Subungual Tumors: An Algorithmic Approach

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Upon completion of this CME activity, the learner should achieve an understanding of:

- The differential diagnosis of subungual tumors
- How to evaluate, diagnose, and treat different subungual tumors

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The presentation of benign and malignant subungual tumors often follows a final common pathway of nonspecific nail deformity; as such, delays in diagnosis are common. Therefore, it is imperative to have a high degree of suspicion for malignant lesions and an organized approach to subungual tumors. To that end, we present a diagnostic algorithm encompassing the most common benign and malignant subungual tumors, along with a summary of the presentation,

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SUBUNGUAL TUMORS (SUT) constitute a diverse group of pathologies, both benign and malignant. Presentation is variable, with a high likelihood of delayed or missed diagnosis. Therefore, it is imperative to have a high degree of suspicion for malignant lesions and an organized approach to SUT. To that end, we present a diagnostic algorithm encompassing the most common benign and malignant subungual tumors, along with a summary of the presentation, imaging, and treatment of these lesions. In this article, we also review the recent literature updates pertaining to SUT.

ANATOMY

The nail apparatus is made up of the germinal matrix, sterile matrix, nail plate, and nail folds (Fig. 1). The nail plate and nail bed are bordered by the eponychium, hyponychium, and paronychium. The germinal matrix creates nail substance and is located mainly under the proximal nail fold, with the most distal extent visible as the white lunula. Most of the subungual space lies between the nail plate and the terminal phalanx. This potential space is small; therefore, any lesions in the subungual space have the ability to both cause nail changes and erode the distal phalanx. Similarly, pathologies of the distal phalanx often alter the subungual space. Because nail deformity is often a final common pathway and therefore a nonspecific finding, imaging has an important role in differentiating among subungual tumors.

ALGORITHM

We present an algorithm for diagnosing the most common subungual tumors (Fig. 2). Diagnosis starts with clinical appearance. Vascular lesions can often be diagnosed by pathognomonic presentations; a small bluish lesion that is sensitive to touch and cold temperatures but decreases in sensitivity when the hand is elevated is likely a glomus tumor. When the diagnosis is in doubt but a vascular lesion is suspected, magnetic resonance imaging (MRI) is diagnostic. All suspected subungual tumors should have plain film imaging to examine for bone destruction. Plain films are also helpful in diagnosing bone and cartilage growth lesions that cause nail deformity. If a tumor-like condition such as a fungal infection or hematoma is suspected, appropriate treatment is initiated. However, if the condition has not resolved after 8 weeks of appropriate management, imaging and biopsy are recommended so as not to delay diagnosis. After a presumed diagnosis is made, excision of the lesion is indicated for diagnostic and therapeutic purposes. For malignant lesions, surgical treatment can include amputation of the affected part and sentinel lymph node biopsies, as discussed subsequently.

BONE GROWTH LESIONS

Subungual exostosis and subungual osteochondromas

Bony lesions causing nail deformity are most likely subungual exostoses or subungual osteochondromas[1] (Fig. 3). Controversy exists regarding whether exostoses and osteochondromas are the same entity; however, recent literature has demonstrated differing histologic features and a pathognomonic translocation, t(X;6)(q22;q13-14), associated only with subungual exostoses.[2] The most common presentation is that of a young adult female with a painful, rapidly growing, and nail-deforming mass on a finger or, more commonly, a toe. A history of trauma or chronic infection may be elicited, because reactive metaplasia is the presumed etiology.[2] Plain radiographs are often diagnostic. Subungual exostoses appear as a dorsal trabecular bony overgrowth with unclear or no continuity of bone cortex or marrow, compared with osteochondromas, which always show marrow and cortical continuity.[1] Magnetic resonance imaging can further define the lesion. Osteochondromas have high signal intensity on T2-weighted images because of the presence of hyaline cartilage cap, which differentiates it from exostosis, which has a hypointense fibrocartilage cap.[3] Both lesions are benign, and treatment is excision, to confirm the diagnosis and for pain relief. Recurrence rates have been quoted between 6% and 12%. Recurrence has been seen more frequently in cases where excision was done without curettage. Therefore, excision with a rongeur followed by curettage to clear the base is recommended.[2,4] On histology, consistent with imaging, a hyaline cartilage cap over endochondral ossification is seen in subungual osteochondromas, compared with fibrous ossification beneath a fibrocartilage cap in subungual exostoses.[2]

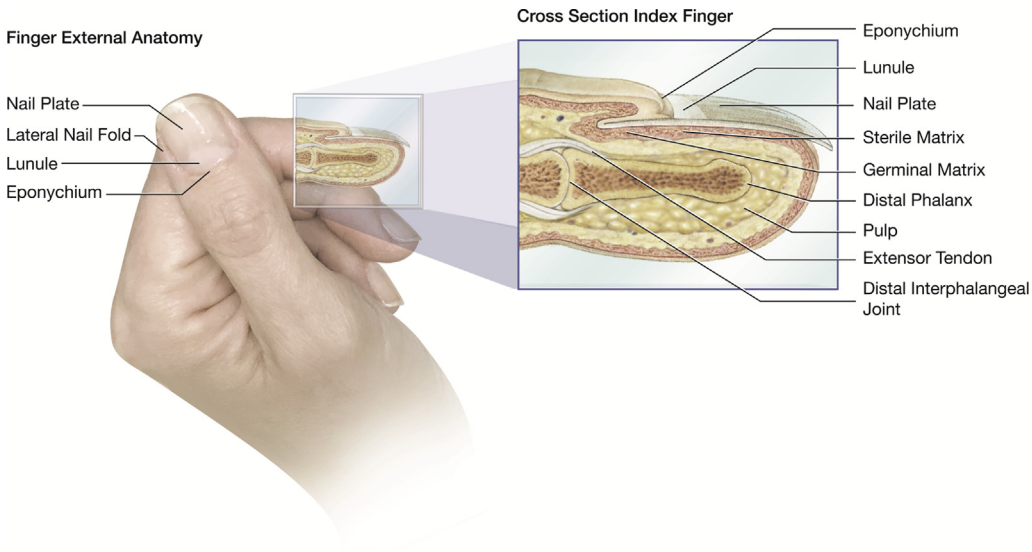

FIGURE 1: Normal anatomy of the nail unit.

