Dermatopathology Quiz Cases 144-150

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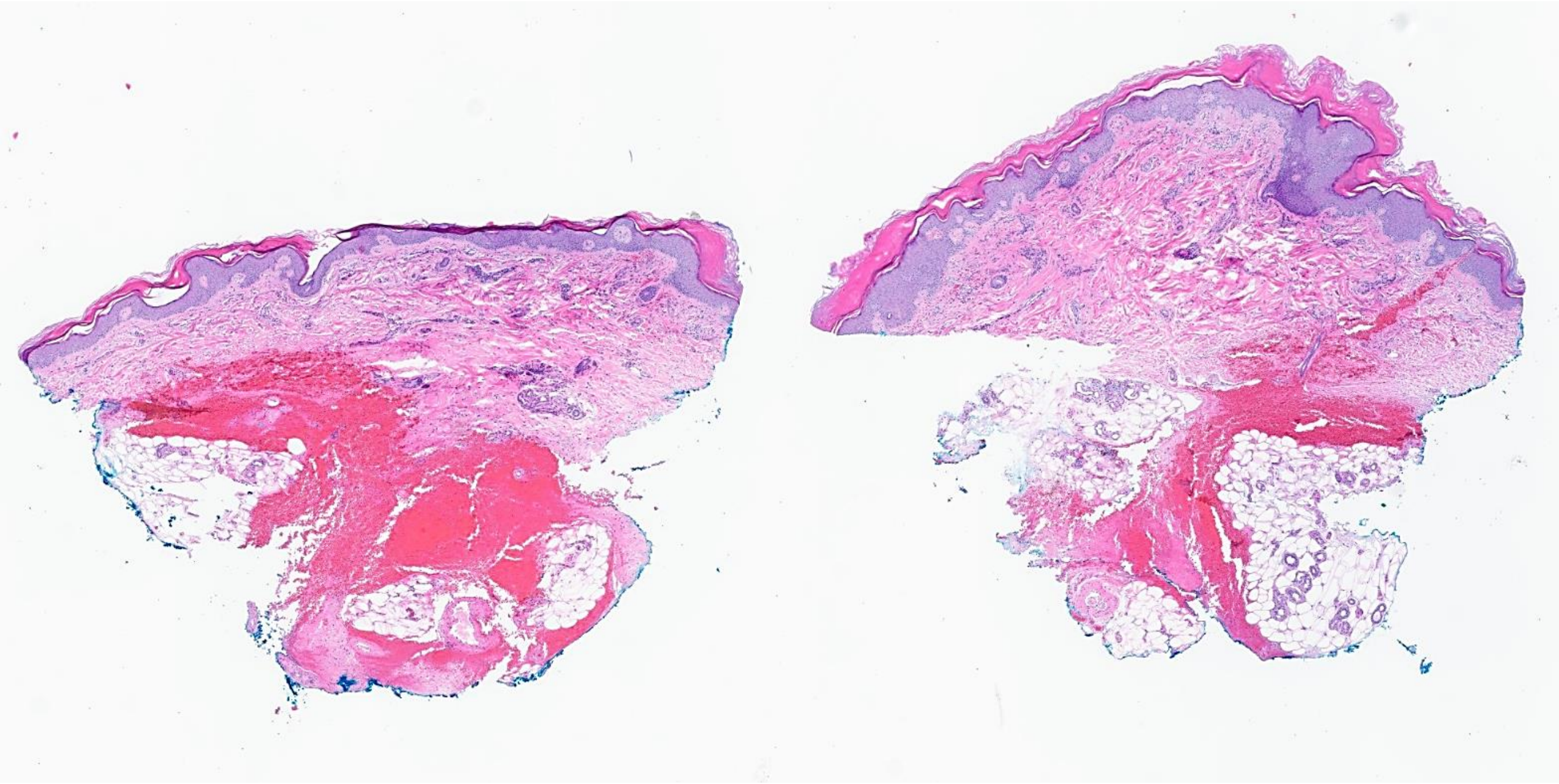
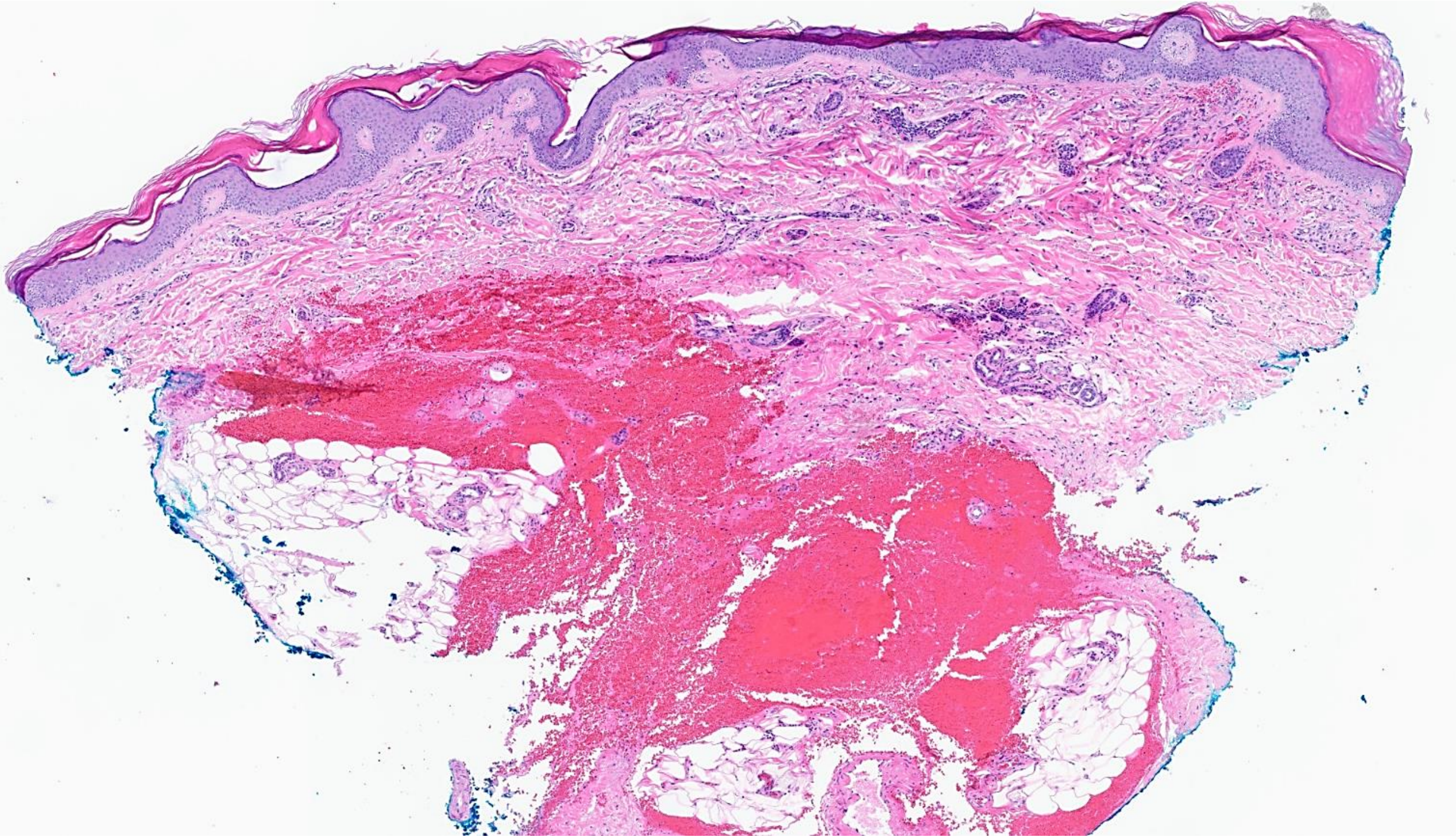
Test your knowledge of