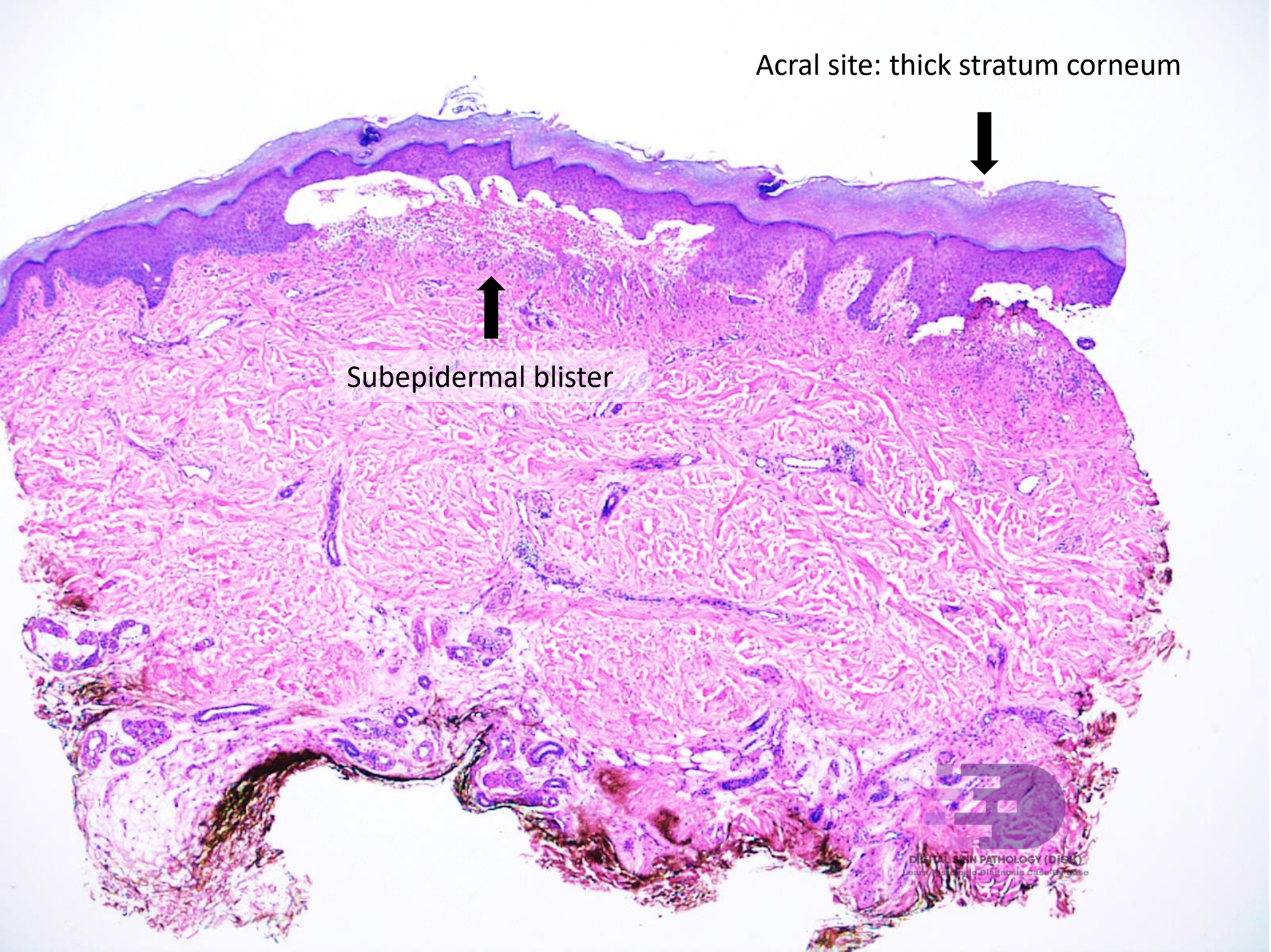
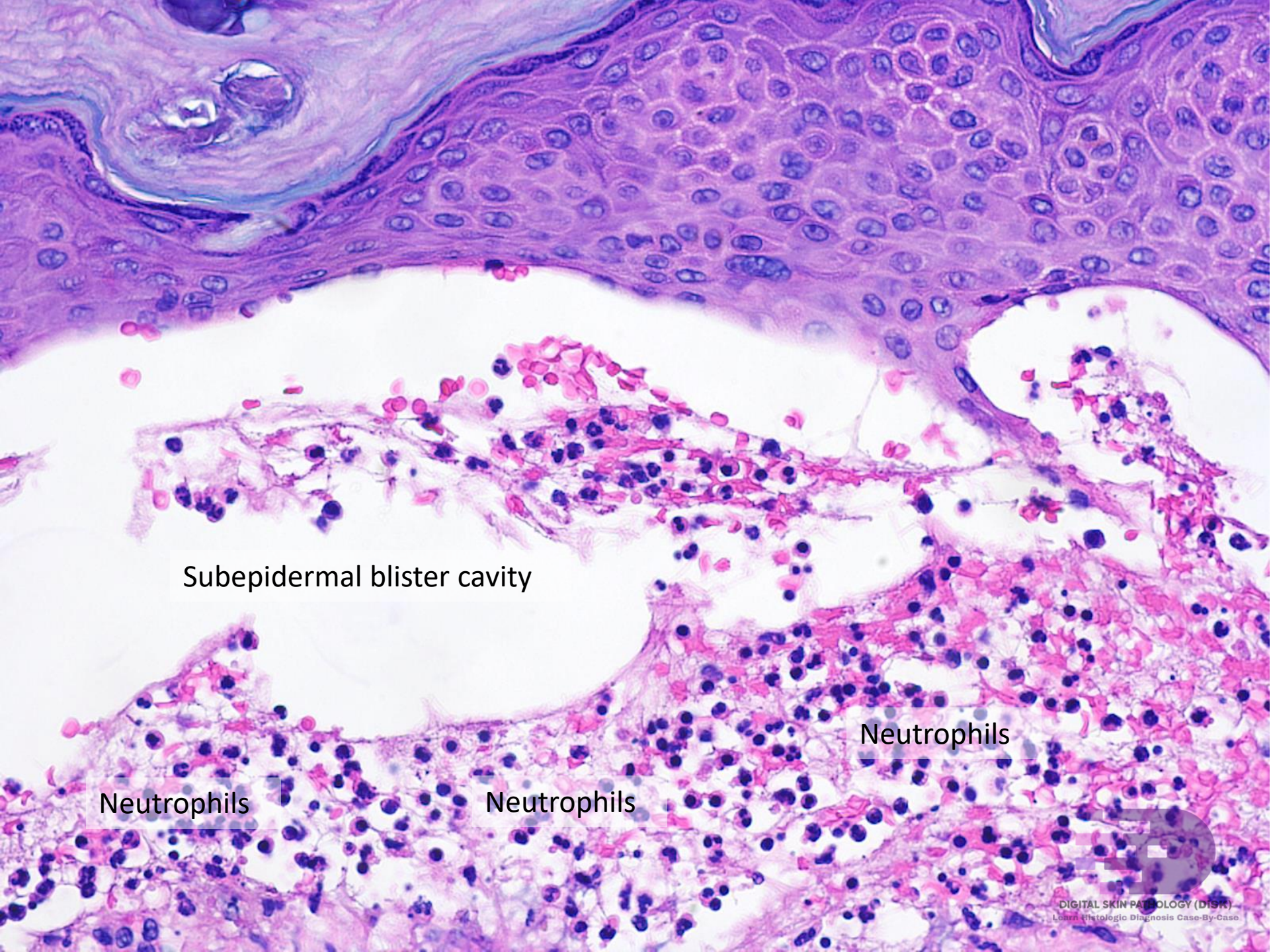
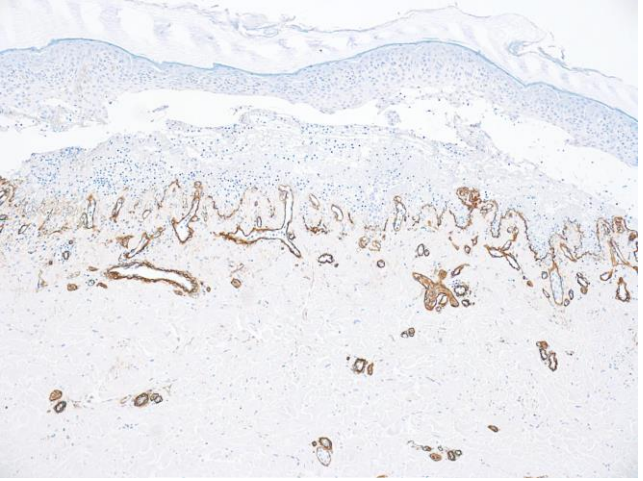
BULLOUS DERMATITIS

