Noxious Nails in Kids
Summer AAD 2018

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Conflicts of Interest

• None for this talk

• Many thanks to Phoebe Rich for sharing cases & slides
Important aspects of Pediatric Nails

• Duration- Congenital?
• Extent
• Texture
• Most common cause in adults (tinea) not as common in children
• The younger the onset, the more likely non-infectious
• Look at hair, mucous membranes
• Underlying bony anomaly?
Which other nail dystrophy has an underlying bone abnormality?

- Nail psoriasis?
- Nail LP?
- COIF?
- Trachyonychia?
Congenital Onychodysplasia of the Index finger (COIF)

- also known as Iso-Kikuchi syndrome
  - micronychia, polyonychia, anonychia, hemionychogryphosis, and misalignment of the nail of the index finger (or other nails)

- Cause?
  - in utero ischemia of the palmar digital artery during limb development?
  - Or dysplastic change in the cap of the distal phalanx
19 year old who is fed up with his small dystrophic nails. What will you do next?

Photo courtesy of Phoebe Rich
19 year old who is fed up with his small dystrophic nails. What will you do next?

- Give him terbinafine, everything is fungus, right?
- Get good medical history and exam?
- Tell him to stop picking his nails?
- Tell him there is nothing you can do and send him home?

Photo courtesy of Phoebe Rich
On exam he has small nails with triangular lunula. Hair, skin and teeth OK, Odd joints especially knees and elbows. What does he have?

- Dystrophic EB
- Nail Patella Syndrome
- Soccer syndrome
- Psoriatic arthritis
Nail-Patella Syndrome

• Autosomal dominant
• 1:50,000
• Nails: triangular lunula, micronychia

Nail-patella Syndrome

The Gene??

- LMX1B
- heterozygous loss-of-function mutations in LMX1B, coding for a LIM homeobox (LIM-HD) transcription factor.
The nail-patella syndrome involves a clinical tetrad of changes in the

• Nails
• Knees
• Elbows
• ________ ?_________ _____ (X-ray)
Nail changes are the most constant feature

- absent
- hypoplastic
- dystrophic

A pathognomonic finding is the presence of _____??____________.
Where will you refer him?

- Ophthalmologists ---- Lester iris-hyperpigmentation of pupillary margin, cataracts, glaucoma
- Nephrologist ---- Glomerulonephritis, kidney failure
- Orthopedist- X-Rays--- knee and elbow abnormalities, absent patella, radial head subluxion, posterior iliac horns
- All the above
LMX1b mutation effect on the Kidney

- Kidney involvement in 30-50% of patients
- Presents with hematuria and proteinuria
- Up to 10% develop end stage renal failure

- LMX1B impairs the development and functioning of podocytes and glomerular filtration slits
What to remember about Nail Patella Syndrome

• Nail Patella syndrome
  – Nail changes
    • Triangular lunula, --- pathognomonic
  – 50 % develop renal impairment
4 girls  4 different painful nails

Photo courtesy of Phoebe Rich
What are you going to do?

• 1. Treat for fungus?
• 2. Order and Ultrasound?
• 2. Biopsy the nail bed?
• 3. Order an X-RAY?
The exact pathogenesis of subungual exostosis is unclear, there many are suggested possible etiologies.

• trauma
• infection
• tumor
• hereditary abnormality
• activation of a cartilaginous cyst
Two theories of exostosis formation

- a reactive process in response to trauma.

- The translocation \( t(X;6)(q22;q13-14) \) has been reproducibly linked to subungual exostosis implying it is a true neoplasm.

• High proportion of cases in the pediatric population (55%),
• female: male ratio is 1:1

• N=255

- 16% of exostosis were in pediatric age group
- 2:1 ratio of female : male
Treatment of subungual exostosis.

- Of 124 patients (of 255) with treatment outcomes
- Recurrence: 5 of 124 (4.0%) cases
- Postoperative infections: 4 of 124 (3.2%)
- Chronic regional pain syndrome: 1 of 124 (0.8%)
Subungual Exostosis

• Clinical?
  – Hard subungual nodule lifting distal or lateral plate
• Benign tumor composed of:
  – trabecular bone with a fibrocartilagenous cap
• Symptom?
  – painful
• Age group?
  – Children and young adults, girls>boys
• Treatment?
  – Surgical removal
• Recurrence rate?
  – 10 % more in kids.
Subungual Exostosis

• Tender subungual mass
• X-ray is diagnostic
Case

• 8 year old boy with a deep depression in the center of his nail present for 1 year

• No trauma

• No manipulation
What next?

• Biopsy nail matrix
• Do a full skin exam
• Ask about family history
• Refer to surgeon
• Biopsy his skin
• Do Nothing
What next?

