Subungual tumors

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Case Report

A 60-year-old man described a 15-year history of intermittent drainage from beneath the nail plate of his left long finger. The drainage began years after the subject sustained an injury in which a thorn became embedded beneath the nail. The patient had performed a number of self-debridements over the years. He had taken oral antibiotics on multiple occasions. In the 6 months prior to presentation, the drainage became more constant along with pain and erythema.

On presentation, the nail plate had a central, 2-mm defect with granulomatous tissue underneath and longitudinal melanonychia. The nail plate was tender and minimal serosanguinous drainage could be expressed. The remainder of the finger and nail complex appeared normal. Radiographs of the finger were normal.

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Under local anesthesia the nail plate was removed. Inspection of the sterile matrix revealed a longitudinal, 3-mm strip of abnormal tissue along the length of the nail. In addition, there was chronic inflammatory tissue surrounding the area near the defect in the nail plate. No foreign body was found. The abnormal tissue was excised and sent to pathology. Cultures were obtained and sent for aerobic and anaerobic bacteria, fungal elements, and mycobacteria.

The patient was seen in the clinic 10 days later (Fig. 1). The surgical pathology report revealed a moderately differentiated squamous cell carcinoma with features suggestive of focal invasion and extension to the border of the resection.

An MRI of the hand (Fig. 2) revealed increased signal within the subungual region with no evidence of involvement of the distal phalanx.

The patient returned to the operating room approximately 2 weeks after the initial surgery. The entire nail complex was excised en bloc with a 2-mm margin of normal tissue (Fig. 3). The final pathology report confirmed the diagnosis of focal squamous cell carcinoma with superficial invasion and no extension to the margins (Fig. 4). The wound was covered with a dermal substitute and placed in a soft dressing. Three weeks later a full thickness skin graft was applied to the site of resection. Six weeks following the placement of the skin graft, the site had fully healed (Fig. 5). At 9 months post-resection, the patient was pain-free and had no sign of tumor recurrence.

Squamous Cell Carcinoma

Squamous cell carcinoma (SCC) is the most common primary neoplasm of the hand and subungual area. It accounts for approximately 90 % of all malignancies involving the hand

Fig. 1 The patient's left long finger 1 week after initial debridement and biopsy. The nail was removed, and abnormal tissue was biopsied, returning as squamous cell carcinoma

[8]. However, the incidence of SCC of the subungual region is quite low [12, 24, 26, 43, 45]. Squamous cell carcinoma in the subungual region is a slow-growing tumor with a variable presentation. As a result, SCC is often misdiagnosed as a more benign process such as onychomycosis, verruca vulgaris, or paronychia infection [27]. The time between the initial presentation and definitive diagnosis averages 24–25 months [12]. It occurs more frequently in men after the fifth decade of life and is typically limited to a single digit [8].

The causes of squamous cell carcinoma are not known. Potential etiologies include ultraviolet radiation [45], human papillomavirus infections, repeated trauma, chronic infections, human immunodeficiency virus, and epidermal dysplasia [24, 27, 45].

The presenting symptoms of SCC include pain, purulent drainage, bleeding, nail plate dyschromia, nail deformity,

Fig. 3 The nail bed was excised en bloc and sent for pathology review. The specimen was determined to be SCC with acceptable margins. The clear margins allowed for the distal phalanx to be preserved

paronychia, and ulceration [24, 36]. These symptoms are not pathognomonic for SCC, and the differential should include paronychia infections, chronic osteomyelitis of distal phalanx, pyogenic granuloma, primary syphilitic chancre, subungual hematoma, epidermoid cyst, subungual glomus tumor, enchondroma of distal phalanx, giant cell tumor, amelanotic melanoma, nevus, fibroma, metastatic tumors, and herpetic whitlow [8]. Even though subungual SCCs are typically low-grade malignancies, bony involvement and metastasis to regional lymph nodes may occur, with approximately 18 % of primary tumors spreading to bone [8, 26, 43].

A definitive diagnosis of subungual SCC is made by biopsy. Treatment options include limited or wide surgical excision, or amputation depending on the involvement of the soft tissue and underlying distal phalanx. Rosen et al. recommended wide surgical excision when the medial aspect of the nail unit is involved or when >50 % of the nail unit is involved with a lateral lesion [36]. Mohs micrographic surgery is preferred in some situations as it allows for histologic verification

Fig. 2 **a** Sagittal T2-weighted MRI of the left hand, which revealed increased signal within the subungual soft tissue and enhancement of the distal middle finger but no evidence of involvement of the distal phalanx. **b** Coronal T2-weighted MRI of the left hand, which revealed increased signal within the subungual soft tissue and enhancement of the distal middle finger but no evidence of involvement of the distal phalanx

Fig. 4 The pathology slide showing focal squamous cell carcinoma in the nail bed en bloc resection

of tumor removal at the time of surgery [14, 45]. In small case series, radiation therapy as primary treatment was effective with low recurrence rates [14, 36]. Currently, there are no evidence-based guidelines on how long to monitor patients with subungual SCC for recurrence.