diagnostic skin pathology

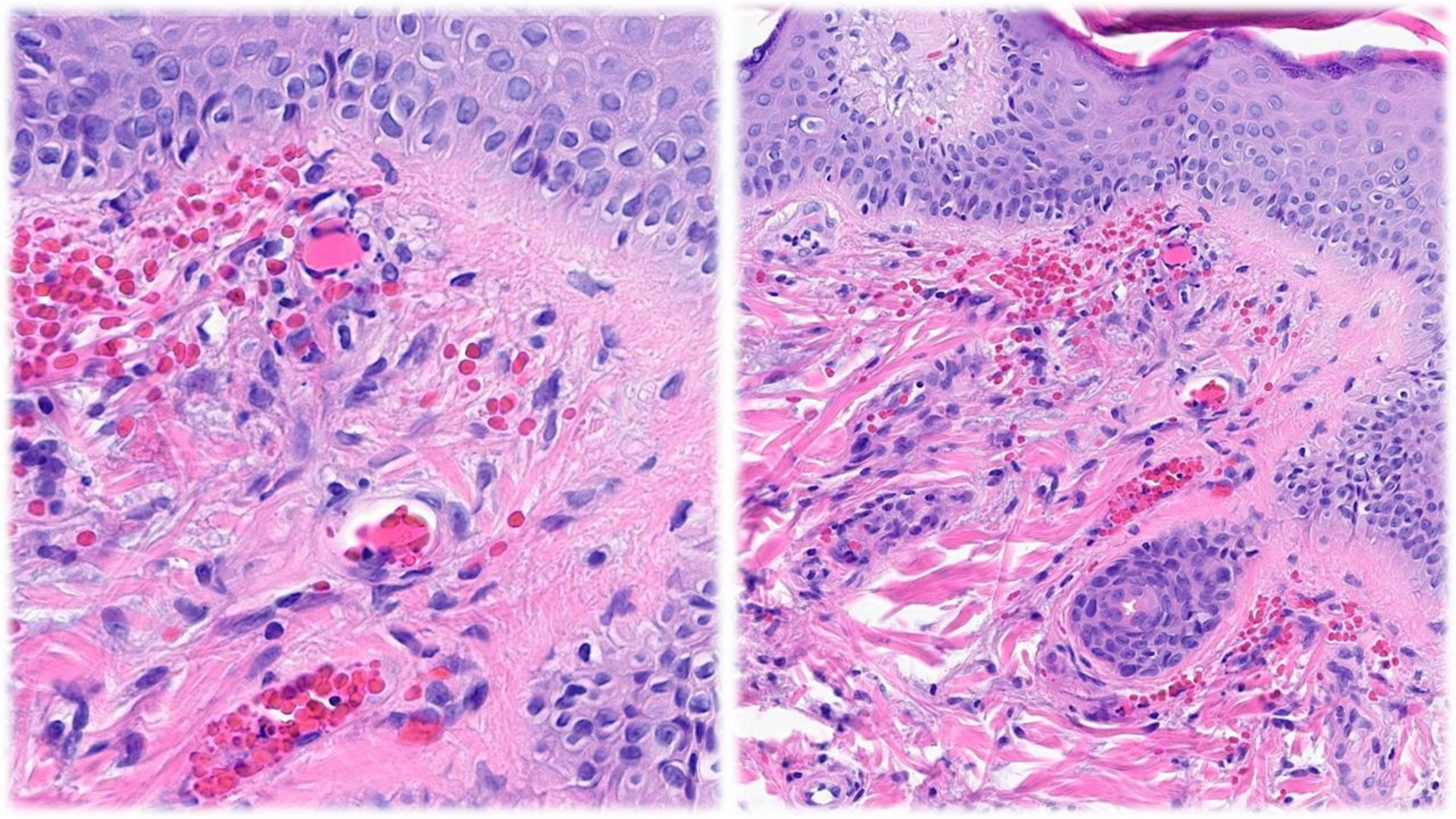
EXAMINE THE UNLABELED IMAGES