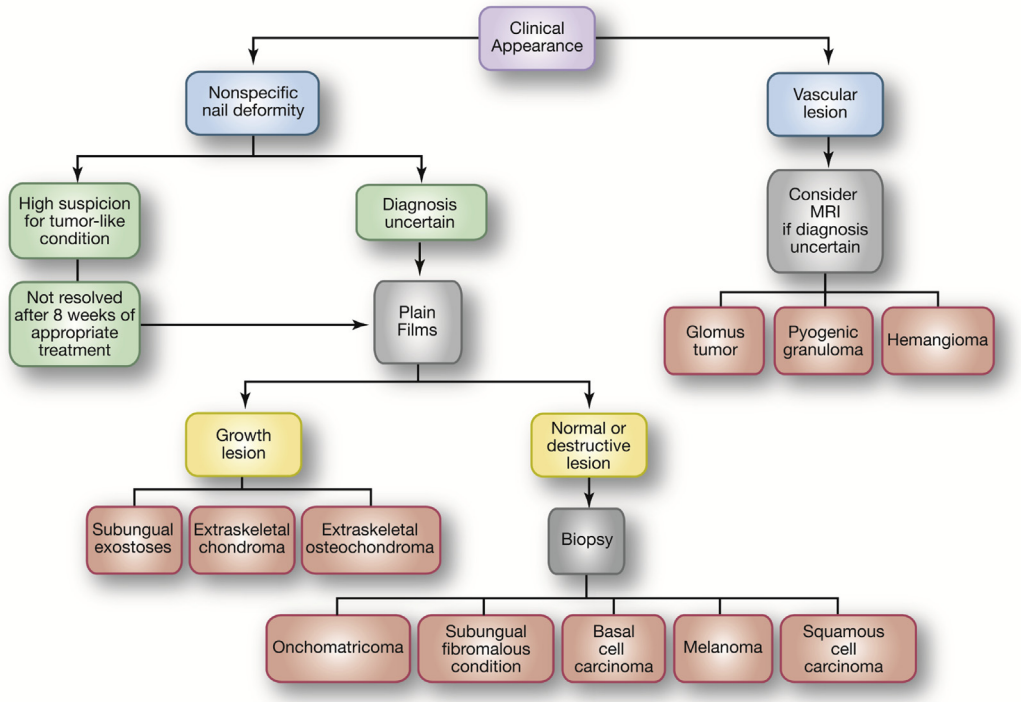

FIGURE 2: Algorithmic approach to subungual tumor diagnosis.

CARTILAGE GROWTH LESIONS

Extraskeletal chondroma

Although 80% of soft tissue chondromas are found in the fingers, subungual chondromas are rare.[5] They present as a slow-growing, variably mobile mass in an adult patient with an associated nail deformity.[1] Because chondromas are thought to arise from fibrous stroma, they can be seen on imaging as a small nodule of cartilage with foci of calcification that is not contiguous to underlying bone (Fig. 4). Treatment involves excision for diagnostic and therapeutic purposes, despite the benign behavior of the lesion. Lobules of hyaline cartilage surrounded by vascular connective tissue confirm the diagnosis of chondroma on histology.

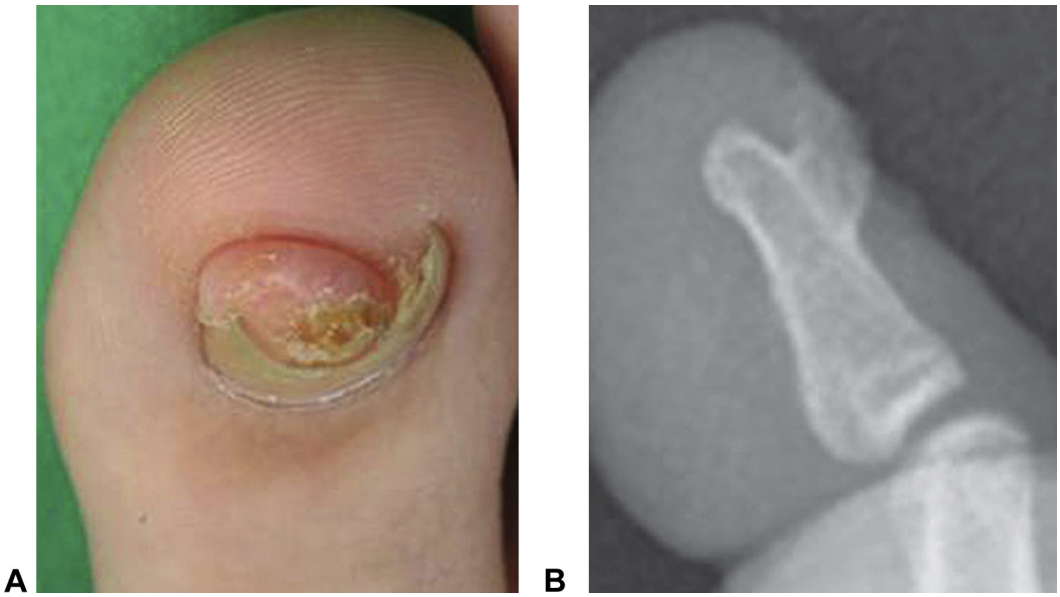

FIGURE 3: Subungual exostosis in an adolescent girl. **A** Exophytic tumor with nail destruction. **B** Lateral radiographs demonstrate dorsal metaphyseal outgrowth of trabecular bone with unclear marrow continuity. Reprinted from Baek HJ, Lee SJ, Cho KH, et al. Subungual tumors: clinicopathologic correlation with US and MR imaging findings. *Radiographics*. 2010;30(6):1621-1636,[1] with permission from the Radiological Society of North America.

