis, and what tests are necessary?**

**FIGURE** Ulcerated tip of the thumb



A spongy, weeping soft-tissue wound over the dorsum of the right thumb.

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### ■ **Diagnosis:** **Subungual melanoma**

Due to the aggressive nature of the wound and the large soft-tissue defect, a plastic surgeon was consulted. Biopsy showed malignant melanoma, and the thumb was amputated at the base of the proximal phalanx. Pathology revealed a 3 x 3.5 cm ulceration at the distal portion of the specimen with malignant melanoma involving the skin, subcutaneous tissue, and bone marrow. Two of 3 axillary lymph nodes were also positive for metastatic malignant melanoma.

### **History and epidemiology**

While public awareness of cutaneous melanoma has been increasing, subungual melanoma remains obscure. First described in 1834 by Alexis Boyer, surgeon to Napoleon, it was later characterized in 1886 by Sir Jonathan Hutchinson, who reported 6 cases of "melanotic whitlow."<sup>1</sup> Hutchinson reported that the lesion was usually first attributed to an injury, and because of this the diagnosis was nearly always missed in the early stages.

Today, subungual melanoma is often neglected by patients and frequently misdiagnosed by physicians. The estimated mean delay in diagnosis ranges from 3 to 24 months—nearly double the diagnostic delay observed with cutaneous melanoma.<sup>1,2</sup>

One study found 52% of subungual melanomas were mistaken for benign or traumatic lesions of the nail bed such as pyogenic granuloma, paronychia, onychomycosis, chronic infection, subungual hematoma, or pigmented nevus. This mistake is not surprising as these lesions are all in the differential diagnosis of a single pigmented nail streak, and all are far more common than subungual melanoma.

Another study found that two thirds of patients underwent some inappropriate surgical procedure before the correct diagnosis was considered.<sup>1</sup> Because of its poor prognosis, often related to delay in diagnosis, maintain a high index of suspicion for subungual melanoma in the proper setting and a sound understanding of which

lesions need to be biopsied.

Subungual melanoma disproportionately affects nonwhites. While the total number of cases of subungual melanoma accounts for only 0.3% to 3% of all new cases of malignant melanoma, one study found subungual melanoma accounted for up to 23% of all malignant melanomas in Japanese persons, 17% of malignant melanomas in Hong Kong Chinese persons, and 25% of malignant melanomas in African Americans.<sup>1</sup>

The thumb and big toe are the most frequently involved regions, perhaps due to the larger proportion of nail matrix on these digits, with 55% of lesions arising on the hands, and more than half of those involving the thumb.<sup>2</sup>

### **Cause is unclear**

The cause of subungual melanoma is thought to be different from that of cutaneous melanoma, but it remains unclear. Because the nail filters out UVB light and subungual melanoma most frequently arises from a portion of the nail matrix that is not sun-exposed, UV exposure is not thought to play the same role in pathogenesis of subungual melanoma as it clearly does in cutaneous melanoma.<sup>1</sup>

Since the time of Hutchinson's original report there have been numerous case reports and several series that describe antecedent trauma in subungual melanoma; however, there has never been conclusive evidence that trauma is a causative factor.<sup>3,4</sup>

### ■ **Clinical presentation**

Nail pigmentation is the first clinical sign of subungual melanoma in more than 75% of cases, but few patients present at this stage. Instead most patients delay presentation until changes in the nail contour are evident, secondary infection supervenes, or ulceration of the nail bed with granuloma formation manifests.<sup>1</sup>

Levit et al<sup>5</sup> surveyed the world literature on "subungual melanoma" in 2000

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**More than half of subungual melanomas are mistaken for benign/traumatic lesions; two thirds of patients have inappropriate surgery**

and, based on their findings, described the ABCDEF mnemonic (**TABLE 1**) to describe the salient features. When considering a nail bed lesion, the presence of any one of these features should raise the clinician's index of suspicion for subungual melanoma, while the presence of multiple features should raise a significantly higher concern.

### Nail pigmentation

The 2 most important signs of subungual melanoma are melanonychia striata (longitudinal brown to black pigmented streaks in the nail) and Hutchinson's sign, which is the spread of brown or black pigment from the nail bed, nail matrix, or nail plate onto the adjacent cuticle or onto the proximal or the lateral nail fold.