Soheil S. Dadras MD-PhD


Acral site: thick stratum corneum
Subepidermal blister



Blister floor flooded with neutrophils



Neutrophils

IHC: Collagen IV

Collagen IV localized to the floor:
Split above the basement membrane

Thickened basement membrane

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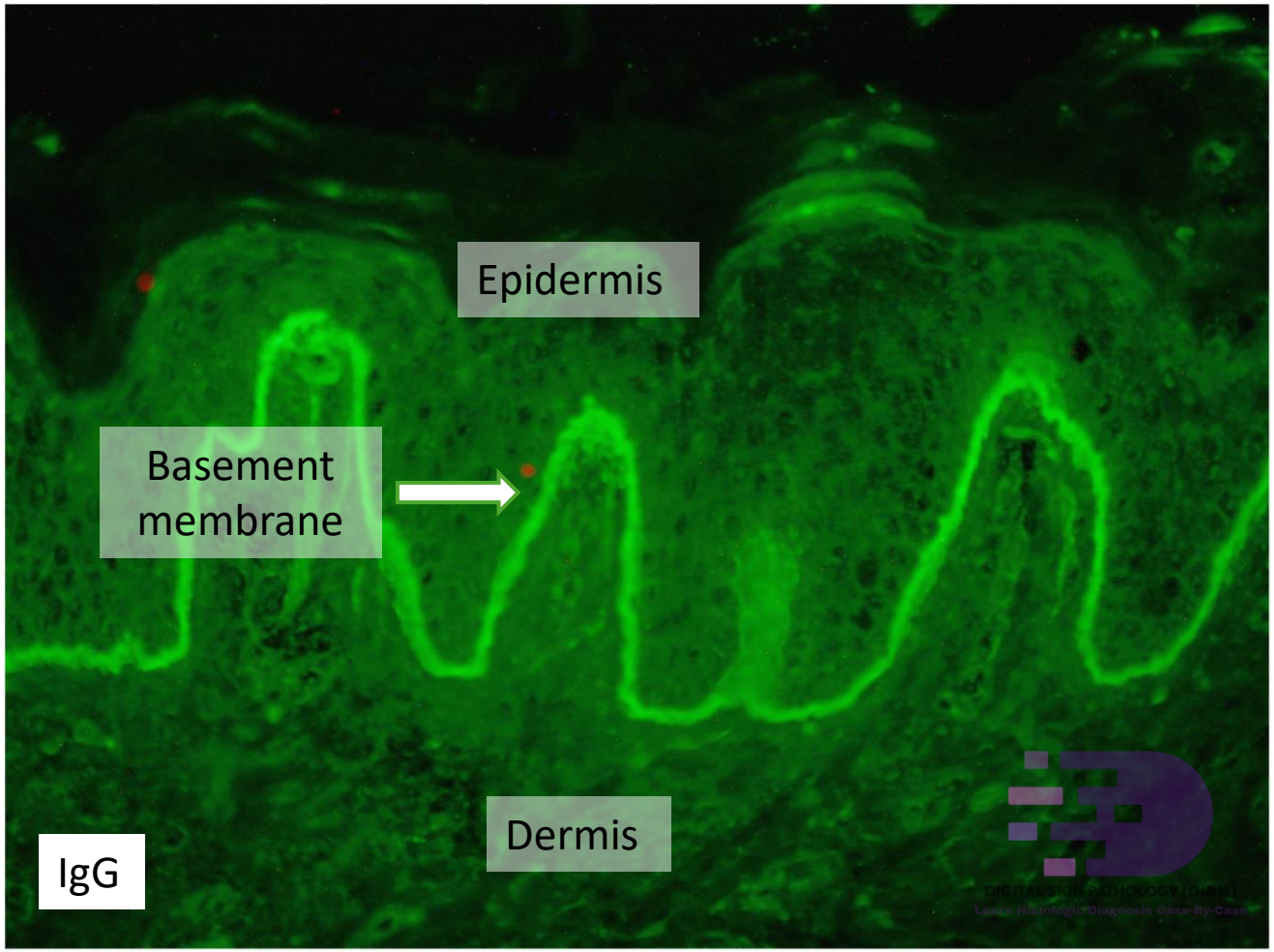
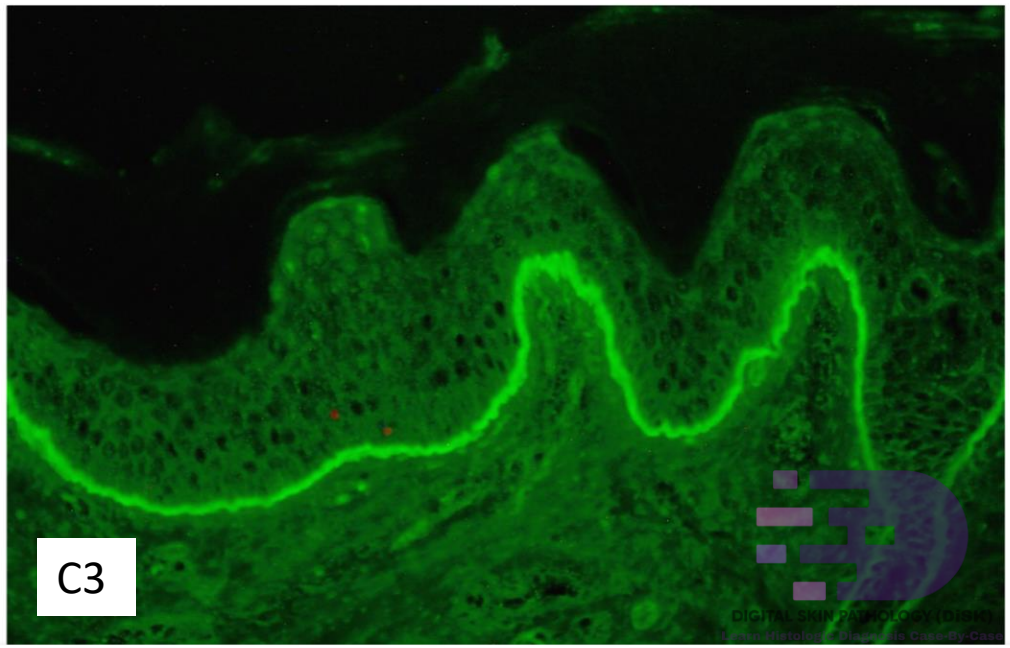
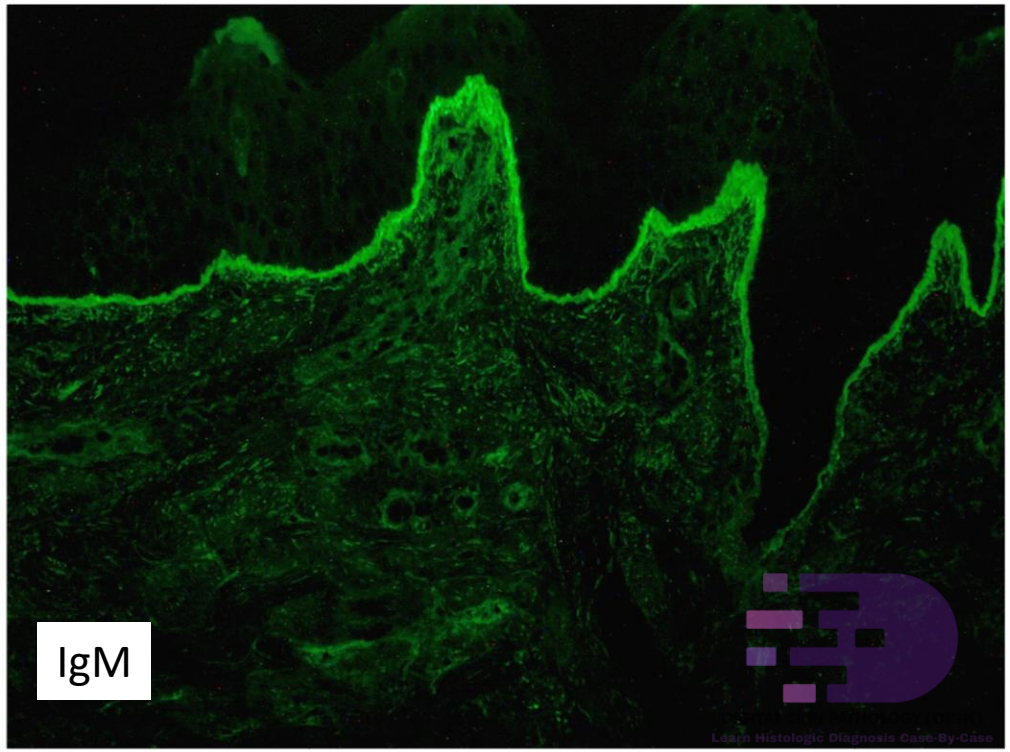
Learn Histologic Diagnosis Case-By-Case







Linear, subepidermal reaction in the basement membrane zone

- **Clinical Information:** 21 year-old Asian female, ?bullous lupus erythematosus (23-1010)

- **DIAGNOSIS:**

  Skin, Right Index, Finger, Punch Biopsy:

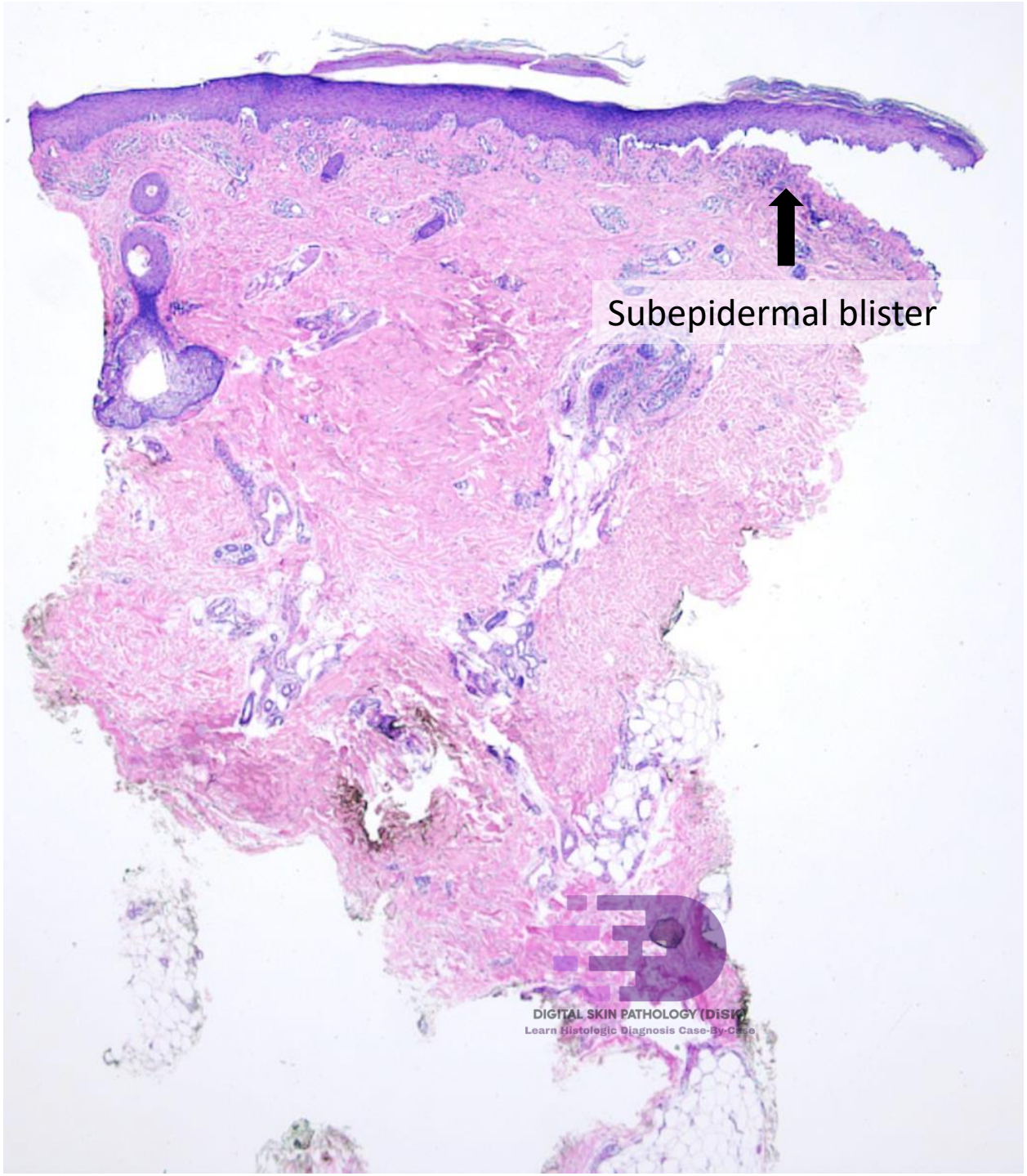
  - Subepidermal bullous dermatitis with neutrophils, compatible with bullous lupus erythematosus.

  Comment: the histopathology and DIF results support the diagnosis. Immunohistochemistry for collagen IV confirms separation above the basement membrane.

  Skin, Right Index, Finger, Punch Biopsy For Direct Immunofluorescence:

  - Positive for linear, subepidermal IgG, IgA, IgM, and C3 reaction.