Malignant Melanoma

Subungual melanoma arises from the nail bed and accounts for 1 to 3 % of all cutaneous melanoma in white patients, and up to 20 % of melanoma in individuals with highly pigmented skin [11]. The tumor most commonly presents on the thumb [4, 30].

Hutchinson initially described subungual melanoma in 1886 when he referred to “a rare form of disease of the nail bed which is malignant, and usually takes the type of melanotic sarcoma” [22]. Although it is rare, early identification is important, as the 5-year survival ranges from 40 to 74 % [11, 30].

Fig. 5 Nail bed at 6 weeks following placement of a full thickness skin graft

The four types of melanoma include superficial spreading, nodular, lentigo maligna, and the least common, acral lentiginous. Although each is possible in the subungual tissue, acral lentiginous melanoma is the most prevalent in that location [23, 30]. Forty-five percent of the patients in the Blessing et al. study and 74 % of patients in the Kato et al. study were shown to have acral lentiginous type tumors [4, 30].

The prognostic factors for subungual melanoma include Clark and Wihm’s levels, the presence of ulceration, age, gender, race, and the staging of the tumor at diagnosis [4, 11, 30]. In the studies evaluated, the patients are older (average ages 55–65) and have a darker skin complexion, but the sex dominance varied by study [4, 30, 34]. Due to the unique anatomy of the nail bed and the dermis abutting the periosteum of the distal phalanx, it is difficult to classify lesions based on Breslow’s system [30, 37]. Although the tumor is similar to other cutaneous variants, the anatomic location of the primary tumor is important for the prognosis of melanoma, with distal lesions having a better prognosis than more proximal lesions [4].

The symptoms of subungual melanoma are vague, as are the findings, including discoloration of the nail, a non-healing wound, a mass, a split in the nail, and bleeding from the nail. These lesions can lack pigmentation and appear relatively benign [11, 30, 34]. The pigmentation of the surrounding nail tissue, called Hutchinson’s sign, paired with nail lifting is indicative of melanoma [22]. The continued linear growth of dark bands subungually, or longitudinal melanonychia, is indicative of melanoma, especially if it is greater than 3 mm wide or wide at the base with distal tapering [23, 37]. Some studies report an increased risk of melanoma secondary to trauma, however, the Cohen study reported trauma as an inciting factor in only 10 % of patients [11]. The connection to trauma has been attributed to the release of fibroblastic growth factor in the healing wound [34]. However, because trauma is common and melanoma is rare, a causal effect cannot yet be drawn [4].

The non-specific findings of subungual melanoma cause a delay in diagnosis averaging 24 months or longer [4, 11, 30, 34]. Common misdiagnoses include onychomycosis, trauma, pyogenic granuloma, paronychia, vascular tumor, squamous cell carcinoma, nevi, or a hematoma [11, 21, 34]. Since the melanocytes of the nail bed are less dense and do not produce melanin, there is an increased likelihood of an apigmented melanoma, which can also increase the delay in diagnosis [37]. Whatever the delay, the disease advances leading to ulceration and metastasis. In one study, only 7 % of the population had stage I disease upon presentation with subungual melanoma versus 80 % of patients with non-subungual cutaneous melanoma [34]. Metzger et al. quantified this delay in diagnosis of subungual melanoma, showing a decrease in the patient’s 5-year life expectancy from 90.9 to 68.5 % [28].

The diagnosis of subungual melanoma begins with a biopsy of the lesion after 4–6 weeks of a newly observed pigmented nail bed lesion [21]. The biopsy is performed down to the periosteum with margins to account for the lateral growth of the lesion [30]. In 2004, Thomas et al. showed a decrease in local–regional recurrence when cutaneous tumors less than 2 mm thick were excised using 3-cm margins as compared to a 1-cm margin [38]. Due to the special nature of the nail bed, these margins are not possible and amputation is recommended following definitive biopsy; a position identical to Hutchinson's in 1886 where he stated “early amputation is demanded” [22, 30].

Debates over amputation type are ongoing. In 1996, Quinn et al. showed no statistical difference between proximal and distal amputations [21, 34]. In 2003, Moehrle et al. demonstrated a three-dimensional histological approach to acral lentiginous melanoma that avoids the need for amputation, without increasing the risk of recurrence [29]. Due to the narrow margins of this approach, it is not acceptable for the wider superficial spreading melanoma and lentigo maligna [29]. In those instances where the lesion does recur, amputation is recommended (Fig. 6).