Many patients with subungual melanoma have a history of a thin pigmented streak that had remained unchanged for years and then suddenly began to enlarge—eventually involving the entire nail bed with subsequent penetration to the eponychium or paronychia, ulceration, or granuloma formation.

**Melanonychia striata.** The differential diagnosis of melanonychia striata is quite long, and most of these streaks are benign (**TABLE 2**). Dark brown or black lines in the nails are common in Asians, African Americans, and in dark-skinned individuals, and may simply represent ethnic variation in pigment. Multiple streaks and streaks that do not extend distally from the proximal nail fold are nearly always benign.

Single streaks greater than 6 mm wide, those appearing in the sixth and seventh decade of life, streaks with a variegated color, or those that exhibit a broader proximal base or undergo any morphological change (indicating an active process) are suspicious for subungual melanoma.

**Hutchinson's sign.** Hutchinson's sign is pathognomonic for subungual melanoma only when accompanied by ulceration of the nail bed or obliteration of the nail plate by granuloma. When present, a tissue diagnosis must always be sought.

**TABLE 1**

### Salient features of subungual melanoma

<b>A</b> = Age (5th to 7th decades), African-American, Asian, American Indian
<b>B</b> = Brown/Black pigment, Breadth (>3mm), Border variegation
<b>C</b> = Change in nail band or lack of change in nail morphology despite, presumably, adequate treatment
<b>D</b> = Digits most commonly involved (thumb, hallux)
<b>E</b> = Extension of pigment onto the proximal/lateral nail fold (Hutchinson's sign)
<b>F</b> = Family or personal history of melanoma

### Amelanotic subungual melanoma

Fewer than 7% of cutaneous melanomas lack pigment. In contrast, 20% to 33% of subungual melanomas are amelanotic. This makes the diagnosis of amelanotic subungual melanoma at best difficult, and often times impossible without a biopsy.<sup>1</sup>

### Management of subungual melanoma

#### Nail biopsy

Untreated melanoma is potentially fatal, while nail biopsy is technically difficult, potentially disfiguring, and can be complicated by scarring or pterygium formation. The physician must thus carefully determine which lesions require biopsy. Except in the special case when the clinician deems the probability of subungual hematoma to be very high (discussed below), it may be best to refer these patients to a specialist when available.

As a general rule any nail lesion, whether pigmented or not, that does not heal with 6 to 12 weeks of conservative treatment should be biopsied. Lesions causing nail dystrophy, ulcerating lesions, and those presenting with Hutchinson's sign should all be biopsied.

**Caucasians.** Managed conservatively, all single pigmented nail streaks in adult Caucasians unresolved within 6 to 12 weeks need to be biopsied. The clinician

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**The early clinical signs of subungual melanoma are nail pigmentation, changes in nail contour, secondary infection, and ulceration of the nail bed**

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**TABLE 2**

### Common differential diagnoses of multiple pigmented nail streaks or periungual pigmentation

DRUGS		
Antimalarials	Hydroxyurea	Sulfonamide
Bleomycin	Ketoconazole	Tetracycline
Cyclophosphamide	Methotrexate	Zidovudine
Doxorubicin	Minocycline	
5-FU	Phenytoin	
SYSTEMIC CONDITIONS		
Addison's disease	Peutz-Jeghers syndrome	
Hemosiderosis	Vitamin B12 deficiency	
Porphyria	Pregnancy	
Radiation therapy	Laugler-Hunziker syndrome	
Subungual melanoma		
MICROBIAL INFECTIONS		
AIDS	Proteus mirabilis	
Blastomycetes	Secondary syphilis	
Candida	Trichophyton	

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**Any nail lesion—pigmented or not—that does not heal in 6 to 12 weeks of treatment should be biopsied**

should thoroughly investigate non-melanotic causes of single pigmented streaks with a careful history and a thorough physical examination. Seek out clues, especially from the patient's drug and treatment history. Unchanged, lightly pigmented streaks already present for many years on adult Caucasians at the time of initial presentation warrant close follow-up, and those with such lesions that remain unchanged after 6 to 12 months of follow-up may be safely discharged with instructions to seek medical evaluation if the lesion shows any subsequent morphological change.