- **Teaching Points:**
  - Full-house DIF results support lupus
  - Make sure the skin submitted for DIF is perilesional (not all blister)
- **Minimal Diagnostic Criteria:**
  - Subepidermal neutrophilic bullous dermatitis
  - IgG (or full-house) linear, granular or stippled pattern using DIF
- **Differential Diagnosis:**
  - Dermatitis herpetiformis
  - Linear IgA bullous dermatitis
  - Cicatricial pemphigoid
  - Epidermolysis bullosa acquisita
  - Bullous urticaria


Subepidermal blister
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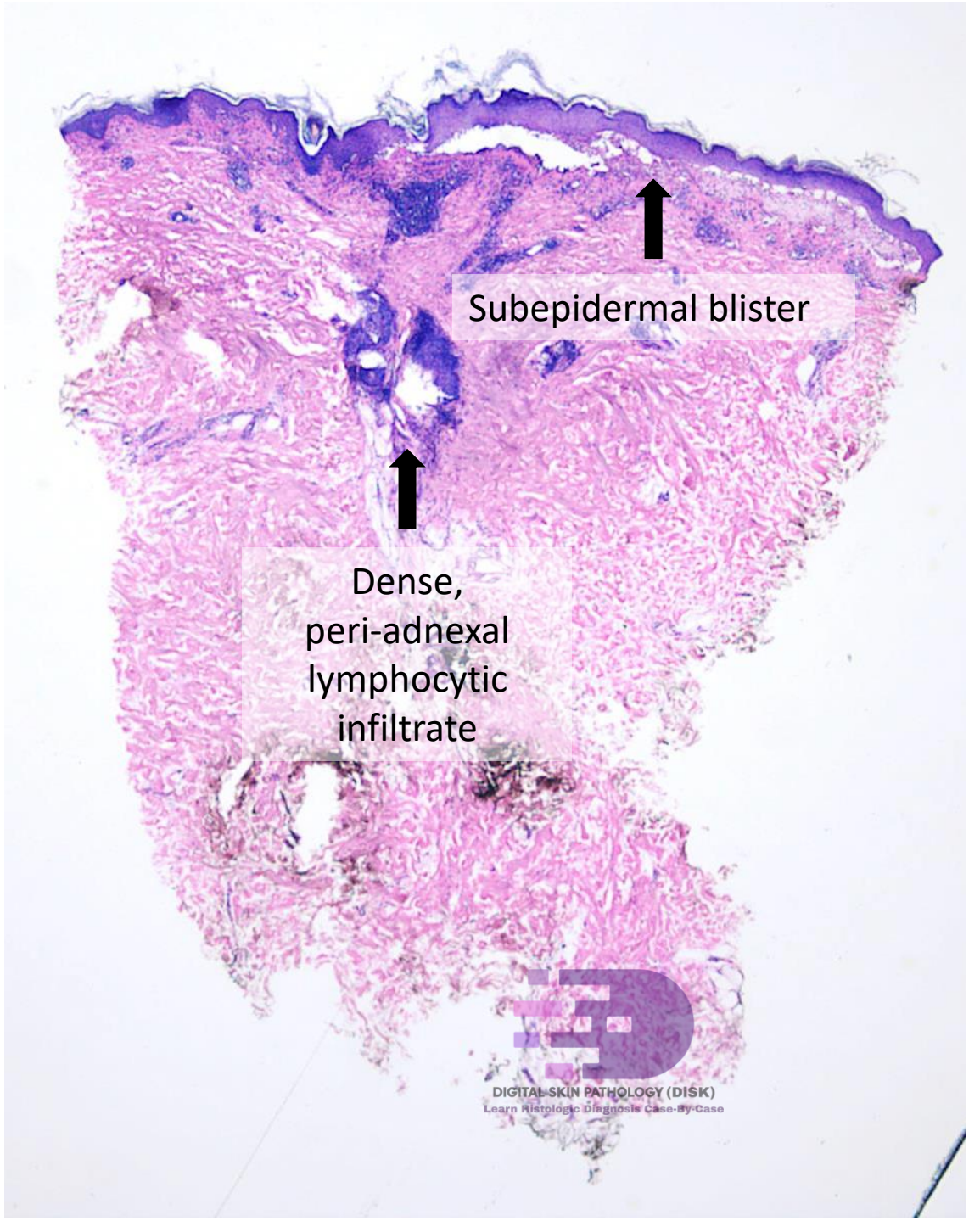
Subepidermal blister
Dense,
peri-adnexal
lymphocytic
infiltrate
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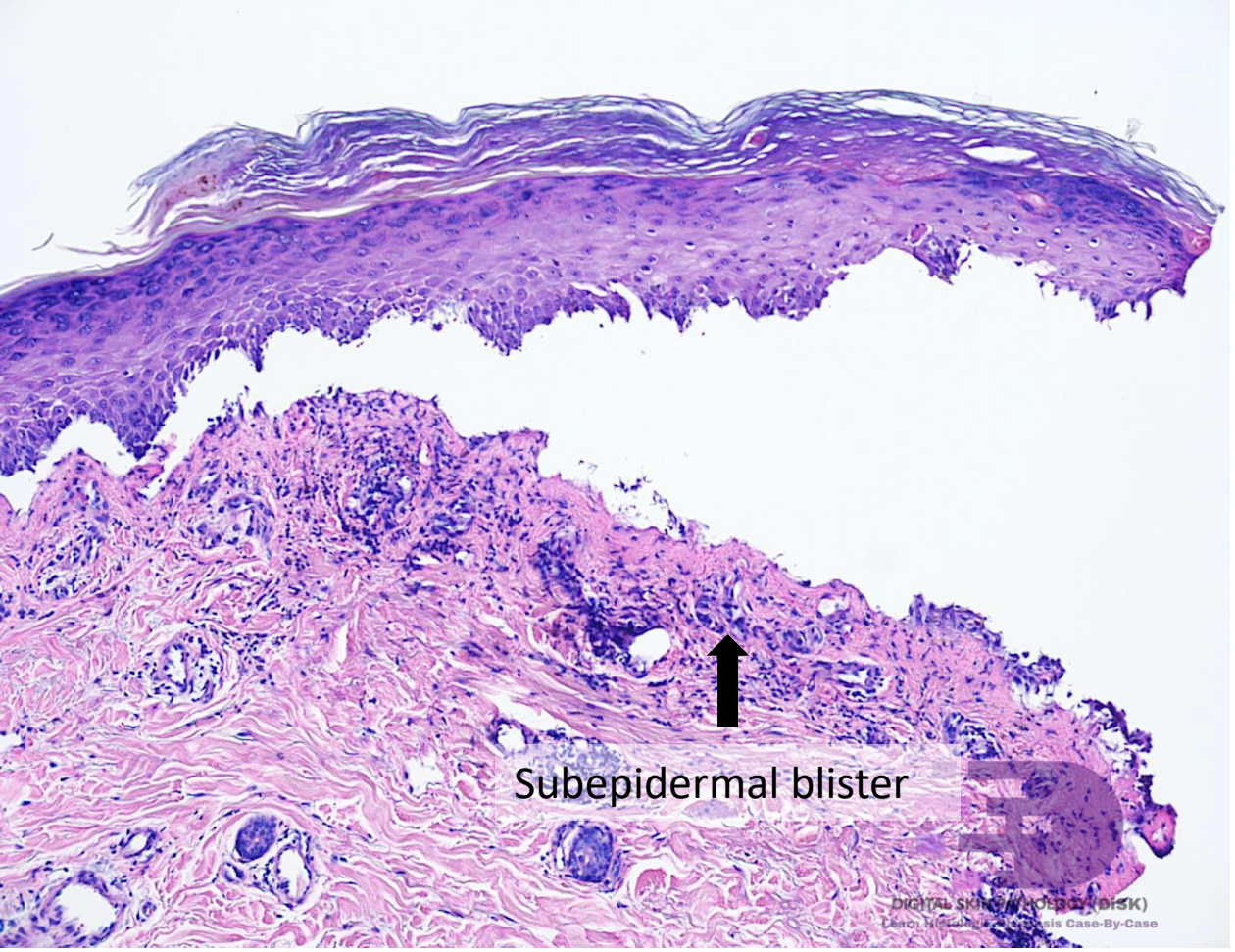
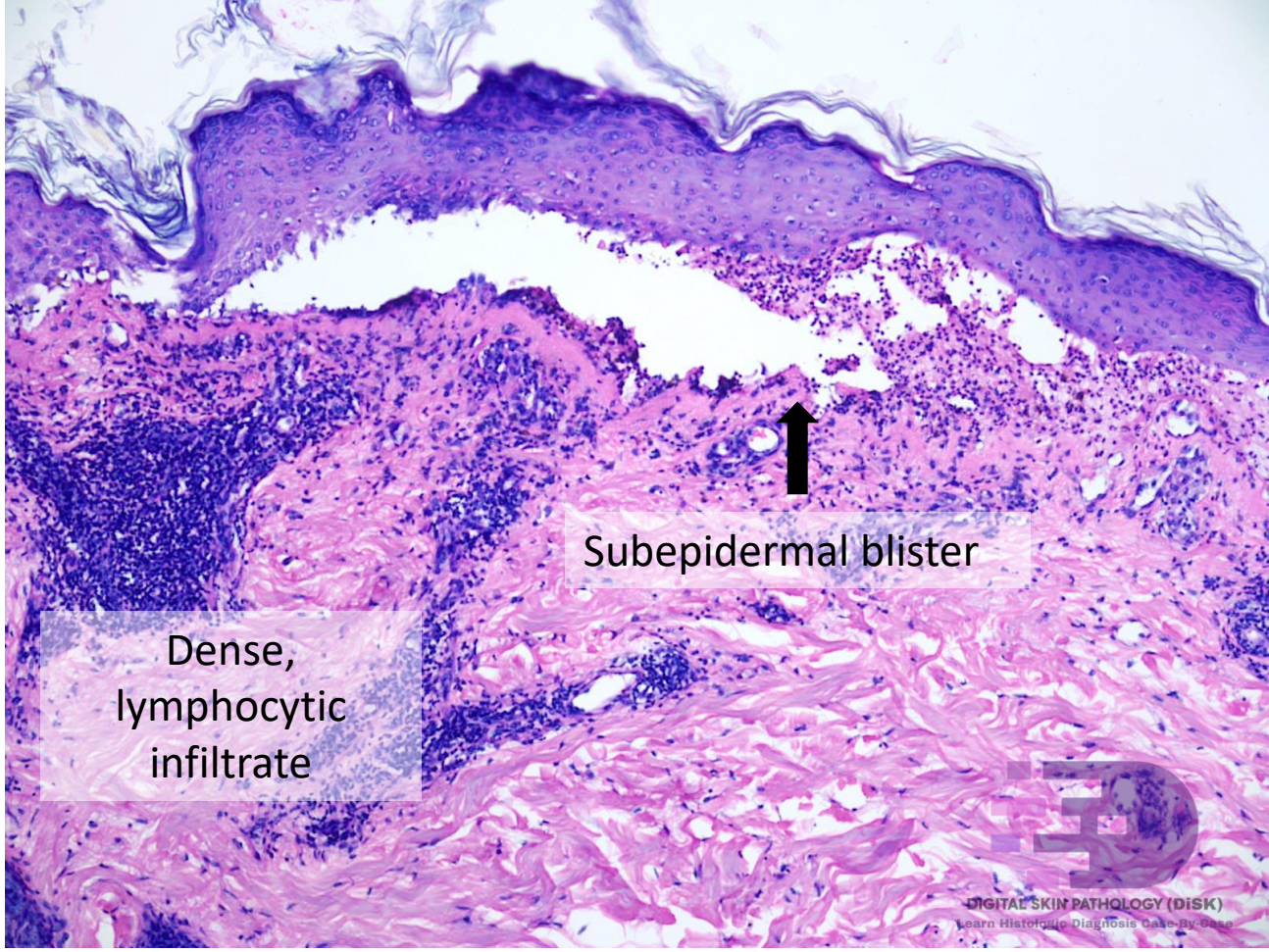
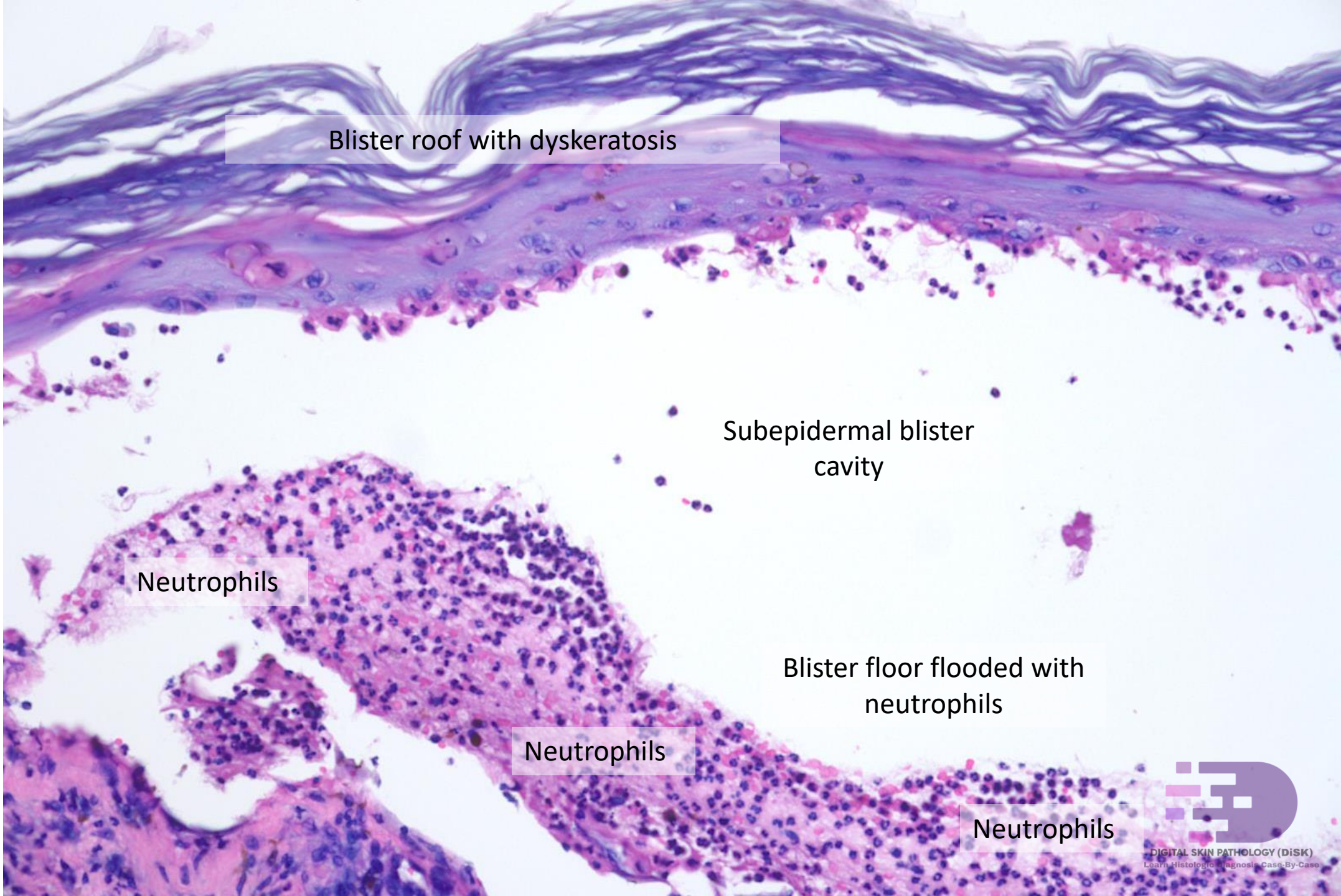