The role of sentinel lymph node biopsy and elective lymph node dissection remains controversial. O'Leary et al. showed no significant 5-year survival benefit to elective node dissection in patients with intermediate thickness (0.76–4 mm) subungual melanomas [30]. Daly et al. caution, however, that although 70 % of their patients were felt to have normal regional lymph nodes, 19 % were positive upon microscopic exam [13]. Although the survival may not differ, the recurrence rates are significantly different when comparing a positive sentinel lymph node versus a known sentinel lymph node metastasis [10]. Logically, the rate of metastasis increased with increasing tumor thickness [10]. Clary et al. suggested that since the likelihood of metastasis was low when tumor thickness was less than 1.5 mm, the treating physician should forgo sentinel lymph node biopsy.

Fig. 6 A recurrent malignant melanoma on a right thumb after a subungual excision. The dark dot on the distal thumb is the lesion. The recurrence was managed with amputation. Picture courtesy of Dr. Peter Murray

Glomus Tumors

A 37-year-old gentleman presented with a 4-year history of hypersensitivity to cold in the left fifth finger. There was small dark blue lesion at the proximal nail fold, on the left fifth digit (Fig. 7). There were no nail changes. The Love's test was positive and cold water increases the pain.

An MRI showed a 3.5×1.9 -mm isointense mass deep at the base of the nail bed on the fifth digit (Fig. 8a, b).

At surgery a freer elevator was used to remove the nail from the nail bed of the right small finger. A small, pigmented lesion was noted in the proximal aspect of the nail bed (Fig. 9). The thin, superficial layer of nail bed overlying the lesion was incised. The tumor was easily shelled from the nail bed. The incised portion of the nail bed was loosely re-approximated with 6-0 chromic and the nail plate was replaced and suture in place. Pathology confirmed the diagnosis of a glomus tumor. Three years later, the patient is pain free, showing no signs of recurrence.

In 1812, glomus tumors were first identified by Wood as a tumor of the subcutaneous tissue that was small, firm, painful, and sensitive to temperature change [44]. Although glomus tumors can be found throughout the body, 75 % are found on the hand, 25–65 % of which arise in a subungual location [7]. The prevalence is quoted as ranging from 1 to 4.5 % of all tumors of the hand [5, 19, 33]. Eighty-eight percent of the patients in the Van Geertruyden et al. study were women with an average age of 44 years [9, 42].

The glomus body is an end organ arteriovenous anastomosis composed of neuromyoarterial tissue that is thought to regulate skin temperature and circulation [7, 8, 39]. The tumors are described as a deep red, blue, or purple, encapsulated, and less than 1 cm in diameter, averaging only a few millimeters [7, 9]. They can occur in clusters, or can be isolated.

Fig. 7 Right fifth finger showing the point of maximal tenderness in a patient with pain and cold intolerance

Fig. 8 **a** T1 axial MRI of right small finger pre-contrast, showing a 3.5×1.9 -mm isointense lesion. **b** T1 axial MRI of right small finger with contrast, showing a 3.5×1.9 -mm contrast-enhanced lesion

The diagnosis of a glomus tumor is based on the triad of symptoms: pain at rest, pain from direct pressure, and intolerance to temperature changes. Exam findings include Love's pin test (direct pressure of a round pin head causing pain), Hildreth's test (applying a tourniquet to the base of the digit which decreases pain), and cold sensitivity (placing the digit in cold water causing increased pain) [3, 35]. Due to the low prevalence of the tumor, the mean duration of diagnosis and treatment is 5–10 years with reports of patients waiting as long as 40 years before a correct diagnosis was made [39, 42]. Although the diagnosis is based on clinical findings, an MRI has a sensitivity and PPV of 90 and 97 %, respectively, and is useful in identifying the exact location and size of a tumor [1, 39]. Al-Qattan et al. recommended surgery based upon clinical findings, even if the MRI was negative [1].

The treatment for glomus tumors is surgical excision [7, 9]. Carroll described nail removal, a technique that can lead to nail deformity [9, 35]. Iselin proposed a lateral approach later modified by Fong that was useful for lesions that were not entirely beneath the nail bed [16]. Most recently, Roan et al. have proposed a split nail technique of excision that leaves the nail and nail bed intact [35]. A small incision is made through the nail directly above the tumor and excision is performed. The nail is then closed with suture and the nail bed and cuticle are left untouched, resulting in an improved cosmetic result [35]. In all of the studies conducted, pain persisted with incomplete excision.

Fig. 9 The right fifth finger after nail removal and a small longitudinal incision through the base of the nail matrix. The glomus tumor appears at the point of the scalpel that was exposed and removed

Subungual Keratoacanthoma

Subungual keratoacanthoma is a benign neoplasm first described by Lamp et al. in 1964 [25]. It usually presents as a painful, rapidly growing lesion on the terminal phalanx, in either a periungual or subungual location [31]. There are cases reports in which a white discharge was present simulating an infection [2, 41].