**Asians and dark-skinned persons.** In contrast to pigmented nail streaks in Caucasians, dark-complected persons commonly exhibit melanonychia striata, and these streaks should not be routinely biopsied unless there has been some morphological change. Multiple streaks, streaks present on multiple nails, and those streaks that do not originate from the proximal nail fold are also unlikely to be melanoma in adults or children of any eth-

nicity, and these warrant clinical observation and a diligent search for another cause.<sup>1</sup> The single exception to this is metastatic melanoma to the nail bed, which may present as multiple pigmented lesions on the same or different nails.

**Children.** Subungual melanoma is quite rare in children of any race, though the incidence is not zero. As such, any new pigmented streak warrants observation by the physician, while pre-existing streaks unchanged for several years may be monitored by the parent and child. Any morphological change in a pre-existing streak or change in a new streak requires biopsy in all adults and children.

### Conducting a nail biopsy

When the clinician believes a diagnosis of subungual hematoma is likely, a simple office procedure and test will often confirm the diagnosis.<sup>6</sup> Any family physician can perform this procedure and test, saving the patient both time and the expense of obtaining a consultation, and sparing both patient and physician the anxiety of waiting days or even weeks to rule out a potentially life-threatening diagnosis.

**Procedure.** First, soak the hand (or foot) in warm water for 10 to 15 minutes to soften the nail plate. Next, drive a 3- or 4-mm punch biopsy through the nail plate, being careful not to injure the underlying nail bed, as any bleeding will invalidate the subsequent test. To minimize the risk of traumatizing the nail bed, avoid local anesthesia. Once you remove the specimen, grasp it with a pair of forceps and inspect it closely.

If the pigment does not adhere to the undersurface of the nail plate, but instead the biopsy specimen is clean, with the pigmented part being the nail bed itself, the diagnosis of subungual hematoma is virtually excluded, mandating a biopsy of the nail bed. If the underside of the nail specimen is pigmented, use a #15 blade to carefully scrape the pigment onto the sample surface of a standard hemocult card. Add a drop of water to the pigment scrapings; then the card is developed in the usual

fashion. A positive test indicates the presence of old blood and confirms the diagnosis of subungual hematoma. You should make sure to follow-up periodically to assure that the pigment recedes as the nail grows, as well as to confirm the absence of any further lesion is still required—keeping in mind that nail trauma precedes a large percentage of subungual hematoma.

### Staging

Once the diagnosis of subungual melanoma is confirmed the depth of invasion must be determined. Clark's level of invasion may be poorly defined in subungual melanoma, due to unique histopathological characteristics of the nail bed. Breslow's absolute depth correlates less closely with prognosis of subungual melanoma than with cutaneous melanoma, but tumor thickness has been found to be a good prognostic indicator of subungual melanoma.<sup>1</sup>

### ■ Treatment: Excision and amputation

Amputation or wide excision are the only accepted treatments for subungual melanoma. However, there is no clear consensus regarding the most appropriate type of excision, biopsy, or level of amputation.<sup>5</sup> Limb perfusion chemotherapy is thought to increase survival in selected cases.

### Outcomes

Subungual melanoma typically has a worse outcome than cutaneous melanoma, but the causes remain unclear. Anatomic location has often been cited as a prognostic marker, and many studies attribute the unusual location of subungual melanomas to their poorer prognosis.<sup>7</sup>

Some recent studies have found that worse outcomes are tied to the fact that subungual melanoma often presents at a much more advanced stage than cutaneous melanoma, while other studies have shown that even when controlled for diseased and stage, subungual melanoma

typically has a worse prognosis than cutaneous melanoma.<sup>1</sup> Racial differences in outcomes may also exist, as one study found that African Americans with subungual melanoma have a 3.5 times greater rate of death than Caucasians (95% confidence interval, 1.4–8.6). When rates were controlled for Clark and Wihm's level, they continued to have a 2.6 times greater rate of death.<sup>2</sup> This indicates that the greater mortality rate is not due entirely to either later stage of disease at presentation or to later diagnosis. ■

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**The only accepted treatments for subungual melanoma are amputation and wide excision**