Subepidermal blister


Subepidermal blister
Dense, lymphocytic infiltrate


Blister roof with dyskeratosis
Subepidermal blister cavity
Neutrophils
Blister floor flooded with neutrophils
Neutrophils
Neutrophils
DIGITAL SKIN PATHOLOGY (DiSK)
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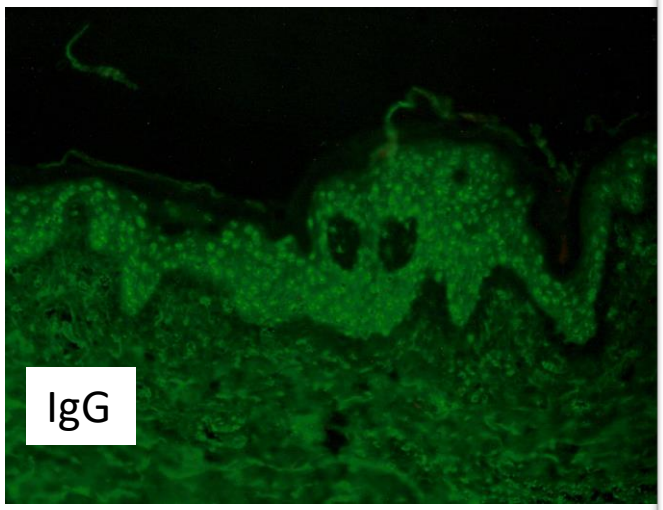
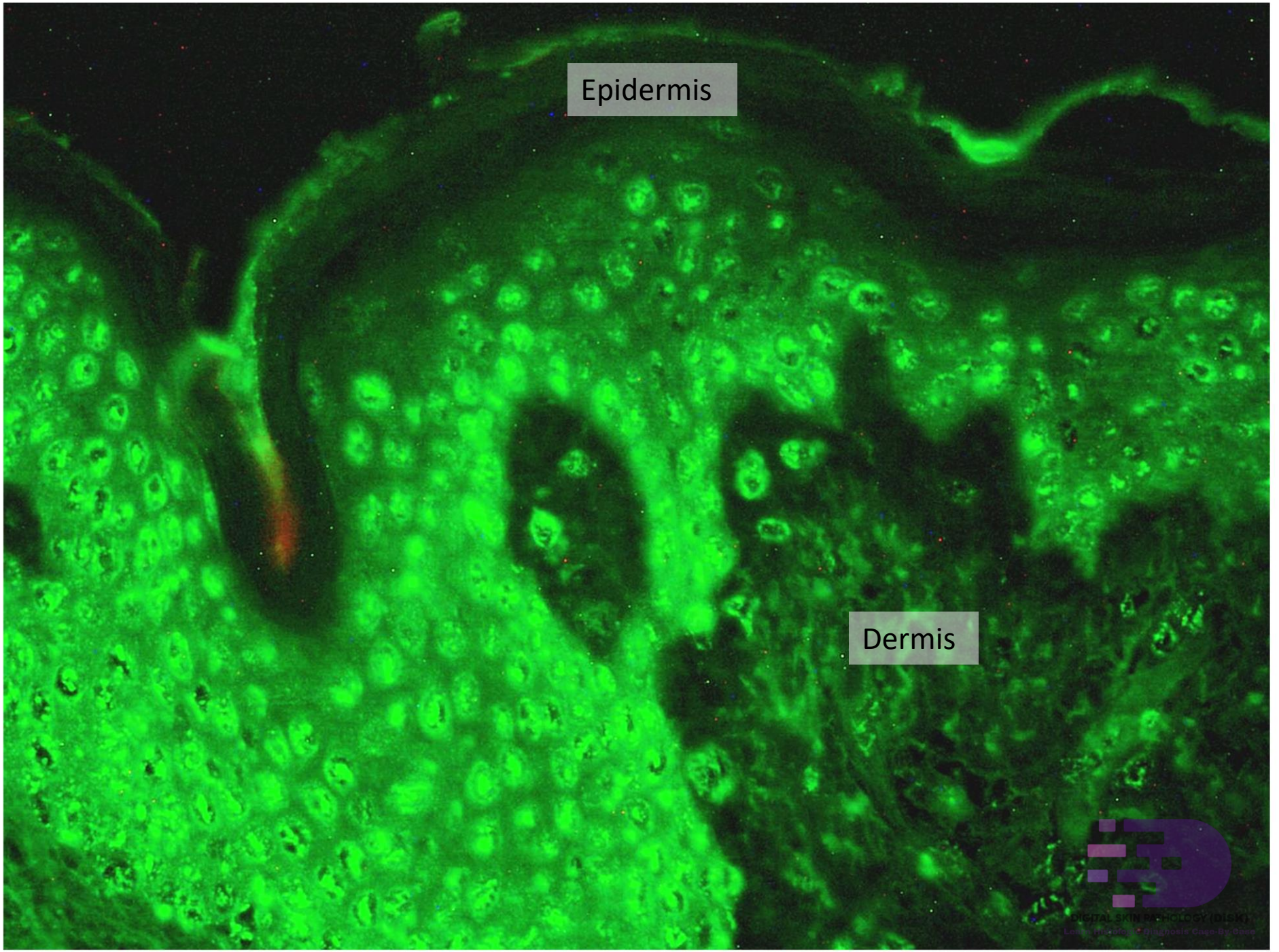


Nuclear, epidermal reaction



- **Clinical Information:** 51 year-old female, L30.9, suspicious for a blistering dermatitis, but patient reports no history of blisters; repeated biopsy with DIF (22-16615).
- **DIAGNOSIS:**

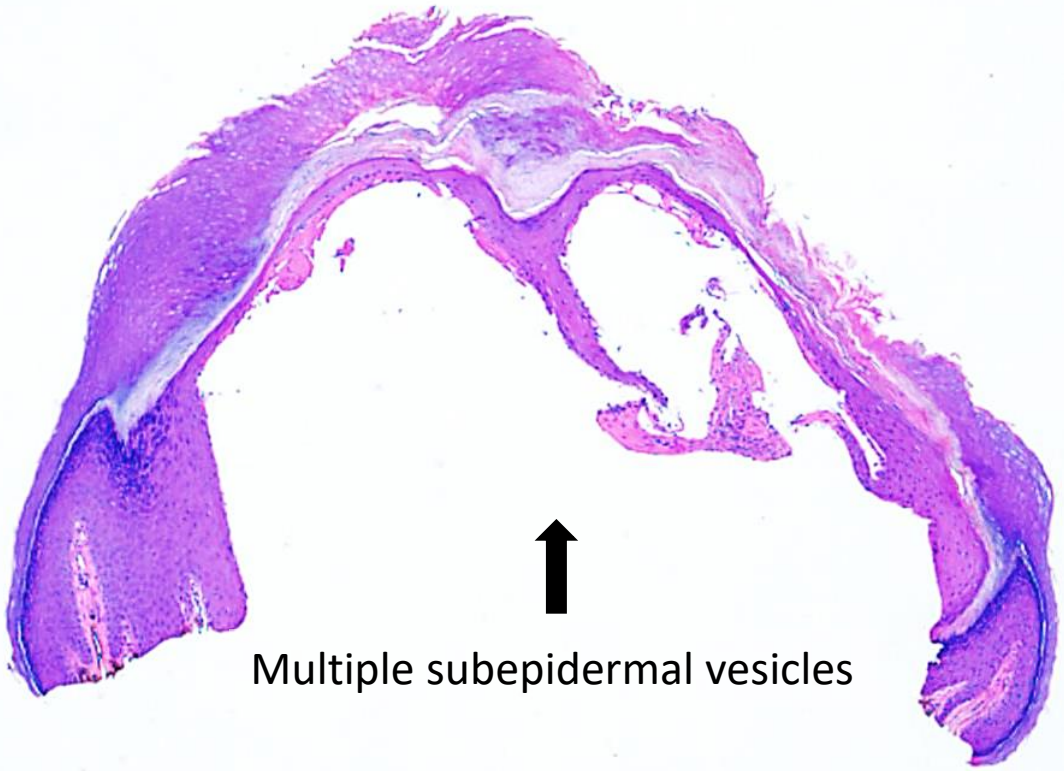
  Skin, Right Flank and Right Buttock, Punch Biopsies:

  - Subepidermal bullous dermatitis with neutrophils and dyskeratosis.

  Skin, Right Flank, Punch Biopsy For Direct Immunofluorescence:

  - Positive for nuclear IgG reaction only.
  - Negative for IgA, IgM, and C3 reaction.

