Case #8
PT-1

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Signalment & History

• 8-month-old, MN, German Shepherd mix
• From a litter of 8 pups found on a reservation near Calgary, Alberta
• Normal until about 12 weeks of age
  – Developed wart-like lesions on all 4 pawpads
  – Only affected dog from the litter
• No CBC or chemistry abnormalities
• No signs of systemic illness
Gross Findings

- Began as swirl-like (yellowish) patterns
  - No discomfort
Gross Findings (cont.)

- Progressed to raised, crusting mounds
- Sloughed off to reveal an open wound
  - Painful
Diagnosis

**Morphologic diagnosis:**
- Pawpad: Marked epidermal acanthosis with orthokeratotic to parakeratotic hyperkeratosis

**Final diagnosis:**
- Familial pawpad hyperkeratosis

**Other considerations:**
- Papillomavirus
- Canine distempervirus
- Nasodigital hyperkeratosis
- Pemphigus foliaceus (pawpad only)
- Nutritional - zinc deficiency or generic dog food
- Hepatocutaneous syndrome
- Systemic lupus erythematosus
Familial Pawpad Hyperkeratosis

• Rare canine cornification defect
  – Probably a subgroup of ichthyosis

• Described in various breeds
  – Irish Terrier
  – Kerry Blue Terrier
  – Labrador Retriever
  – Golden Retriever
  – Mongrel

• Autosomal recessive inheritance?
  – Suggested in Irish Terriers
  – Several palmoplantar keratodermas described in people
Cornified Cell Envelope (CCE)

• Durable protein-lipid polymer
  – Formed inside the cytoplasmic membrane of differentiating keratinocytes
  – Eventually resides on exterior of cornified cells
  • Mechanical & chemical barrier

FORMATION IS A MULTISTEP PROCESS
Release of keratohyalin granules

LORICRIN binds desmosomal structures

Transglutaminase binds proteins to cell membrane

Profilaggrin cleaved to FILAGGRIN

Forms highly insoluble protein component

Terminal differentiation (FILAGGRIN degraded)


Palmoplantar Keratodermas in People
Possible Correlation in Dogs?

GENETIC MUTATION $\rightarrow$ ABNORMAL PROTEIN $\rightarrow$ ABNORMAL CCE

• Keratins
  – Abnormal structural integrity
    • Dysfunctional keratins 1 & 9
  – Irish Terriers:
    • PCR analysis did not implicate keratins 2 or 9

• Loricrin
  – Abnormal CCE development
  – Dysfunctional apoptosis of differentiating keratinocytes

• Desmosomal proteins
  – Blistering disorders
Palmoplantar Keratodermas in People
Possible Correlation in Dogs?

• Connexins
  – Form gap junctions

  Abnormal Ca^{2+} signaling
  ↓
  Abnormal regulation of CCE formation

• Cathepsin C
  – Intracellular protein degradation
    • Specific function in keratodermas unknown
Conclusions

• Familial pawpad hyperkeratosis
  – Rare disease in dogs
  – Specific genetics of the disease remain unknown

• Outcome for “Camry”
  – He is doing well
    • Paw soaks
    • Antibiotics as needed
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