VASCULAR LESIONS

Glomus tumor

Glomus tumors are generally benign, vascular hamartomas. They develop from the glomus body, a neuromyoarterial structure in the reticular dermis that is responsible for regulating circulation and thermoregulation within the skin. The most common presentation is that of an adult woman with a small, oval, bluish or reddish painful lesion visible through the nail plate. Upon examination, the lesion is sensitive to touch (Love's pin test), which reduces in sensitivity on elevation and applying a pneumatic tourniquet inflated to 250 mm Hg (Hildreth's test) and increases with cold temperatures[6] (Fig. 5). Because this presentation is relatively diagnostic, advanced imaging is needed mainly in situations in which clinical findings are equivocal. Chen et al[7] reported a sensitivity and specificity of 100% with color Doppler and a sensitivity of 90% and specificity of 50% with MRI, which make ultrasound the diagnostic test of choice. Glomus tumors appear as hypervascular lesions on ultrasound and hyperintense on T2 imaging.[1] Excision is the treatment of choice for glomus tumors. A midlateral approach, nail plate removal (Fig. 5), and the use of Mohs surgery have been described.[8] Recurrence rates between 4% and 15% have been reported.[6] Because data on surgical excision using Mohs technique are limited to case reports, the superiority of one excision technique over another cannot be assessed. Glomangiosarcomas represent about 1% of glomus tumors and are locally aggressive but rarely metastasize.[9] Treatment for these malignant tumors remains wide local excision. The most common histopathology is a benign tumor with vascularity, glomus cells, and smooth muscle cells. Malignant tumors are differentiated from benign forms on histology by a higher mitotic rate and nuclear atypia.[9]

Hemangioma

Hemangiomas of the subungual space present most commonly as a bluish tinged nail with pseudo-clubbing (Fig. 6). Incidences of congenital hemangioma have also been reported. Advanced imaging is diagnostic. On T2-weighted MRIs, hemangiomas appear as a high−signal intensity lesion in the papillary dermis or epidermis (unlike the reticular dermis for glomus tumors).[1] There is no consensus regarding treatment of subungual hemangiomas. Excision, shave biopsy with cauterization, and sclerotherapy have been reported.[4]

Pyogenic granuloma (lobular capillary hemangioma)

Primary clinical characteristics distinguishing pyogenic granulomas (PGs) from other subungual vascular tumors are their rapid growth and tendency to bleed (Fig. 7). The etiology can be reactive after trauma or peripheral nerve injury.[4,10] Less commonly, PGs are seen in relation to medications such as retinoids and antiretrovirals, or related systemic inflammatory

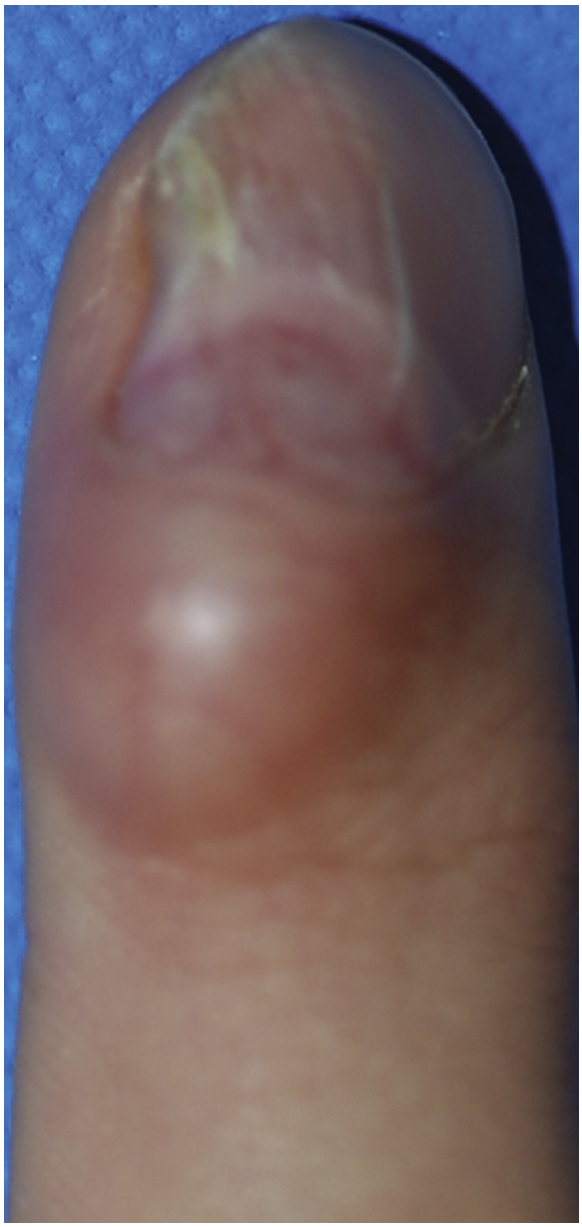

FIGURE 4: Soft tissue chondroma of left index finger in a young man, causing a dystrophic nail. Reprinted from Baek HJ, Lee SJ, Cho KH, et al. Subungual tumors: clinicopathologic correlation with US and MR imaging findings. *Radiographics*. 2010;30(6):1621-1636,[1] with permission from the Radiological Society of North America.

states.[10] Imaging can aid in diagnosis. Pyogenic granulomas have characteristics similar to those of glomus tumors or hemangiomas on MRI. Ultrasound can be a more specific test, because PGs are more echogenic than other subungual vascular tumors.[1] Although reports exist of successful treatment with sclerotherapy or topical steroids, standard treatment is excision, for diagnostic as well as therapeutic purposes. We do not recommend treatments that do not provide tissue diagnosis, even for this benign condition, because multiple cases have been reported of amelanotic melanoma and other malignant tumors masquerading as a PG.[10] Histologic analysis reveals branching capillary lobules within a mass of inflammatory cells and connective tissue.

CYSTIC LESIONS

Epidermal inclusion cyst

Epidermal inclusion cysts are common and can present as a mass with pseudo-clubbing and nail deformity. Bone erosion or compression fractures can also occur in the distal phalanx. These cysts are thought to result from trauma, leading to the subdermal entrapment of epidermal tissue. Ultrasound imaging can confirm the suspected diagnosis; the cysts will appear as hypoechoic subungual round masses without internal vascularity.[1] Excision is usually curative, although there may be recurrences. On histology, a stratified squamous cyst lining is seen, with a laminated keratin center.