  Comment: Direct immunofluorescence demonstrates positive nuclear reaction for IgG in the epidermal keratinocytes; the other usual patterns are negative. Nuclear IgG pattern has been reported in patients with Sjogren's syndrome (68%), systemic lupus erythematosus (15%), and other connective tissue diseases (20-40%). Notably, up to 10% of healthy individuals also display epidermal nuclear IgG deposits, therefore limiting the specificity of this finding. The combined histopathology and DIF results point to a connective tissue disorder; however, correlation with appropriate serology is needed.
- **Teaching Points:**
  - Nuclear, epidermal IgG reaction may suggest lupus or another connective tissue disorder, but it is not specific
- **Minimal Diagnostic Criteria:**
  - Subepidermal neutrophilic bullous dermatitis
- **Differential Diagnosis:**
  - Dermatitis herpetiformis
  - Linear IgA bullous dermatitis
  - Cicatricial pemphigoid
  - Epidermolysis bullosa acquisita
  - Bullous urticaria



Multiple subepidermal vesicles

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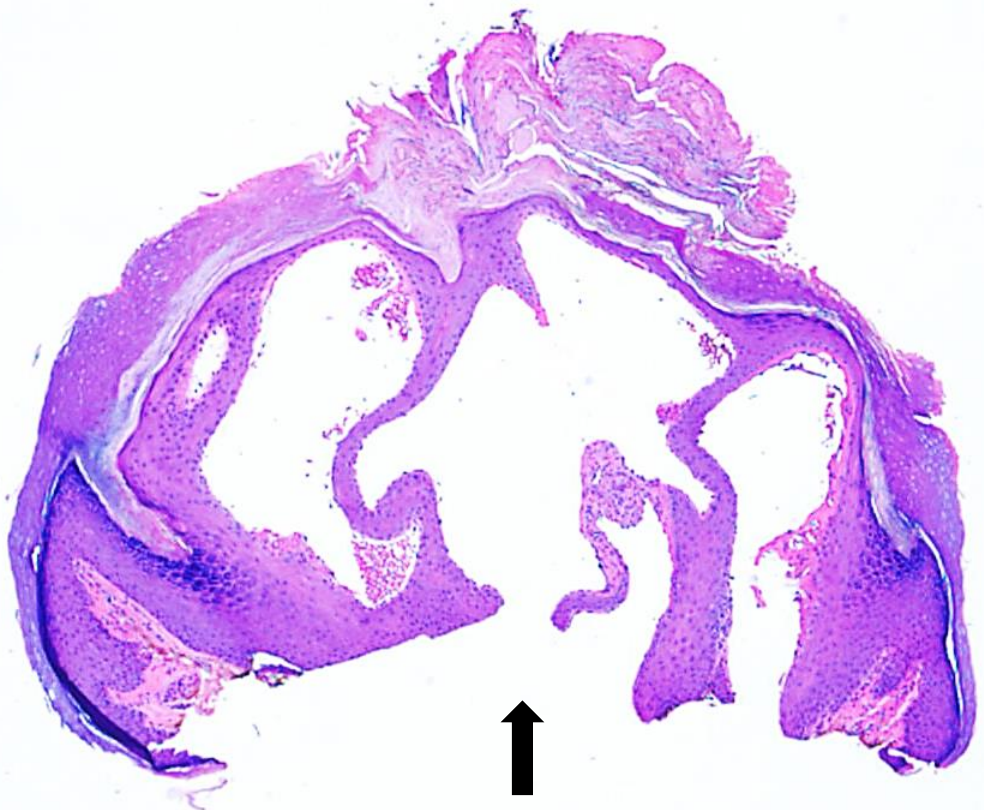

Multiple subepidermal vesicles

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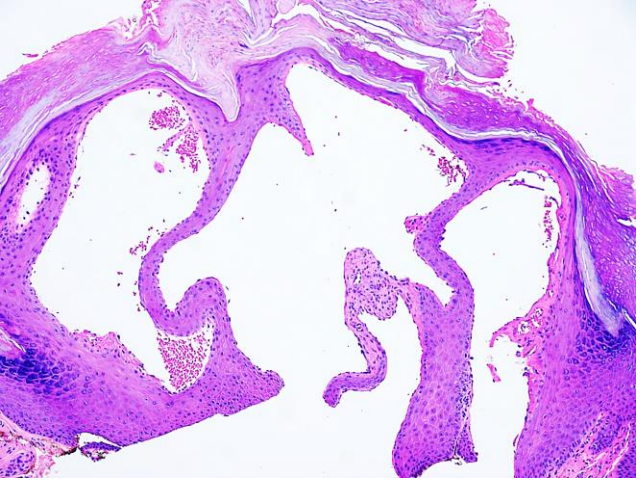