Subungual keratoacanthoma appears to be most common in middle age Caucasians with a slight predilection for men [2, 31]. Compared to squamous cell carcinoma patients, subungual keratoacanthoma patients are younger and the onset of symptoms is more rapid [41]. Lesions can be found on the hands and the feet, but has a predilection for the hands, particularly the first three fingers, especially the thumb [2]. The tumor can begin as a painful paronychia-like lesion and change to one with cheesy or purulent exudates suggestive of a bacterial infection [25].

Keratoacanthoma lesions are associated with the X-linked dominant disorder incontinentia pigmenti (Bloch-Sulzberger) in females [41]. Bloch-Sulzberger disease can lead to miscarriages of affected male fetuses, hence the importance of accurate diagnosis and genetic testing.

Subungual keratoacanthomas differ from keratoacanthomas (KA) throughout the rest of the body, calling into question whether they are classified correctly. Baran et al. identified five characteristics that distinguish subungual KA from KA in other locations: (1) they occur on non-hair-bearing skin, (2) they lack an epithelial collarette, (3) they typically have less inflammation, (4) they tend to be deeper, and (5) there are more dyskeratotic eosinophilic cells [2].

The differential diagnosis for subungual keratoacanthoma is infection, squamous cell carcinoma, subungual warts, glomus tumor, malignant melanoma, and giant cell tumor [2, 25]. Sun exposure, tar, mineral oil, steel wool, and human papilloma virus have been suggested as contributing factors to the formation of subungual keratoacanthoma [31].

Diagnosis of subungual keratoacanthoma is made histologically, looking for an exoendophytic dome-shaped nodule with a central horn [2]. A cup-shaped erosion of the distal phalanx may be seen on radiographs [2, 31].

Rapid growth noticed within weeks of onset helps differentiate a keratoacanthoma from a SCC. Because of the many similarities between these two lesions, debate continues as to whether the tumors are different or a variant of one another [6].

The treatment of subungual keratoacanthoma is surgical. Curettage can be performed, but local excision is preferred. Oliwiecki et al. reported no recurrences in 11 cases of local excision compared with three recurrences in nine patients that underwent curettage [31]. Amputation is performed, either on patients that have had recurrence or in those patients with extensive bone destruction. Baran et al. caution that amputation should be reserved for those cases in which multiple recurrences have occurred, or in those cases where a clear differentiation cannot be made from SCC [2].

Onychomatricoma

Onychomatricoma is a rare fibro-epithelial nail bed tumor that usually affects middle-aged patients [17, 18]. It was first described in 1992 by Baran and Kint, and is defined by four cardinal characteristics; a yellow thickened longitudinal band on the nail plate with prominent ridging, increased transverse curvature of the nail, splinter hemorrhages in the proximal nail portion, and a funnel-shaped deformity of the nail plate with filamentous extensions originating from the matrix (Baran and Kint paper describing onychomatricoma first) [18, 32, 40]. Onychomatricoma is the only known tumor to be formed from the nail matrix, thus producing a primary nail deformity [40]. The tumor can also present with less common symptoms such as a cutaneous horn presentation, or a longitudinal melanonychia, which may be mistaken for melanoma [15]. Along with melanoma, the differential for onychomatricoma also includes squamous cell carcinoma, subungual keratoacanthoma, Bowen's disease, subungual exostoses, and subungual warts [20].

Onychomatricoma tumors can exist for extended periods of time before diagnosis. The symptoms are non-specific, with nail-bed bleeding, pigmentation changes, or a nail plate abnormality [18, 20]. The tumor is commonly found concurrently with fungal infections, making the definitive diagnosis more challenging [15]. A unique characteristic to the onychomatricoma is the active production of nail plate substance, which causes changes to the nail itself, including thickening and discoloration [18]. This metabolic process assists in the diagnosis of the tumor. Onychomatricoma produces e-cadherin and beta-catenin in the cell membranes of the invaginations, but does not produce nuclear beta-catenin, allowing for differentiation between it and other matrix tumors at the cellular level [17].

Pathologically, the tumor has two distinct growth patterns. The first, near the lanula is a fibrous core with

numerous "glove finger" projections into the nail [17, 32]. The finger-like expansions will enter small, longitudinal "worm-like" holes of the nail [17, 18]. The second growth pattern is proximal to the first, under the nail fold, and is composed of epithelium and keratinous zones of nail matrix in a classic "V shape" [17, 32].

Treatment of onychomatricoma is surgical excision, and there are no documented cases of recurrence with complete excision.

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