• Biopsy nail matrix
• Do a full skin exam
• Ask about family history
• Refer to surgeon
• Biopsy his skin
• Do Nothing
Lichen Striatus

- 2.6 % of pts with LS have nail dystrophy

Nail Lichen striatus

- The median patient age was 11 years (range: 4–33 years),
- female:male ratio was 3:4.
- All patients had both typical skin lesions and nail abnormalities. involved a single digit (n = 5).
- nail change was longitudinal fissuring (n = 4)
- Treated with topical corticosteroid and tacrolimus
Lichen Striatus of nail

- Clinical diagnosis
- No nail biopsy
- Skin biopsy if lesions present but not necessary
- NO TREATMENT IS NECESSARY.
Case

• Lifelong funny short nails
• Dad too.
• What does she have?
Racquet Nails vs Normal nails

- Normal nail: length is greater than width
- Racquet nail: width is longer than length

- Usually congenital
- Thumb most common
- Often inherited as autosomal dominant
- Usually has underlying brachydactyly
Letter to the Editor

Acquired racquet nails: a useful sign of hyperparathyroidism

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This teenager comes in with these nail changes. What is the diagnosis?

- Congenital malalignment
- Onychomycosis
- Pachyonychia congenita
- Clouston’s syndrome
This child comes in with these nail changes. What is the diagnosis?

• Congenital malalignment
• Onychomycosis
• Pachyonychia congenita
• Clouston’s syndrome
Pachyonychia Congenita

• A rare congenital disorder that is inherited as an autosomal dominant.

• It is caused by mutations in keratin genes
Which is of the following is the least helpful in diagnosing PC

- Recognizing the clinical appearance and features.
- **A skin biopsy of the affected tissues**
- Molecular genetic studies to detect mutations in the affected keratin genes.
- Contacting the Pachyonychia Congenita Project.
PC

- Uncommon AD disorder of keratinization with hypertrophic nails and plantar hypereratosis and pain.
- Oral leulokkeratosis, follicle hyper, hoarsemess, natal teeth
- Keratin gene defects KRT6A, KRT6B, Krt16, KRT17. Formerly PC-1, PC-2, now PC-6a etc.
NAIL KERATINS

Keratin 6, 16 and 17

Mutations in Keratins 6 and 16 lead to Pachyonychia Congenita Type 1

Mutations in K 6 and 17 lead to PC-2
Clinical Features of PC

• Nails
• Palms and soles
• Skin
• Oral cavity
Clinical features of PC.  **Nails**

- Nail changes are most severe with mutations of K6a and K16.
- Abnormalities of nails are apparent early in life.
- Nails are thickened (pachyonychia), often with brownish discolouration.
- All fingernails are commonly involved; toenails to a lesser degree. Specific K16 mutations do not affect fingernails.
Mouth

• White patches on tongue and inside cheeks (leukokeratosis)
• Sores at sides of mouth (angular cheilitis)
• Tooth abnormalities (natal or prenatal teeth. k17)
Clinical. Palms and Soles

• Thickened or calloused palms and soles (palmoplantar hyperkeratosis or keratoderma particularly, resulting in pain when walking
• Focal palmoplantar keratoderma may be the only feature of pachyonychia congenita in patients with mutations of K6c.
• Pain is common and can be very severe, particularly in patients with mutations of K6a and K16
• hyperhidrosis (excessive sweating)
• Blisters precipitated by friction and warm weather
Cysts (skin)

- **Steatocystoma** and pilosebaceous **cysts** are common, particularly in patients with mutations of K17 and to a lesser extent, K16a.
- Cysts may or may not be painful.
Important Mutations in PC

• Keratin genes KRT6a and KRT16 in Type 1
  – Gene locus 12q13 in KRT6a,
    Gene locus 17q12-q21 in KRT 16

• KRT6b and KRT17 in Type 2
  – Gene locus 12q13 in KRT6B,
    Gene locus 17q12-q21

• There was ablation of endogenous K6a expression in two keratinocyte cell lines after transfection with the siRNA’s against K6a3.


Treatment

• Patients reported surgical treatments being most effective for cysts
• and mechanical treatments the most effective conventional therapeutic for nails
Does she have PC?

- Began early in life
- Significant alopecia
- Son has some nail changes

Photo courtesy of Phoebe Rich
Clouston's hidrotic ectodermal dysplasia
Clouston’s syndrome

• 1. ectodermal dysplasia that is characterized by abnormalities of the skin, hair and nails.
• 2. Clouston syndrome is caused by changes (mutations) in the GJB6 gene
• 3. Is inherited in an autosomal dominant manner.
Clouston's hidrotic ectodermal dysplasia

- partial or total alopecia,
- dystrophy of the nails,
- hyperpigmentation of the skin (especially over the joints),
- clubbing of the fingers.
Clouston's hidrotic ectodermal dysplasia

• is caused by mutations in a connexin gene, GJB6 or connexin-30
3 year old with slightly abnormal great toenails. Using topical antifungals for 2 years. Dad has ugly nails and mom wants to prevent it. What next?