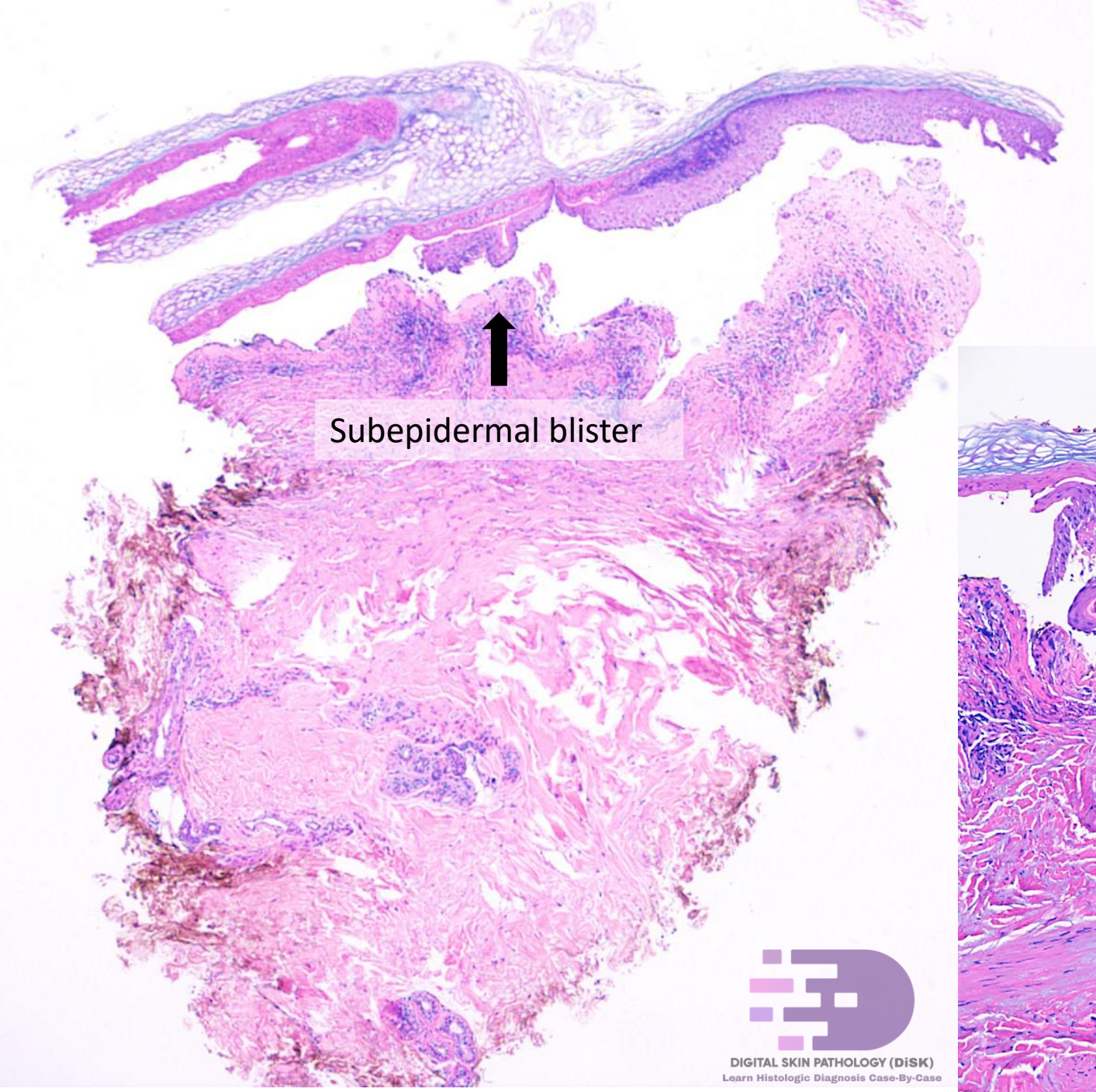
Multiple subepidermal vesicles

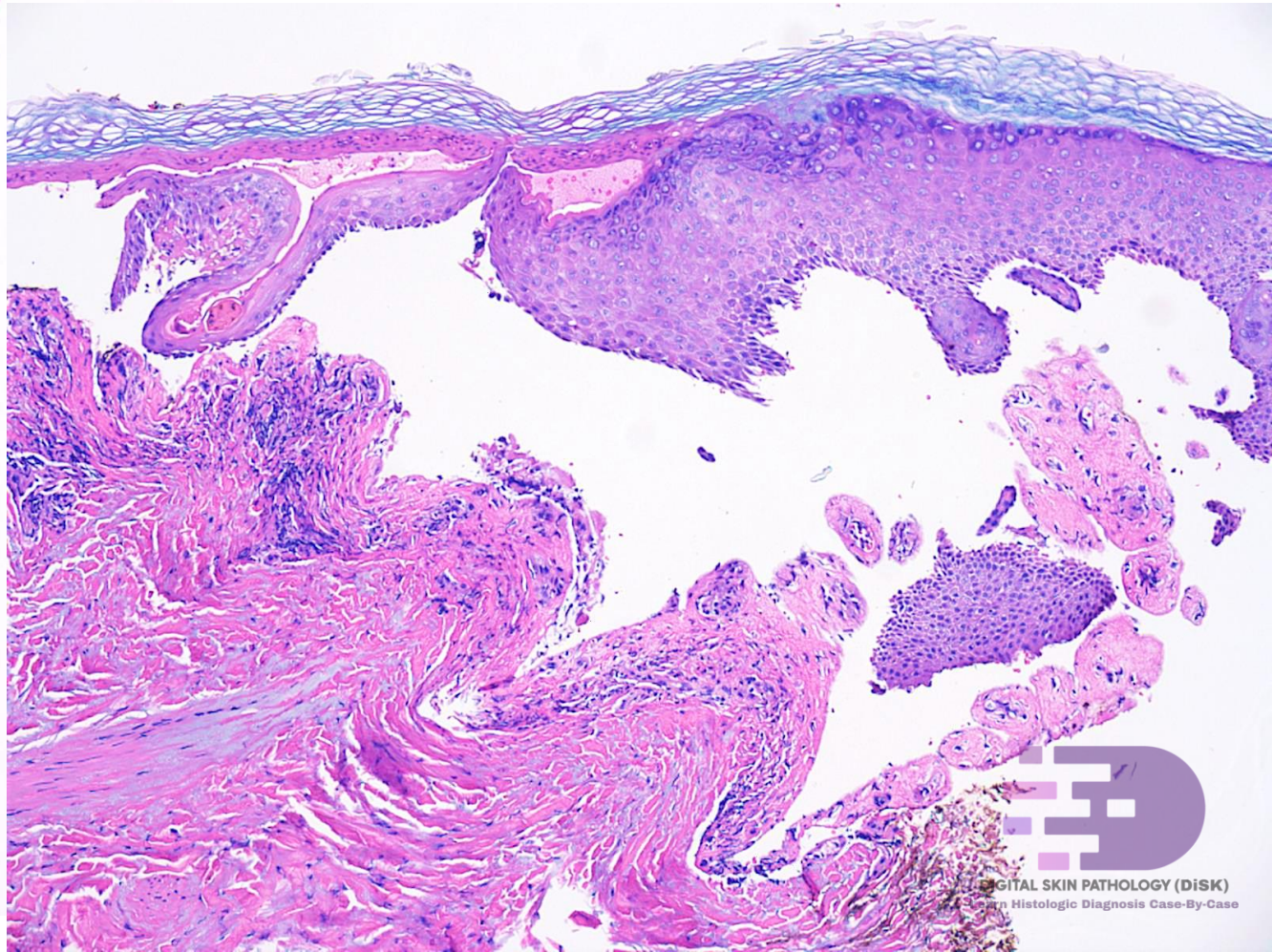
Valve-like structures

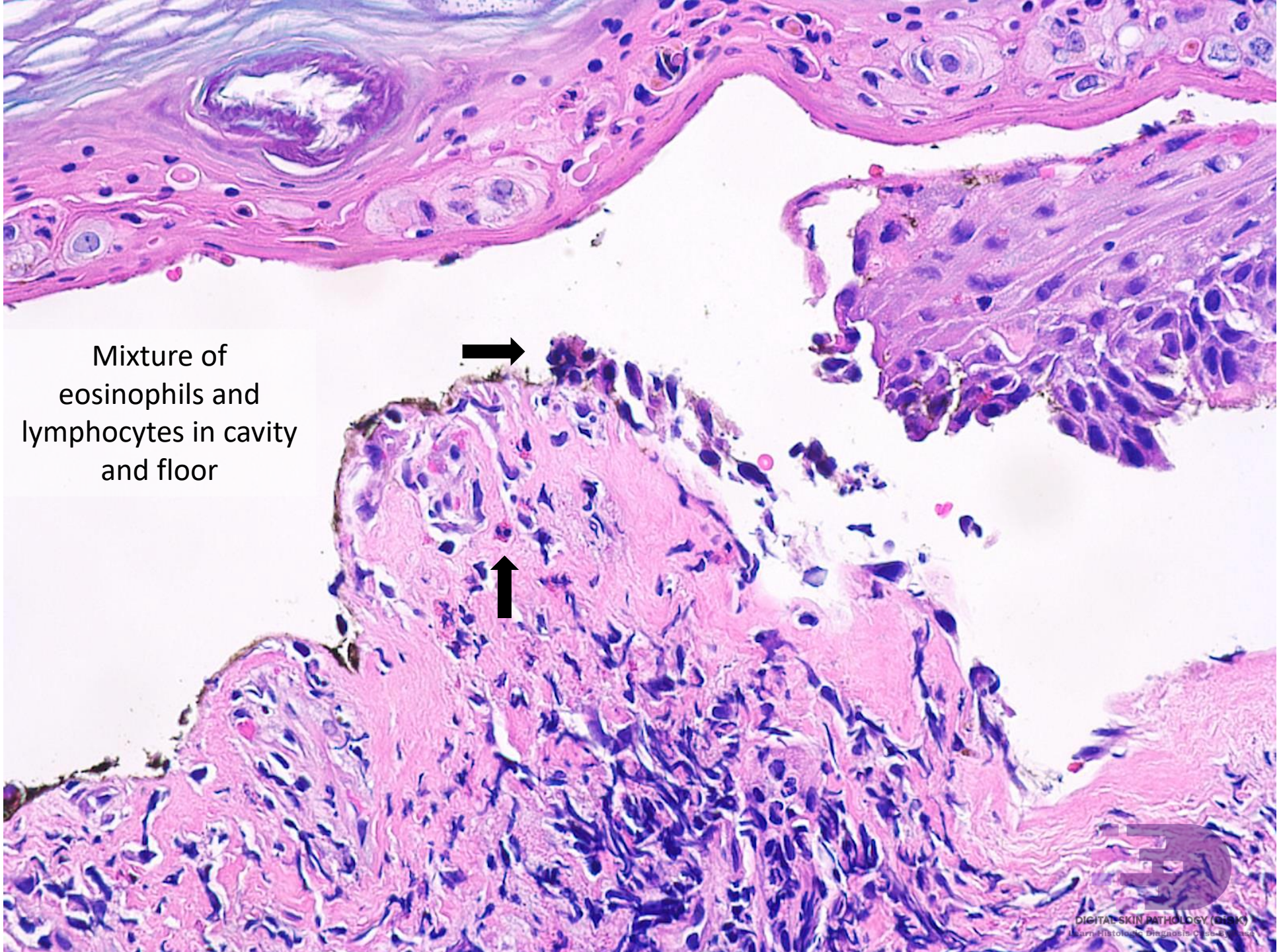
Vesicles lined by single layer of endothelium

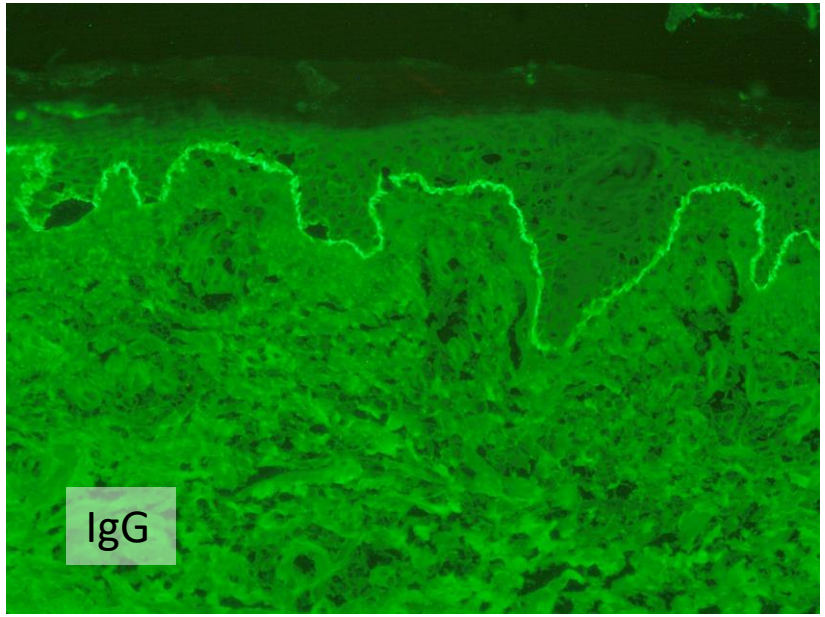
- **Clinical Information:** 60 year-old male, N48.9, penile lesion (22-07950).
- **DIAGNOSIS:**

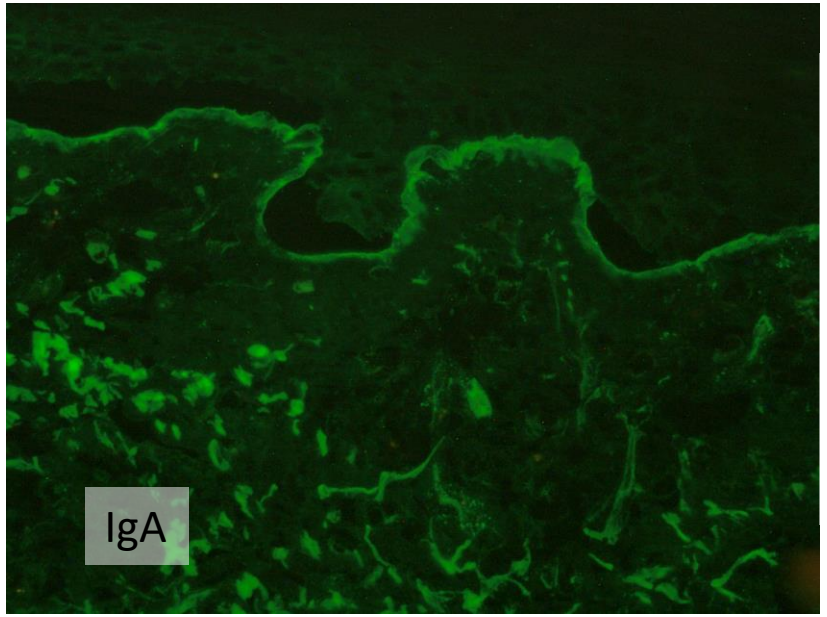
  Skin, Penis, Shave Biopsy:
  - Lymphangioma circumscriptum.
- **Teaching Points:**
  - Not all that blisters is a vesiculobullous disorder
  - Look for endothelial lining
  - When endothelial lining is found, then not a vesiculobullous disorder
- **Minimal Diagnostic Criteria:**
  - Multiple subepidermal vesicles impart the clinical impression of “fish eggs”
  - Empty space is lined by a row of flat (lymphatic) endothelial cells
  - IHC for podoplanin (D2-40) will typically highlight the endothelial cells
- **Differential Diagnosis:**
  - May mimic the roof of subepidermal blister (low power)
  - Deep or superficial and deep variant of Lymphangioma circumscriptum


Subepidermal blister
DIGITAL SKIN PATHOLOGY (DiSK)
Learn Histologic Diagnosis Case-By-Case

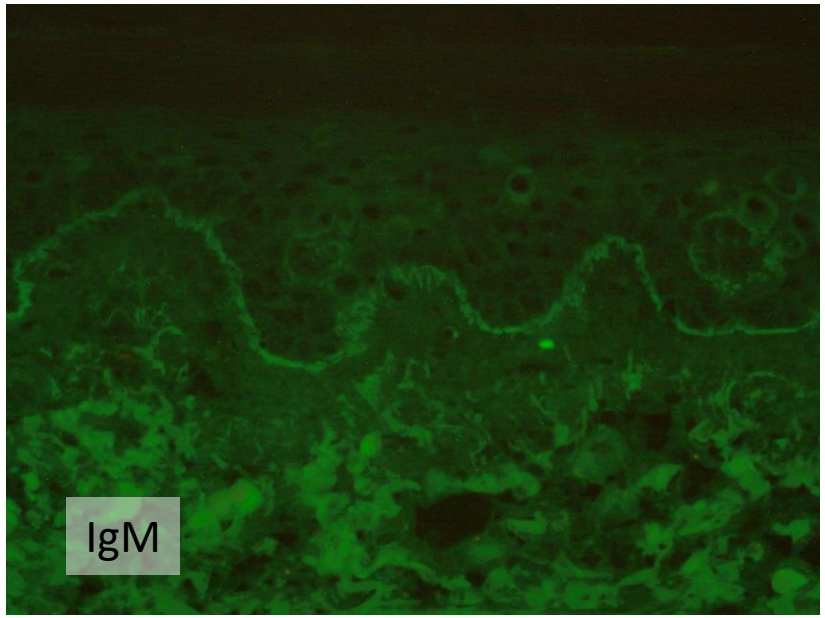

DIGITAL SKIN PATHOLOGY (DiSK)

