Nail pathology II: Non-melanocytic Neoplasms

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Epithelial and other neoplasms of the nail unit
- Some are counterparts to those found elsewhere
- Some are entities unique to this site
- Unusual features can create diagnostic quandaries
- Diagnosis often depends on the adequacy of the specimen and the clinical history

Epithelial and other neoplasms
- Benign
  - Onychopapilloma
  - Subungual epidermoid inclusions
  - Onychomatricoma
  - Onychocytic matricoma
  - Superficial acral fibromyxoma
- Malignant
  - SCCIS/SCC
  - Keratoacanthoma
  - Subungual tumors of incontinentia pigmenti
  - Onycholemmal CA
  - Onychocytic CA (?)
  - Papillary adenoCA
Onychopapilloma

- Clinical findings
  - Erythronychia
  - Splinter hemorrhage
  - Melanonychia
  - Leukonychia
  - Distal hyperkeratosis
  - Distal splitting

Histologic features

- Hyperplasia of distal matrix and nail bed epithelium, papillated distally
- Distal subungual hyperkeratosis/parakeratosis
- Hemorrhage
- Matrical metaplasia (eosinophilic, anucleated cell layer in nail bed)
- Large and multinucleate distal nail bed keratinocytes
- Sometimes pigmentation (melanocytic activation)
- Often need intact lesion to make definitive diagnosis
Verruca vulgaris

SUMMARY.—This paper describes the evolution of subungual epidermoid inclusions and discusses their etiology. They are shown to develop from the epidermis of the nail bed and to be different from the epidermoid inclusions of the nail matrix. The inclusions may lose their connections with the epidermis and come to lie deep within the dermis of the nail bed. Although the inclusions are usually microscopic in size they may be large and should be considered in the differential diagnosis of nail bed swellings.

The etiology of these lesions is still obscure. They may follow trauma and are found in finger clubbing and it is probable that different stimuli can produce them.
Subungual epidermoid inclusions

- Small aggregates of keratinocytes or cysts that can be found under the epithelium of the nail bed
- An incidental finding, or associated with nail dystrophy, especially a shortened and dystrophic nail plate, or clubbing
- A history of trauma is common, and there may be associated underlying bony abnormalities as well
- There may be associated hyperkeratosis of the nail bed
- Less cystic variants can be mistaken for squamous cell carcinoma or other neoplasms

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Onychomatricoma
Baran and Kint

Onychomatricoma. Filamentous tufted tumour in the matrix of a funnel-shaped nail: a new entity (report of three cases)

Summary

Identical lesions of the nails were observed in three patients. The main signs were a yellow elevation along the entire length of the nail, with splinter hemorrhages in its proximal portion. A tendency towards transverse overcurvature of the affected nails, and episodes of a bluish tumor under the nail had been noticed and the proximal cuticle had become thinned. The patient were sufficiently brave to lead to the clinical suspicion of a filamentous tufted tumour in the matrix of a funnel-shaped nail, an entity not previously described.

Onychomatricoma
Clinical presentation

Nodule

Hollow area within tumor

Nail bed

Courtesy of Monica Lawry, MD

Thickened nail plate

Transverse overcurvature

Splinter hemorrhages
Specimen for pathology

Onychomatricoma

Clinical features:
- Mean age 50.5 (24-68), lighter-skinned patients
- Fingers most often affected, esp. thumb and index
- Female to male 2.16:1
- Thickened yellowish nail, transverse overcurvature, splinter hemorrhages, sometimes pigmented
- Nodular area corresponding to the matrix
- Rarely recurs after surgery

Onychomatricoma

Key histologic features:
- Multiple fibroepithelial projections
- Thick V-shaped keratogenous zone, mimics normal matrix
- Matrical hyperplasia of varying degree
- “Glove-finger” appearance of nail plate and matrix interaction
- Altered nail plate thin proximally, thick distally, with multiple cavities (wormwood)
- Fibrocellular stroma of varying degree
  - CD34+, CD99, S100, EMA-
  - More cellular superficially, perpendicular collagen bundles deeply
  - Myxoid stroma similar to superficial acral fibromyxoma, rare

Normal nail

Thick, altered nail plate
Pigmented onychomatricoma

Courtesy of A. Christine Miller, MD
“Pleomorphic” OM

- Only seven cases now reported:
  - 2 as "unguioblastic fibroma"
  - 2 possibly as pleomorphic fibroma
  - 2 in a large series of 19 cases of OM
- Although pleomorphic, no history of adverse biologic behavior


Ki-67

Nail clipping for diagnosis
Onychomatricoma
Differential Diagnosis - Histologic

- Angiofibroma (Koenen's tumor)
- Acquired digital fibrokeratoma
- Cellular digital fibroma
- Perineurioma
- Pleomorphic fibroma
- Superficial acral fibromyxoma
- Verruca vulgaris
- SCC in situ (rarely)

Superficial acral fibromyxoma

Courtesy of Brad Naylor, DPM
Superficial acral fibromyxoma
Clinical features
• A benign spindle cell proliferation
• Predilection for hands and feet, fingers and toes, often with close relationship to nail unit
• Broad age range (mean, 43)
• Duration 3 mos to 30 years
• Size 0.6 cm-5 cm, may impinge on bone
• Behavior: most did not recur after excision