• 1. Start oral antifungals
• 2 remove her toenails surgically?
• 3 tell her not to wear shoes
• 4. Take a culture because it must be fungus
Lateral Malalignment of the great toenail

- Congenital lateral deviation of great toenail due to rotation of the matrix
- ? AD inheritance vs improper in utero fetal positioning
- May cause nail fold inflammation, ingrown, paronychia,
- Some (? Half) may spontaneously resolve.
Pediatric onychomycosis

• Overall prevalence in children – 0.3%
• San Diego prevalence -
• Increased incidence with age
• Decreased ? Thinner, faster-growing nail plate in children
• Risk factors – family disease
• No FDA approved systemic therapy

Feldstein S et al Clinics in Dermatology 2015
Totri C et al Pediatric Dermatology 2016
How to treat pediatric onychomycosis

• Systemic review – 26 trials; children <18 yrs
• Pooled data - 70.8% cure rate systemic overall, 80% combined therapy
Onychomycosis in children: Safety and efficacy of antifungal agents

Aditya K. Gupta MD, PhD1,2 | Rachel R. Mays BSc1 | Sarah G. Versteeg MSc1 |
Neil H. Shear MD3 | Sheila F. Friedlander MD4

1Mediprobe Research Inc., London, ON, USA
# Peds Onycho....How to Treat?

<table>
<thead>
<tr>
<th>Antifungal</th>
<th>Dosage</th>
<th>Duration</th>
<th>Notes</th>
<th>Monitoring guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciclopiox</td>
<td>8% lacquer daily with weekly professional debridement</td>
<td>48 wk</td>
<td>Considered safe for aged $\geq 12$</td>
<td>-</td>
</tr>
<tr>
<td>Efinaconazole</td>
<td>10% solution daily</td>
<td>48 wk</td>
<td>Safety and efficacy not established</td>
<td>-</td>
</tr>
<tr>
<td>Tavaborole</td>
<td>5% solution daily</td>
<td>48 wk</td>
<td>Safety and efficacy not established</td>
<td>-</td>
</tr>
<tr>
<td><strong>Oral</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole (tablet)</td>
<td>3-6 mg/kg weekly</td>
<td>FN: 12-16 wk</td>
<td>TN: 18-26 wk</td>
<td>-</td>
</tr>
<tr>
<td>Griseofulvin (microsize)</td>
<td>10 mg/kg daily up to 20-25 mg/kg daily</td>
<td>FN: 36-52 wk</td>
<td>TN: 9-12 mo</td>
<td>Children aged $\geq 2$</td>
</tr>
<tr>
<td>Itraconazole (capsules)</td>
<td>5 mg/kg for pulse 200 mg daily</td>
<td>FN: 6 wk,</td>
<td>FN: 2 pulses,</td>
<td>Liver tests, exercise caution in liver dysfunction</td>
</tr>
<tr>
<td>Terbinafine (tablets)</td>
<td>$&lt;20$ kg, 62.5 mg/d (1/4 tablet) 20-40 kg, 125 mg/d (1/2 tablet) &gt;40 kg, 250 mg/d (1 tablet)</td>
<td>FN: 6 wk,</td>
<td>TN: 12 wk</td>
<td>-</td>
</tr>
</tbody>
</table>

This review was limited to the United States and Canada. Information is based on package inserts obtained from the National Institutes of Health, U.S. National Library of Medicine, Daily Med; U.S. FDA-Approved Drug Products Database; and Health Canada Drug Product Database.

Check the regulatory status of each drug in your jurisdiction. Check for current dosing and monitoring guidelines. The above is presented as a guide.

Gupta AK et al  Peds Derm 2018
Systemic therapies for pediatric onychomycosis

- None FDA approved for this purpose
  - Griseofulvin
  - Terbinafine
  - Itraconazole
  - Fluconazole

- T. capitis doses used

- Prolonged therapy required – at least 3 mos for terbinafine, 6-9 mos for griseofulvin
What about topical therapy for pediatric onychomycosis?

• Pediatric nails – thinner, faster growing, better circulation

• Topical alternatives (none FDA approved for kids) (particularly appropriate for non-matrix disease)
  – Ciclopirox 8%
  – Efinaconazole 10%
  – Tavaborole 5%

• One pediatric study,* ciclopirox, showed 71% M.C & 70% ET in 20 children at 32 weeks

Rosen TD et al  Journal Drugs Dermatology 2015
*Friedlander SF et al 2013 Ped Dermatology
Elewski BE et al  tavaborole solution for onychomycosisJAAD 2015
But cost is a problem

• Insurance companies NOT anxious to cover

• Some pharma companies provide “coupons”

• It requires commitment on the part of the patient/parent

• But many parents prefer this to oral therapy