

Beyond Atopic Dermatitis: Unmasking Rare Mimickers

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Takeaway Message:

- Maintain a broad differential diagnosis in suspected cases of atypical eczema especially moderate to severe atopic dermatitis.
- Early and accurate diagnosis is paramount for initiating disease-specific management, improving outcomes, and providing appropriate genetic counseling.

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Recognizing the Implications of Misdiagnosis

Background

Atopic dermatitis (AD) is a common diagnosis for eczematous presentations. However, a subset of patients presents with severe, atypical, or treatment-refractory "eczema" that signals an underlying rare disorder

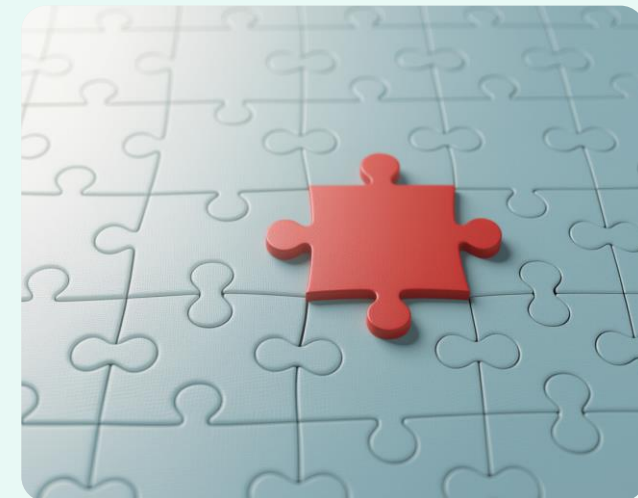
Consequences

- Delayed diagnosis of the underlying condition
- Inappropriate or ineffective treatment strategies
- Increased risk of complications related to the underlying disease
- Financial burden due to prolonged and ineffective treatments
- Parental stress and anxiety

Importance

Allows for targeted, disease-specific management

Improves patient outcomes and reduces morbidity



Primary Immunological Deficiencies: Hyper-IgE Syndrome

A rare primary immunodeficiency characterized by elevated IgE levels, eczema, and recurrent infections.

- **Clinical Presentation:**
- Severe eczematous dermatitis, often starting in early infancy.
- Recurrent skin and respiratory infections (e.g., *Staphylococcus aureus*).
- Coarse facial features , Skeletal and dental abnormalities (e.g., retained primary teeth).
- **Diagnostic Clues:**
- Early onset
- Lack of response to standard treatments
- Markedly elevated IgE levels, eosinophilia
- Genetic testing for mutations in genes:
STAT3, *DOC8*, *PGM3*, *IL6ST*, *ERBIN*, *ZNF431*.



Case 1 – HIES (4 months)

Presentation:

- Severe, recurrent, chronic eczematoid rash at birth
- Recurrent purulent papules on the scalp
- Special facies emerge with age.
- Refractory to potent topical corticosteroids and meticulous daily skin care
- A history of two pneumonia episodes during infant

Diagnostic Red Flags:

- Early onset
- Lack of response to standard treatments
- Lab result: WBC $32.8 \times 10^9/L$, EOS: $4.5 \times 10^9/L$, IgE: 28000 KIU/L;
- **Diagnosis:**
- c.1145G>A (exon13, NM_139276) (9 months old)
- **Treatment:** Dupilumab + sulfonamides



4-months old



1 year and 3-month-old



1 year and 5-month-old



Baseline 2y9m
(2023.7)



Complete clearance
(2023.8)

Netherton Syndrome: A Genodermatosis Disorders

Netherton Syndrome:

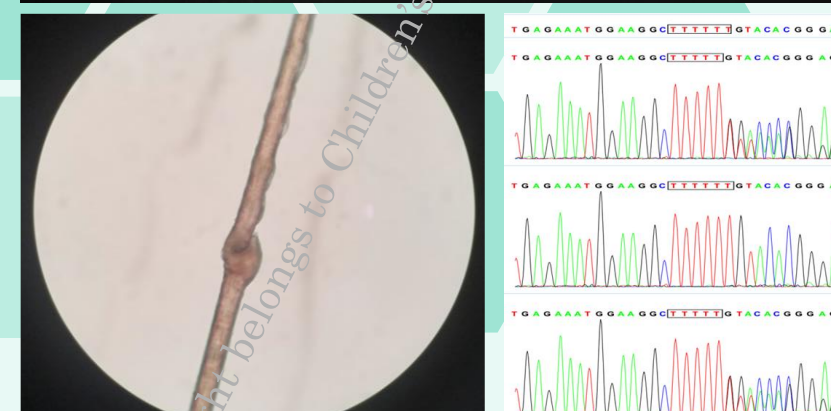
A rare autosomal recessive genodermatosis caused by mutations in the *SPINK5* gene, encoding LEKTI.