Myxoid cyst

The vast majority of myxoid cysts arise owing to osteoarthritis and degeneration of the distal interphalangeal (DIP) joint capsule, leading to egress of joint fluid. The frequency of the subungual location for this common pathology is likely underreported because of unfamiliarity with the presentation, but it has been estimated to be 8% to 30% of myxoid cysts.[11] These cysts usually present as a subungual mass beneath the proximal nail fold, causing increased nail curvature or other nail deformity, red or blue nail discoloration, and sometimes pain (Fig. 8). Intermittent discharge of mucoid joint fluid is common.[11] Plain films are usually all that is required, because an associated osteophyte at the DIP joint is suggestive of the diagnosis. Ultrasound imaging is nonspecific, and although MRI can be diagnostic, such advanced imaging often is not required. Definitive treatment in adults includes surgical excision, including any associated offending osteophytes; nonsurgical treatments such as needle aspiration or sclerosant have been reported but have a higher recurrence rate.

SOLID LESIONS

For nonvascular, solid subungual tumors, imaging is generally nonspecific. Therefore, biopsy is generally the first step in managing any solid subungual lesion. Even lesions that appear infectious should be biopsied expeditiously if they do not resolve with a short course of appropriate therapy. A good principle is to

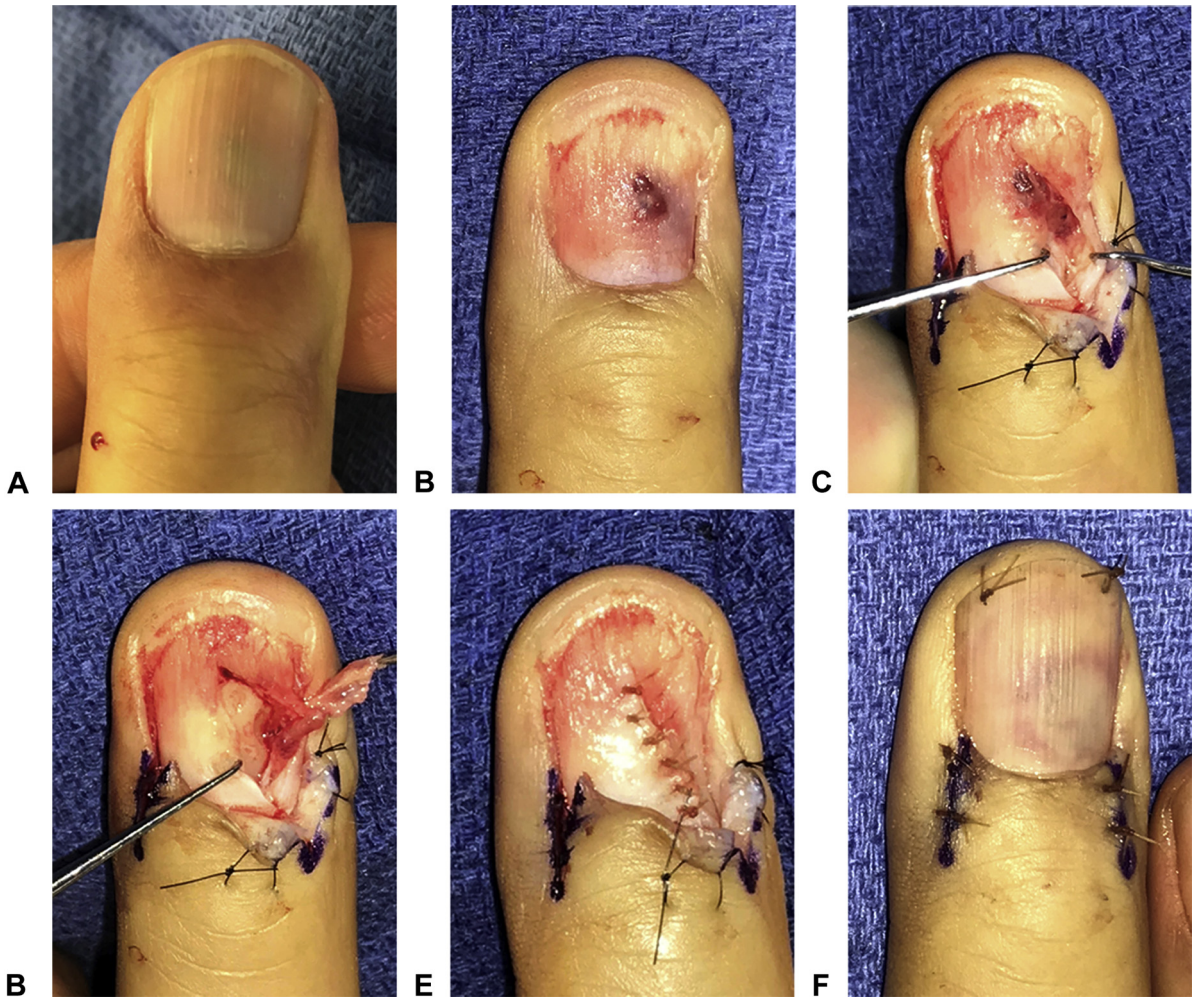

FIGURE 5: **A** Glomus tumor in the index finger of a woman, presenting with a small, bluish, painful lesion. **B**–**D** Excision of the tumor through a nail plate removal approach. **E** Primary closure of the sterile matrix with absorbable suture to prevent future nail deformity. **F** Stenting of the eponychial fold with the removed nail plate to prevent scarring and improve the chances for normal nail regrowth.