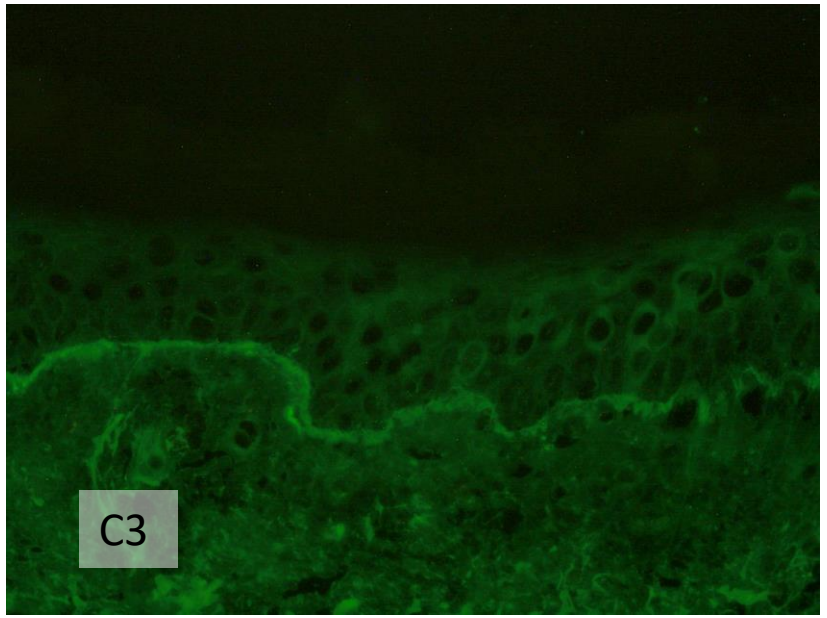

Mixture of eosinophils and lymphocytes in cavity and floor





Full house linear, subepidermal reaction in the basement membrane zone





DIGITAL SKIN PATHOLOGY (DiSK)
Learn Histologic Diagnosis Case-By-Case

- **Clinical Information:** 89 year-old female, R21 2.5 cm placid bullae of superior anterior lateral right shin. Few superficial resolving erosions scattered on the right anterior lower leg with larger patch inferiorly with the rim of hemorrhagic, scaling and central pinpoint bleeding; and smaller, round eroded and scaly patches scattered superiorly, rule out bullous pemphigoid vs. pemphigus foliaceus (22-53703).
- **DIAGNOSIS:**

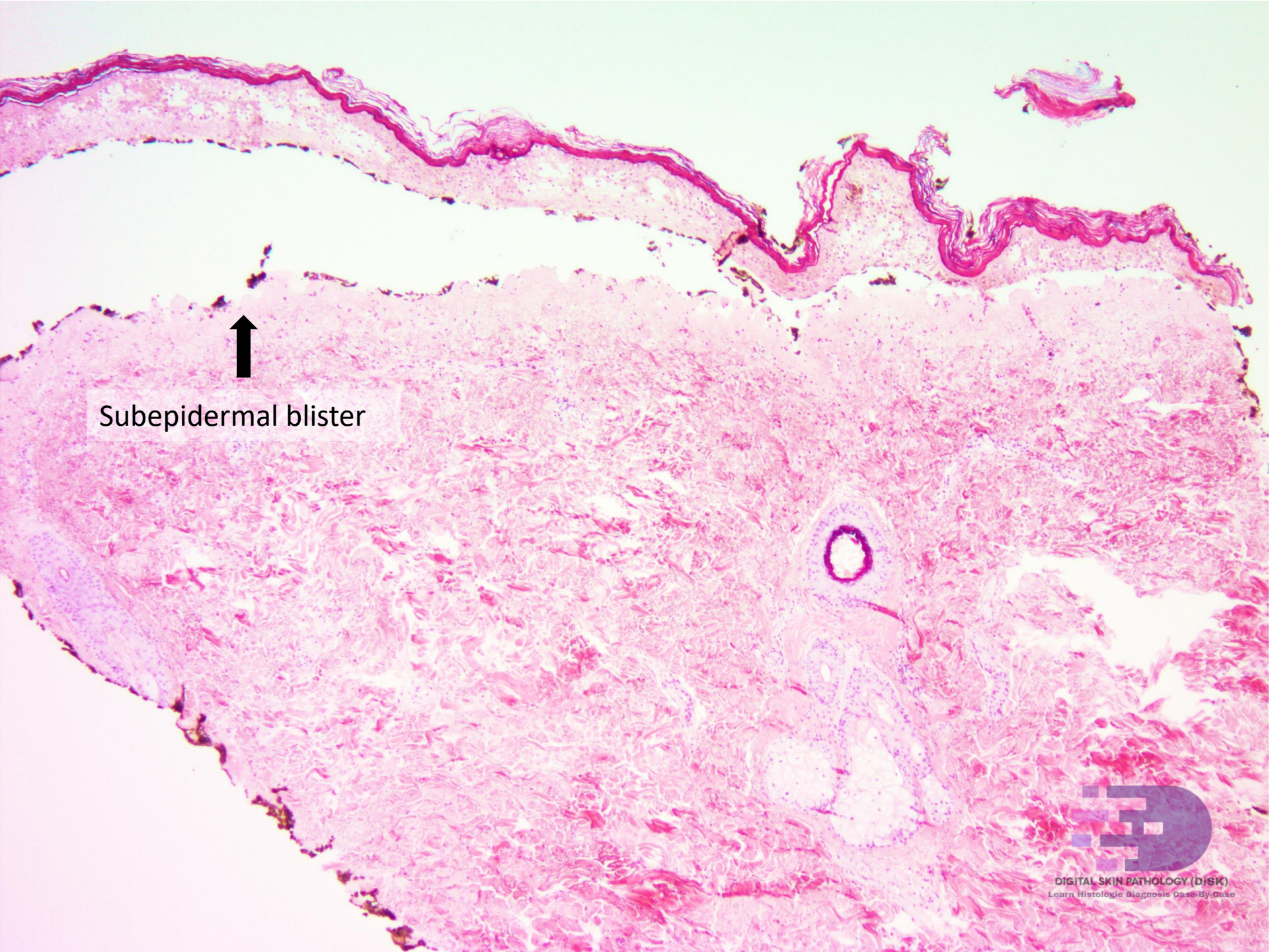
  Skin, Right Anterior Lower Leg, Punch Biopsy:

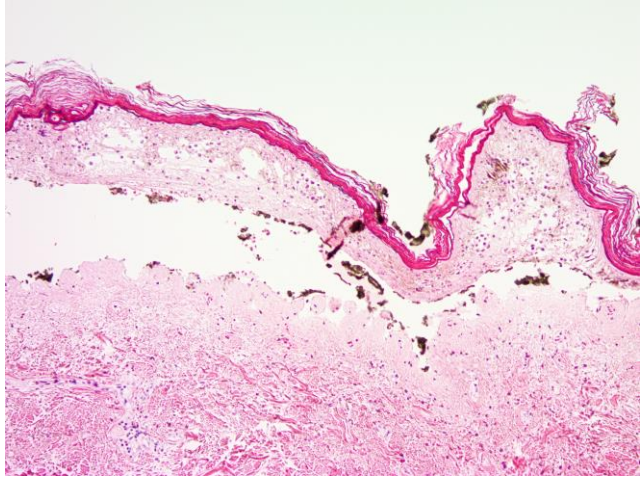
  - Subepidermal bullous dermatitis with eosinophils.

  Skin, Right Anterior Lower Leg, Punch Biopsy For Direct Immunofluorescence:

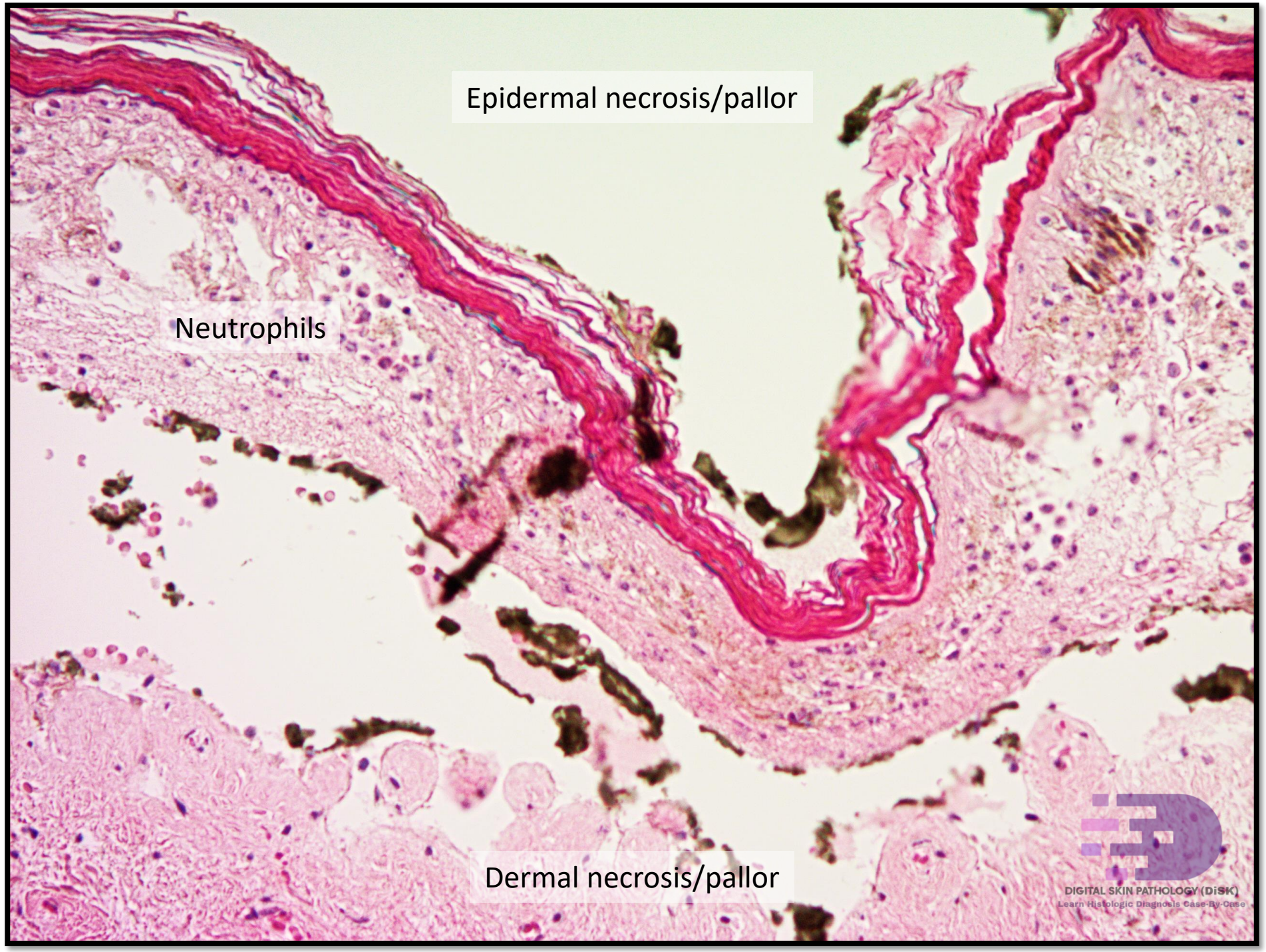
  - Positive for linear, subepidermal IgG, IgA, IgM, and C3 reaction.