- **Unique Characteristics::**
- **Atopic Diathesis:** Increased susceptibility to allergies and eczema.
- **Ichthyosis Linearis Circumflexa:** Distinctive migratory, serpiginous, scaling lesions.
- **Trichorrhexis Invaginata:** "Bamboo hair" - a characteristic hair shaft abnormality.
- **Diagnosis::**
- Hair microscopy to identify trichorrhexis invaginata
- Genetic testing to confirm *SPINK5* mutations



Case 2 – Netherton Syndrome (4 months)

- **Presentation:**
 - Generalized erythroderma
 - Alopecia
 - Failure to thrive
 - three episodes of pneumonia
- **Diagnostic Process:**
 - Microscopic examination of eyebrow hairs revealed trichorrhexis invaginata ("bamboo hair").
 - Genetic testing confirmed a *SPINK5* mutation.
- **Outcome:**
 - Diagnosis of Netherton syndrome,
 - Despite IVIG and antibiotics, the infant died from severe lung infection



Metabolic Disorders in Dermatological Presentations

Inherited Metabolic Disorders: can present with dermatological manifestations that mimic atopic dermatitis.

- **Multi-Carboxylase Deficiency:**

- Inborn errors in the metabolism of biotin in which there is defective activity of propionyl CoA carboxylase, 3-methylcrotonyl CoA carboxylase and pyruvate carboxylase.

- **Types :**

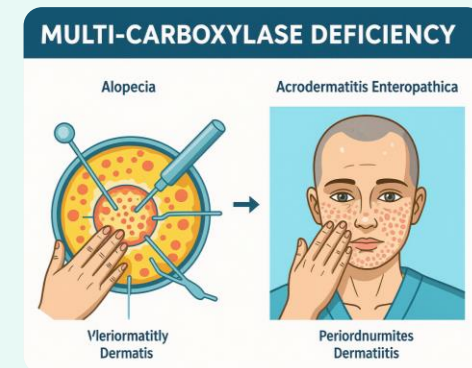
Holocarboxylase synthetase deficiency - neonatal

Biotinidase deficiency - late onset

- **Fetures:** eczematous dermatitis, feeding difficulties, alopecia, developmental delays, neurological symptoms

- **Diagnostic Approach:** Metabolic screening to identify specific markers;
Genetic analysis

- **Treatment:** Biotin supplementation



Case 3 – Holocarboxylase synthetase deficiency (3 months)

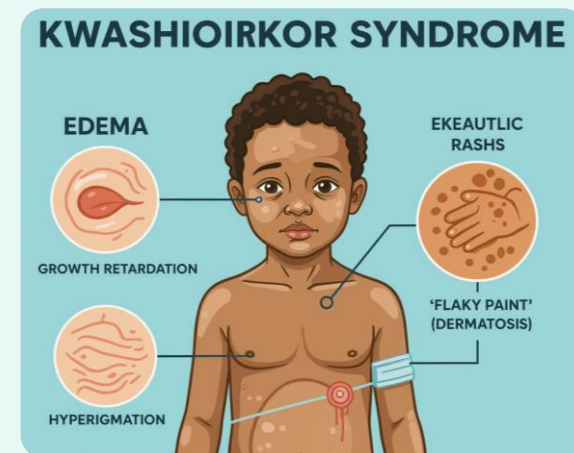
- **Presentation:**
 - Widespread eczematous erythema
 - Leaf-like scaling
 - Mild dysphoria
- **Lab findings:**
 - Elevated lactate and Urinary methylcrotonamide
- **Therapeutic Intervention:**
 - Biotin replacement therapy was initiated.
- **Outcome:**
 - Rapid resolution of the rash following biotin replacement therapy.



Profound Protein-Energy Malnutrition: Kwashiorkor Syndrome

Kwashiorkor Syndrome:

- A severe form of malnutrition caused by protein deficiency.
- **Systemic Effects:**
 - Edema, growth retardation, and immune dysfunction.
- **Dermatological Manifestations:**
 - Eczematous rashes, hyperpigmentation, and desquamation ("flaky paint" dermatosis).
- **Diagnostic Considerations:**
 - Nutritional assessment and investigation of underlying causes of malnutrition.



Case 4 – Kwashiorkor Syndrome (5 months)

- **Presentation:**
 - Infant initially diagnosed with food allergy
 - Treated with amino acid-based formula (AA formula)
 - Developed generalized edema, erythema, and skin desquamation after starting AA formula
- **Diagnostic Error:**
 - Initially misdiagnosed as widespread AD.
- **Lab results:** significant decrease in total protein and albumin levels
- **Management:** gradually resumed normal milk feeding.
All the rashes completely disappeared within 4 weeks.



Take-Home Messages

- **Key Points:**
 - Early disease onset and poor response to conventional therapies necessitate consideration of diagnoses beyond atopic dermatitis.
 - Recognize clinical red flags.
- **Targeted Investigations:**
 - IgE levels
 - Hair microscopy
 - Metabolic panels
 - Nutritional assessment
 - Genetic testing
- **Importance:**
 - Maintain a broad differential diagnosis in suspected cases of atypical eczema.
 - Early and accurate diagnosis is paramount for initiating disease-specific management, improving outcomes, and providing appropriate genetic counseling.



Thank you for your attention !

Juan Xiang

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