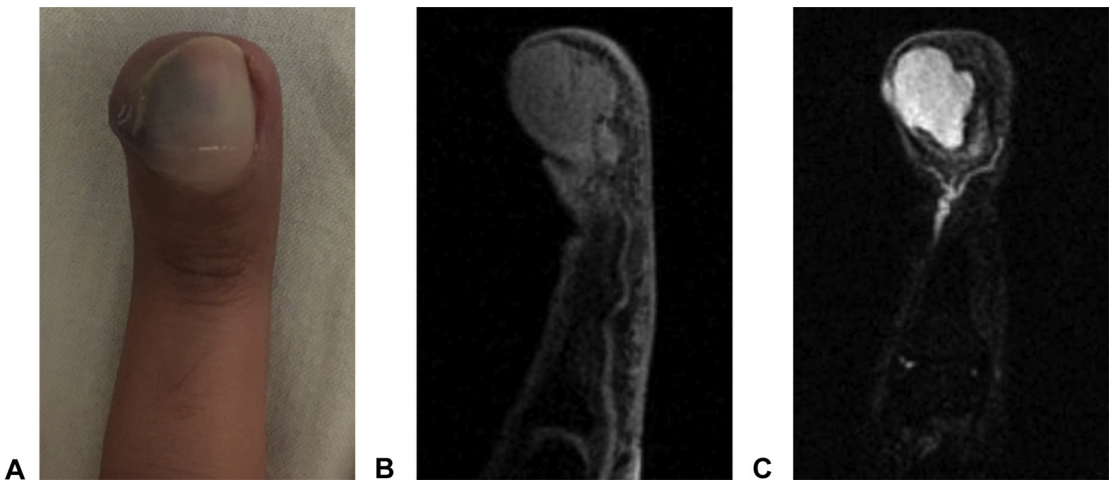

FIGURE 6: **A** Hemangioma in the middle finger of a woman, causing nail discoloration and elevation. Upon MRI, an expansile, homogeneous, lobulated mass is seen that is **B** hypointense on T1 images, and **C** hyperintense on T2 images. On magnetic resonance angiography sequence, the lesion was enhanced centrally and then gradually filled the periphery.

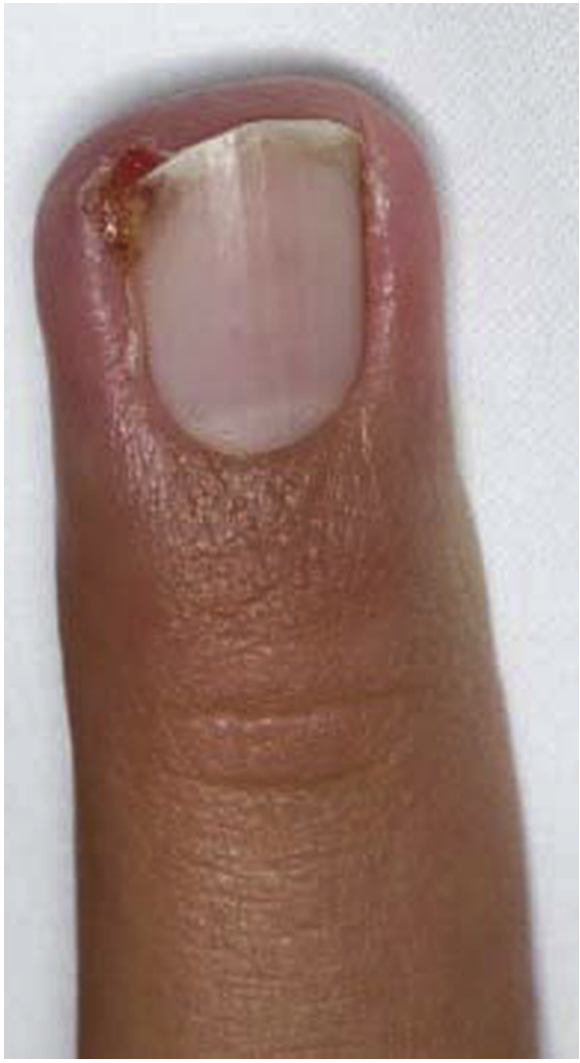

FIGURE 7: The presentation of lobular capillary hemangiomas is variable. In this case, a periungual vascular appearing papule is seen. Reprinted from Willard KJ, Cappel MA, Kozin SH, Abzug JM. Benign subungual tumors. *J Hand Surg Am*. 2012;37(6):1276-1286,[4] with permission from The American Society for Surgery of the Hand.

have no more than 8 weeks between presentation and a tissue diagnosis for any subungual lesion.[12] The type of biopsy (excisional, shave, or punch) depends on the practitioner's level of suspicion for malignancy. Characteristics such as induration, pigmentation, and size greater than 6 mm are all concerning and should prompt a punch biopsy so that the lesion depth can be determined. A standard technique for punch biopsies is demonstrated in Figure 9.[13] At our institution, shave biopsies are not performed for subungual lesions. If greater than 3 mm of tissue is desired for sampling, we use a longitudinal incision and meticulous closure to avoid a future permanent nail deformity.

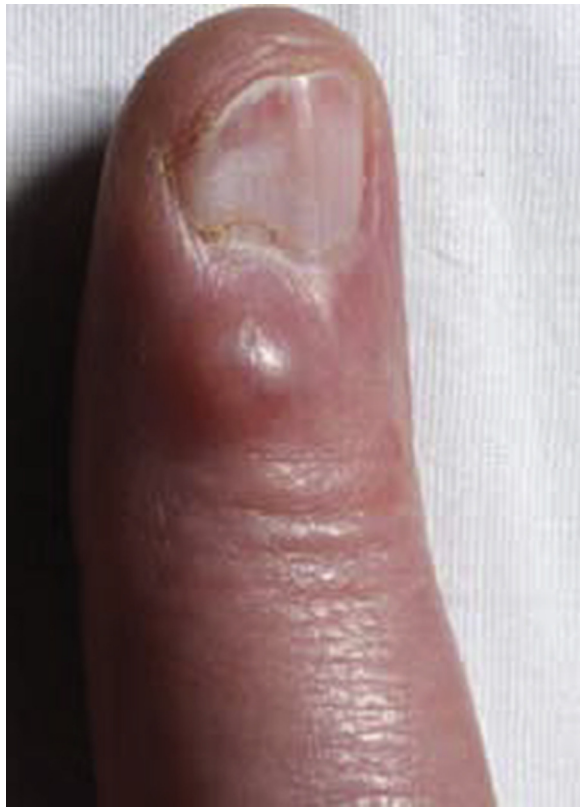

FIGURE 8: Myxoid cysts present as a subungual, cystic-appearing mass under the proximal nail fold, causing nail deformity. Intermittent discharge from the cyst is common. Reprinted from Willard KJ, Cappel MA, Kozin SH, Abzug JM. Benign subungual tumors. *J Hand Surg Am*. 2012;37(6):1276-1286,[4] with permission from The American Society for Surgery of the Hand.