  Comment: Overall, the histopathology and DIF results support bullous pemphigoid.
- **Teaching Points:**
  - Although unusual, other immunoreactants (like IgA and IgM) can also be seen using DIF
  - Lack of dyskeratosis excludes pemphigus disease group on histopathology
- **Minimal Diagnostic Criteria:**
  - Subepidermal eosinophilic bullous dermatitis, without dyskeratosis
  - Eosinophils and lymphocytes seen in the cavity and/or the floor
- **Differential Diagnosis:**
  - Bullous drug reaction
  - Bullous arthropod assault
  - Epidermolysis bullosa





Tissue pallor:
Necrosis of skin
And adnexa


Epidermal necrosis/pallor
Neutrophils
Dermal necrosis/pallor
DIGITAL SKIN PATHOLOGY (DiSK)
Learn Histologic Diagnosis Case-By-Case

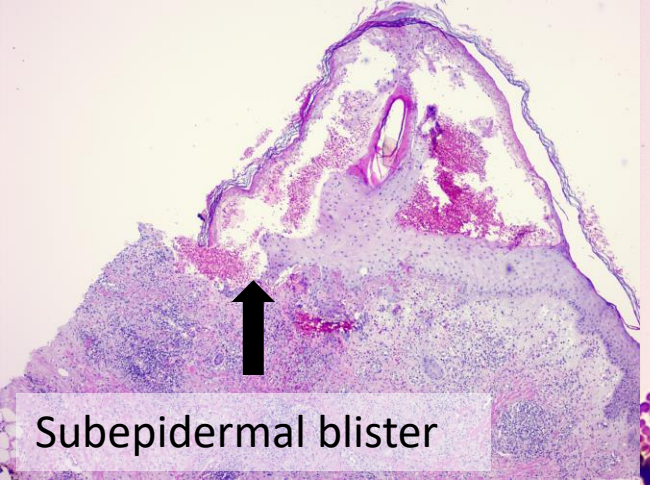
- **Clinical Information:** 56 year-old with erythematous eruption with erosions and blisters on the chest and abdomen, r/o blistering disorder (24-3316).
- **DIAGNOSIS:**

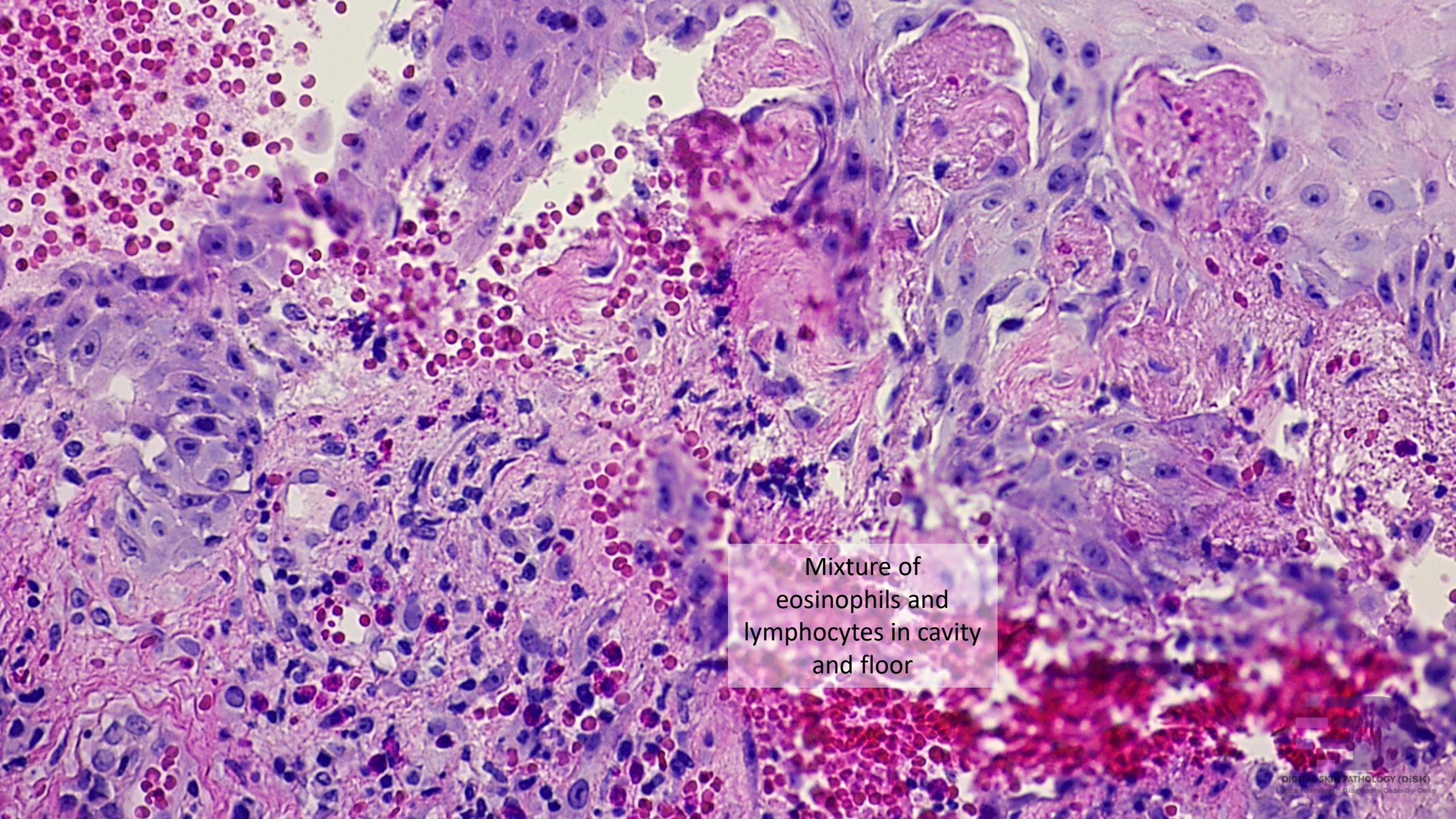
  Skin, Chest, Punch Biopsy:
  - Full-thickness epidermal necrosis and cell-poor subepidermal blister.

  Skin, Chest, Punch Biopsy For Direct Immunofluorescence:
  - Negative for IgG, IgA, IgM, and C3 reaction.

  Comment: Overall, the histopathology supports thermal injury, e.g., burn. Clinical correlation is recommended.

  Follow-up: Further inquiry into the history showed chronic alcohol abuse, stated to the first responders, “wanted to light up my grill” when found at home alone and confused. The next day clinical exam showed charred skin in some areas on the chest.
- **Teaching Points:**
  - Cell-poor subepidermal blister
  - Epidermal, dermal necrosis (depending on the degree of burn)
- **Minimal Diagnostic Criteria:**
  - Tissue pallor
  - Necrosis of skin and adnexa
  - Cell-poor subepidermal blister
- **Differential Diagnosis:**
  - Porphyria cutanea tarda
  - Cryotherapy
  - Toxic epidermal necrolysis
  - Blister over scar
  - Bullous amyloidosis
  - Cell-poor bullous pemphigoid
  - Vascular (arterial) insufficiency


Subepidermal blister


Mixture of eosinophils and lymphocytes in cavity and floor
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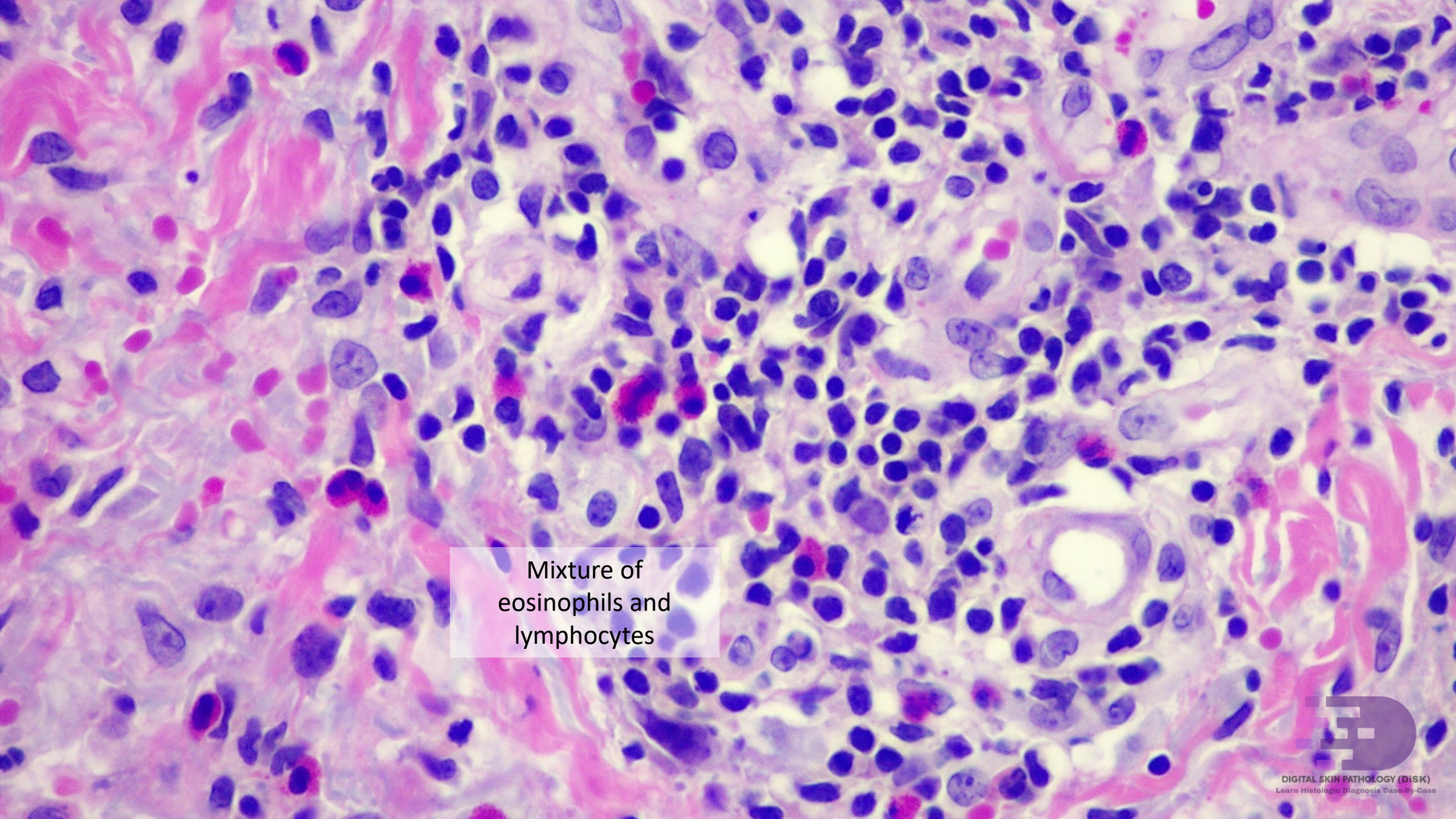
Mixture of eosinophils and lymphocytes
DIGITAL SKIN PATHOLOGY (DiSK)
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Clinical Information: 76F with two pruritic tense bullae on the right and left lower extremities that have been very itchy. Bullous arthropod v. BP v. PV v. ACD v. Less likely DH, EBA (24-37422)

DIAGNOSIS:

Specimen #1 - Skin, Right Lower Leg, Punch Biopsy:

-Subepidermal bullous and perivascular lymphocytic dermatitis with eosinophils. See comment

Comment 1: The histologic differential diagnosis includes bullous arthropod bite reaction and bullous dermal hypersensitivity to a drug or other ingestants. Additional levels (two sets) are examined. A PAS stain is negative for fungal forms.

Specimen #2 - Skin, Right Lower Leg, (DIF) Punch Biopsy:

- Direct immunofluorescence is negative (for IgG, IgA, IgM, C3 and fibrinogen).

Comment 2: The frozen-section histopathology demonstrates intact epidermis without microvesicles.

Teaching Points:

- Lack of dyskeratosis excludes pemphigus disease group on histopathology
- DIF is part of complete work-up to exclude immunobullous disorders, make sure the skin submitted for DIF is perilesional (not all blister)

Minimal Diagnostic Criteria:

- Subepidermal eosinophilic bullous dermatitis, without dyskeratosis
- Eosinophils and lymphocytes seen in the cavity and/or the floor

Differential Diagnosis:

- Bullous drug reaction
- Epidermolysis bullosa
- Bullous pemphigoid