Superficial acral fibromyxoma
Histologic features
• Spindled to stellate cells
• Random, loose storiform or fascicular patterns
• Myxoid to collagenous, prominent mast cells
• Occasional multinucleate cells, rare mitoses
• CD34+, CD99 variable +, EMA focal/-
• Nestin positive, RB1 loss
• Probable fibroblastic differentiation
Pleomorphic fibroma

Angiofibroma
Onychocytic Matricoma Presenting as Pachymelanonychia Longitudinal. A New Entity (Report of Five Cases)

Courtesy of Mark Holzberg, MD

FIGURE 1. Pachymelanonychia longitudinal of the finger right §.
Papillomatous
Keratogenous

Melanocytes and melanin

Nail dystrophy began 3 years ago, slowly more raised

Courtesy of Drs. Jane Bellet and Ken Ellington
SCC of the nail unit

- Most common tumor of nail unit, but still uncommon
- Atypical clinical presentations the rule
  - Dystrophy, onycholysis, ulceration, paronychia, nail loss, and rarely longitudinal melanonychia
- Predisposing factors
  - Immunosuppression
  - Oncogenic HPV
  - Radiodermatitis

Squamous cell carcinoma

- In situ
- Invasive
Partial nail plate avulsion reveals nail bed abnormality.
SCCIS of the nail unit
Pigmented SCCIS

Subungual keratoacanthoma
Painful subungual tumor of incontinentia pigmenti

- Well-recognized but rare complication of IP, a late manifestation
- Corresponds to the verrucous stage, IP
- Fingers > toes
- DDX: subungual keratoacanthoma, verruca, epidermoid cysts, subungual fibroma, chronic paronychia
- Intense pain and osteolysis may occur
- Excision or amputation may be necessary
- Retinoids have been used with some promise
Onycholemmal carcinoma: A morphologic comparison of 6 reported cases


Clinical features:

- Female to male 1:1
- Middle age to older patients
- Finger: thumb: toe: unknown 3:1:1:1
- Symptoms/signs: ulceration, swelling, paronychia-like, onycholysis, periungual erythema, pain
- May abut the bone but no bony involvement
- Indolent course (no aggressive behavior)
- Treatment: Mohs surgery, excision, nail unit excision, radiation, amputation
- Conservative treatment advocated
• Histologic features
  – Cytologically bland
  – Poorly circumscribed, infiltrative pattern
  – Lobular and cystic
  – Abrupt keratinization (reminiscent of proliferating pilar tumor)
  – Authors consider this an acral SCC
  – 1 case studied was negative for HPV


Fig 1. Clinical image of onycholemmal carcinoma. A. Nail distortion, von Hamel nail or “black bead” sign. B. Charcot cryst: irregular epidermal hyperplasia and aching of nail bed.

Fig 2. Histopathologic features of onycholemmal carcinoma. A. Isolated vertical and horizontal orientation of basal and suprabasal cell layer with central apparent keratinization. B. Increased vascularity at the hillock between thinning areas. C. Early chronic inflammatory cell infiltrate adjacent to the neoplastic proliferation. D. Acantholytic and keratinizing tumor cells and keratin pearls.

- 51 yo woman, ulceration of left ring finger, 4 years
- Began with trauma, then formed a longitudinal split
- Gradual destruction of whole nail bed
- First biopsy inconclusive

Invasive
Retiform contour
Matrix-like cytology
Keratinization
Digital papillary adenocarcinoma

History

- First described by Helwig, 1979 (AAD CPC)
- Rare low grade malignant adnexal tumor
- Formerly, aggressive digital papillary adenoma (ADPA)
- Despite somewhat bland histologic appearance, some cases found to behave aggressively
- 2000, Duke et al propose ADPA is malignant without a benign counterpart, renaming as PDA to reflect this behavior, suggest aggressive treatment
- 2009, Hsu et al suggest that wide excision may be adequate for some more limited cases (use Ki-67 proliferation index as a guide)

Digital papillary adenocarcinoma

Clinical features

- Painful or painless cystic mass, acral skin, volar surfaces of fingers and toes
- Male predominance
- Unusual presentations include as PG, hemangioma, SCC-like, osteomyelitis, soft tissue infection, and paronychia
- Preferred location: between nail unit and DIP
Digital papillary adenocarcinoma

Histology

- Mixed papillary, tubuloalveolar, solid, cystic patterns; variable atypia, mitotic rate, necrosis
- Squamous metaplasia, clear cells, spindle cells
- Stains with S100, CEA, p63
  - Also EMA, ER, PR, CK7, CK77, PHLDA, SMA, AR
- May contain myoepithelial cells
- No histologic features predict biologic behavior
- Ki-67 proliferation rate?

Digital papillary adenocarcinoma
Differential diagnosis

- Metastatic carcinoma
- Tubular apocrine adenoma
- Hidradenoma

Digital papillary adenocarcinoma
Prognosis and treatment

- Local recurrence in 5%, up to 50% if not widely excised
- Metastasis 12-14%, often to lung (70%)
- In some series, metastatic rate approaches 50%
- Treatment: wide local excision, amputation, Mohs surgery, sentinel node sampling?

Take home points

- Epithelial and other neoplasms may have distinctive features in the nail unit
- Orientation of the tissue may be key to recognition
- Determining benign versus malignant can sometimes be tricky
- Some diagnoses are unique to this site
- Be on the lookout for new entities!