Subungual fibromatous condition

Subungual fibromas are almost exclusively found in adult patients with tuberous sclerosis; they occur in up to 50% of cases in this population.[14] The most common findings are hyperkeratosis and a pink or red papule that lifts or otherwise deforms the nail plate (Fig. 10). Subungual neurofibromas present similarly and are found in patients with neurofibromatosis or are nonsyndromic but related to trauma.[4] Neurofibromas are usually painless. Treatment for subungual fibromas and neurofibromas is surgical excision. On histology, both have thick stromal collagen, although the neurofibromas will be rich in Schwann and other perineural cells.

Onchomatricoma

Onchomatricomas are rare, benign, and slow-growing tumors of the nail matrix. The typical clinical presentation is an adult patient with a solitary, painless subungual mass associated with

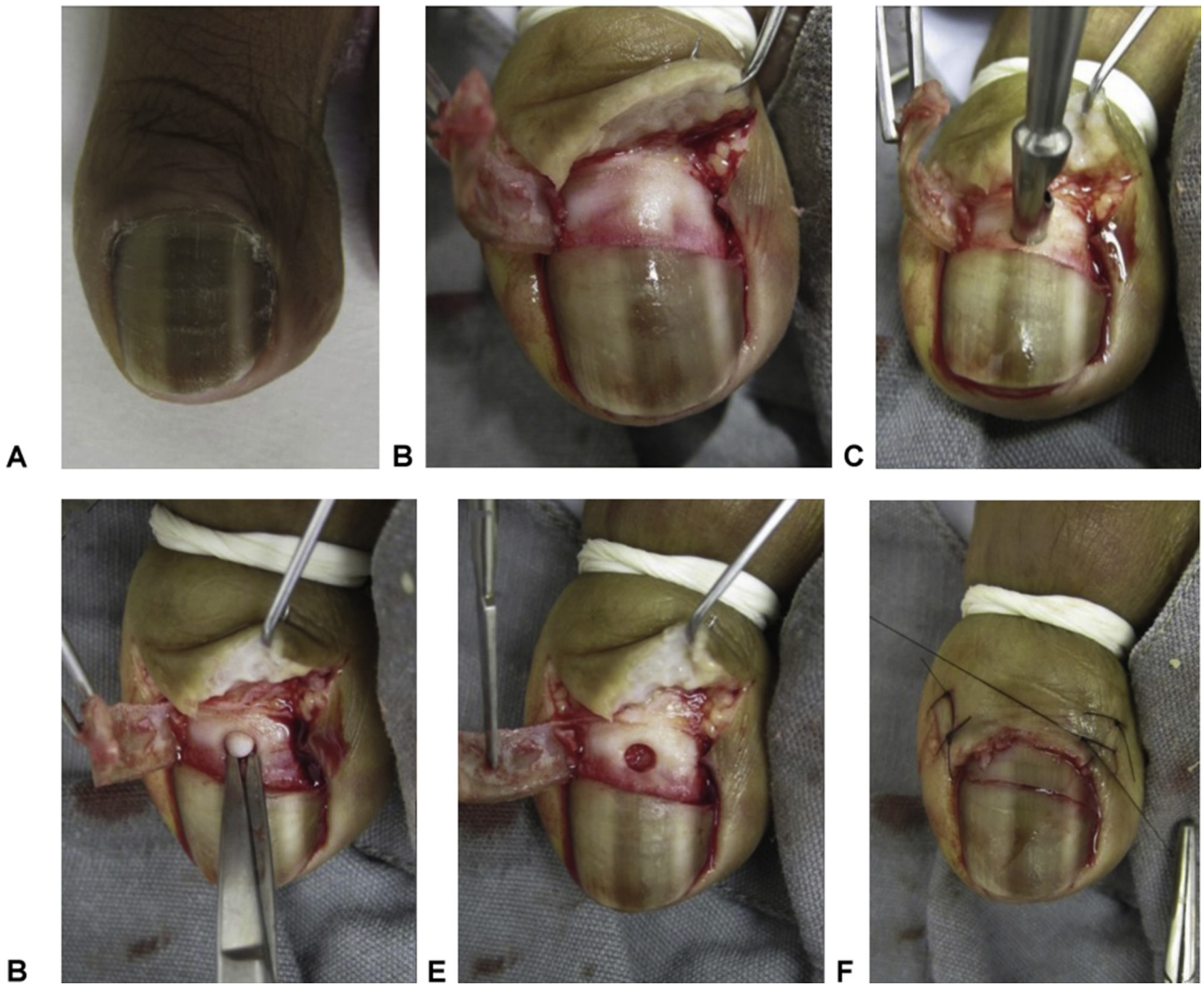

FIGURE 9: A Punch biopsy of medial melonychia. **B** The nail plate should be removed and **C**–**E** a 3-mm punch biopsy should be performed of the affected nailbed. **F** The nail plate can then be sutured in place to protect the nail bed. If more than 3 mm of tissue sampling is required, the biopsy site should be closed primarily or reconstructed in a delayed fashion to mitigate future nail plate deformity. Reprinted from Domínguez-Cherit J, Gutiérrez Mendoza D. Best way to perform a punch biopsy. *Dermatol Clin*. 2015;33(2):273-276,[13] with permission from Elsevier.

onychodystrophy, splinter hemorrhages, and a yellowed nail.[15] These tumors can be pigmented, and thus confused for subungual melanomas. As a tumor of the nail matrix, the underlying bone is not involved on plain radiographs. Magnetic resonance imaging demonstrates a characteristic Y-shaped deformity in the proximal nail plate. The treatment of onchomatricomas is excision. Recently, a small case series demonstrated successfully using Mohs micrographic surgery to improve tissue conservation of the nail unit.[8] Histopathology revealed a fibroepithelial tumor with finger-like projections that perforated the nail plate and a biphasic growth pattern that mimicked normal nail matrix histology.

Basal cell carcinoma

Subungual basal cell carcinoma is extremely rare, with fewer than 20 reported cases in the literature. Reported presentations include long-standing pigmented or ulcerated lesions with an indolent course. Diagnosis is often delayed. Basal cell carcinoma rarely metastasizes but it can be locally aggressive, and treatment is excision to clear margins. Surgical excision of basal cell carcinoma has a 5-year cure rate of 99%.[16]

Squamous cell carcinoma

Squamous cell carcinoma (SCC) is the most common primary malignancy of the subungual

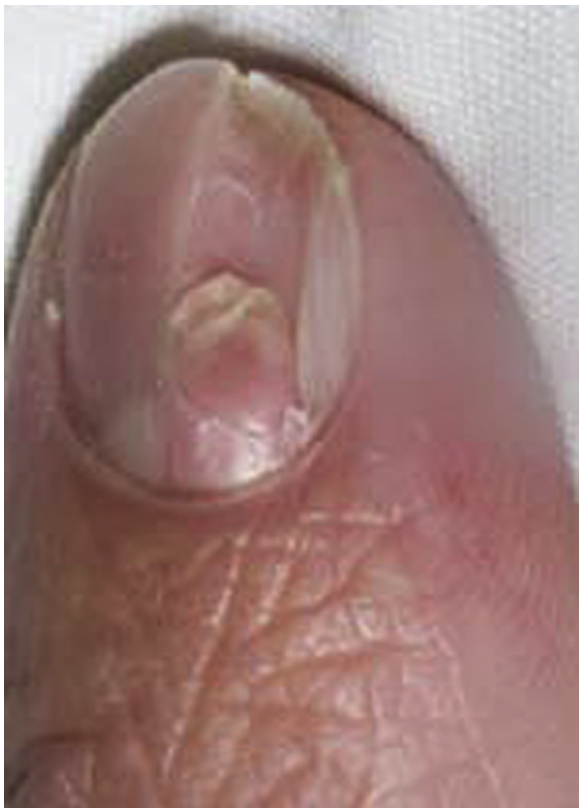

FIGURE 10: Subungual fibromas commonly present as a hyperkeratotic pink or red papule that lifts or otherwise deforms the nail plate. Reprinted from Willard KJ, Cappel MA, Kozin SH, Abzug JM. Benign subungual tumors. *J Hand Surg Am.* 2012;37(6):1276-1286,[4] with permission from The American Society for Surgery of the Hand.

space.[17] It commonly presents as onychodystrophy or discoloration, hyperkeratosis, ulceration, or a mass and is associated with nonspecific pain. It can easily be misdiagnosed as an infection (Fig. 11). Sun exposure and human papilloma virus infection have also been implicated in the development of subungual SCC. At the time of diagnosis, there is often substantial local invasion, with involvement of the distal phalanx in 20% to 50% of cases.[1] A recent review of the literature[17] found a 1.6% rate of distant metastasis, 40% of which were fatal. Biopsy is the diagnostic test of choice. Histopathology reveals keratin pearls, atypical pleomorphic keratinocytes with frequent mitoses, and perinuclear vacuolization. Plain films should be obtained routinely to evaluate bone involvement.[1] If invasive cancer is suspected, a clinical examination of regional nodal basins and a chest computed tomography scan ahead of any definitive resection is recommended.[17] Whereas topical treatments, phototherapy, and radiation therapy have all been reported as treatment for subungual SCC, wide excision is the standard of care.[18]

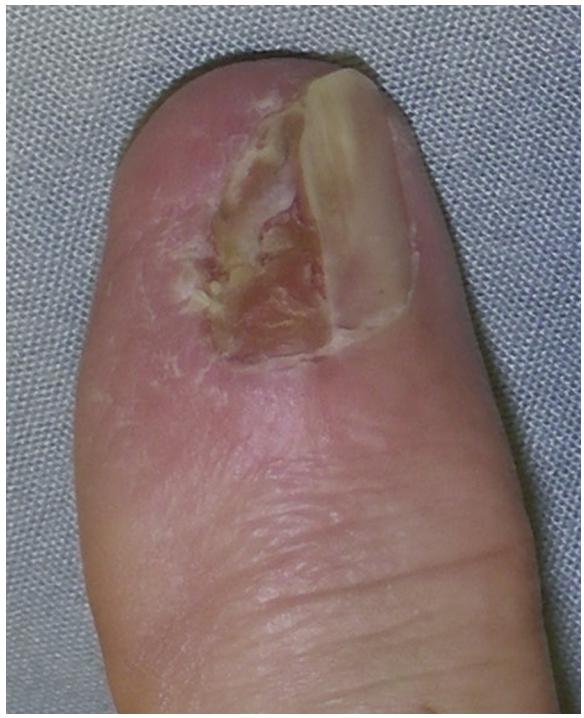

FIGURE 11: Subungual squamous cell carcinomas have a variable presentation. The most common presentations include nail plate destruction with hyperkeratosis, mimicking a fungal infection.

Mohs surgery has been used to treat subungual SCC, although a higher recurrence rate has been noted with this method of excision compared with surgical excision.[8,17] No consensus exists regarding the recommended excision margins; however, if bone is involved, amputation is recommended to at least the level of the first uninvolved joint. Recurrences usually occur within the first year; thus, follow-up every 6 months for the first year, and then annually for 2 years, is recommended.[18]

Melanoma

Malignant melanoma is by far the most lethal of the subungual malignancies, which makes it an extremely important differential diagnosis for any subungual lesion, regardless of pigmentation. Poor prognosis is associated with node positivity, ulceration, and amelanosis. Between 12% and 33% of subungual melanomas are node-positive on diagnosis, with a median survival of just 4.6 years.[19] Because sun exposure is not a risk factor for subungual melanoma, compared with other cutaneous melanomas, different races are affected equally. Pigmented lesions are concerning for melanoma (Fig. 12), particularly pigmentation of the eponychium (Hutchinson sign). However, subungual melanomas can often be amelanotic and have a notoriously variable presentation.[19] Imaging is

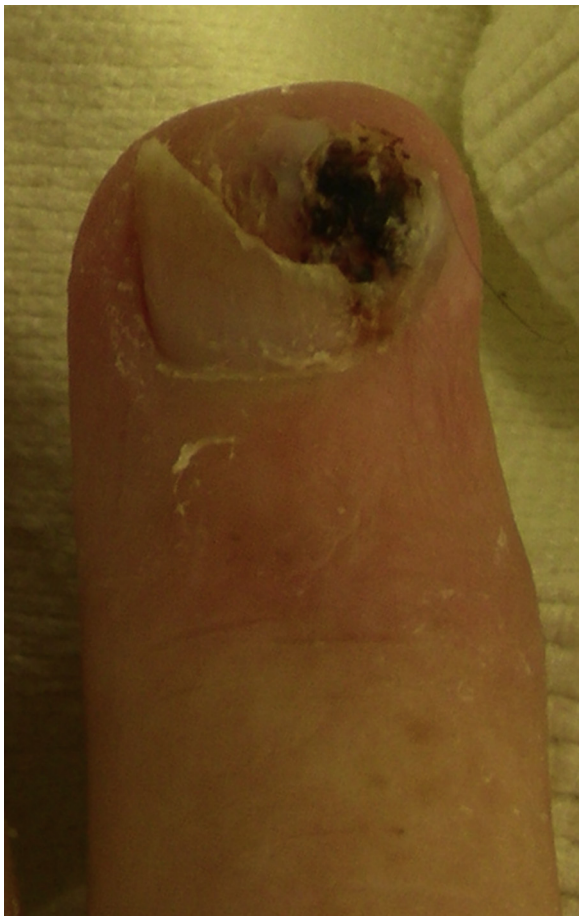

FIGURE 12: Pigmented lesion on the left index finger of a man, which is concerning for melanoma.

mostly nonspecific, but findings of intratumoral hemorrhage on advanced imaging should heighten suspicion.[1] Biopsies of the nail matrix should be full thickness to determine the depth of invasion if the biopsy reveals melanoma. Full-thickness biopsies should be elliptical and longitudinally oriented with a 1- to 3-mm margin. Shave biopsies have been described; however, if the biopsy reveals melanoma, surgical planning can be seriously jeopardized (Table 1). Hence, shave biopsies should be used only in instances of low suspicion. Sterile matrix lesions distally can be biopsied with a punch biopsy with minimal risk for nail deformity. On histopathologic analysis, spindle-shaped melanoma cells infiltrate the dermis, with elongation of rete ridges and lentiginous proliferation of atypical melanocytes. Further studies are indicated once diagnosis and depth of invasion are confirmed. For biopsy specimens greater than 1 mm thick, chest radiographs and liver function tests are recommended; for specimens greater than 4 mm thick, a computed tomography–positron emission tomography and brain MRI are routinely performed.

TABLE 1. Current National Comprehensive Cancer Network Guidelines for Melanoma Excision Margins Based on Depth of Lesion Upon Biopsy

Tumor Thickness, mm	Recommended Clinical Margins, cm
In situ	0.5–1.0
≤1.0	1.0
1.1–2.0	1.0–2.0
2.1–4.0	2.0
>4.0	2.0

Recent reviews have not demonstrated a correlation between the depth of subungual melanoma and node positivity.[19] Hence, sentinel lymph node biopsy (SLNB) is recommended for all invasive subungual melanomas.[19] This recommendation is controversial, and certain resources including the National Comprehensive Cancer Network still stratify the recommendation for SLNB based on a Breslow thickness of greater than 1.0 mm, or greater than 0.75 mm for melanomas with high-risk features.[19] If the SLNB is positive, a full node dissection is recommended. The most current data available, from the Multicentre Selective Lymphadenectomy Trial 2,[20] suggested that completion lymphadenectomy after a positive SLNB decreases lymph node field relapse but does not confer a survival benefit. Thus, SLNB is the strongest predictor of survival but does not affect it. Until further evidence is brought to bear on the subject, SLNB should be offered to all patients with invasive subungual melanoma for staging of regional nodes.

The historical treatment recommendation for invasive subungual melanoma was to amputate at the phalanx proximal to the area involved with the primary lesion.[21,22] For the nail bed, amputation would thus be at the level of the proximal interphalangeal joint or metacarpophalangeal joint for the thumb. Multiple case series have since been published demonstrating equivalent oncologic outcomes and improved function with amputations occurring at the first uninvolved joint, usually the DIP in fingers and the interphalangeal for the thumb.[19,21] Even greater tissue-sparing approaches have been described, with partial distal phalanx amputations and wide local excisions, and with equivalent recurrence-free survival.[23,24] However, as Cochran et al[22] noted in their review of this topic, a lack of important data (tumor-specific information and tumor depth) in these reports precludes drawing real conclusions about the safety of a more conservative tissue resection.

Tissue-sparing approaches with wide local excision and skin graft are more accepted for melanoma *in situ*. Whereas surgical treatment remains the standard of care for melanoma, recent technological advancements have led to identifying genetic mutations for targeted molecular therapies. Specifically, for hand and foot melanomas, c-Kit–positive mutations have been identified as having an increased prevalence, which suggests new avenues for biologic therapy in the future.[19]

This article presents a review of the most common subungual tumors, both benign and malignant. The importance of tissue diagnosis of any lesion that does not resolve within 8 weeks with appropriate treatment is emphasized. Although all roads lead to biopsy, organizing one's thoughts by imaging findings and general tumor characteristics can narrow the differential diagnosis and help determine whether a complete excision or full-thickness biopsy is more appropriate. Finally, particularly in the digits, tumor resection must be balanced with preservation of hand function. This must be done without compromising tumor excision in malignant lesions. The goals of reconstruction include providing a durable, sensate reconstruction with consideration given to donor site morbidity, patient preferences, profession, hand dominance, and comorbidities. It is often better to amputate part of the finger than to compromise overall hand function with a stiff finger.

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