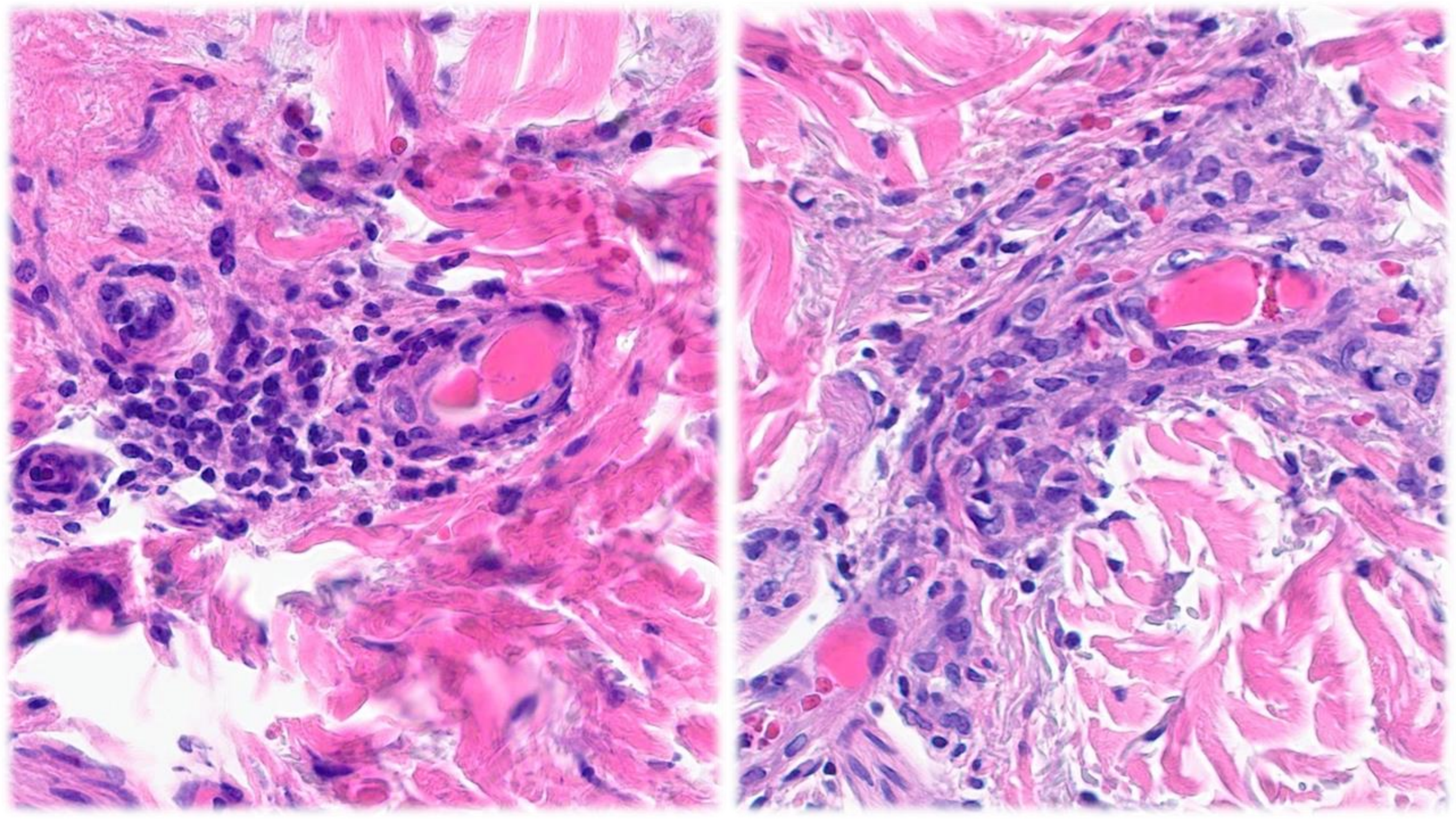
ANSWER THE QUESTIONS

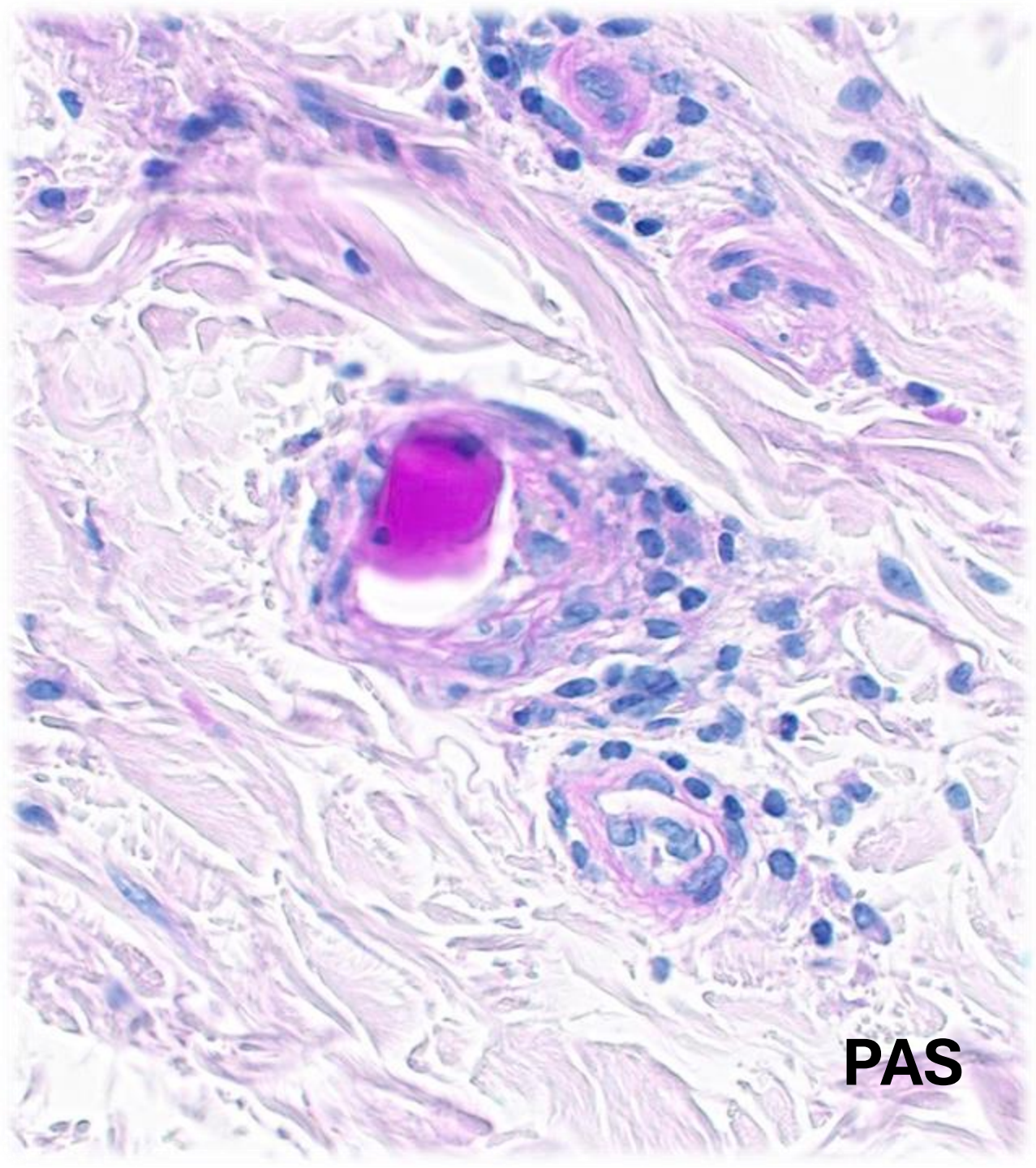
FIND THE ANSWER KEY AND SUMMARY







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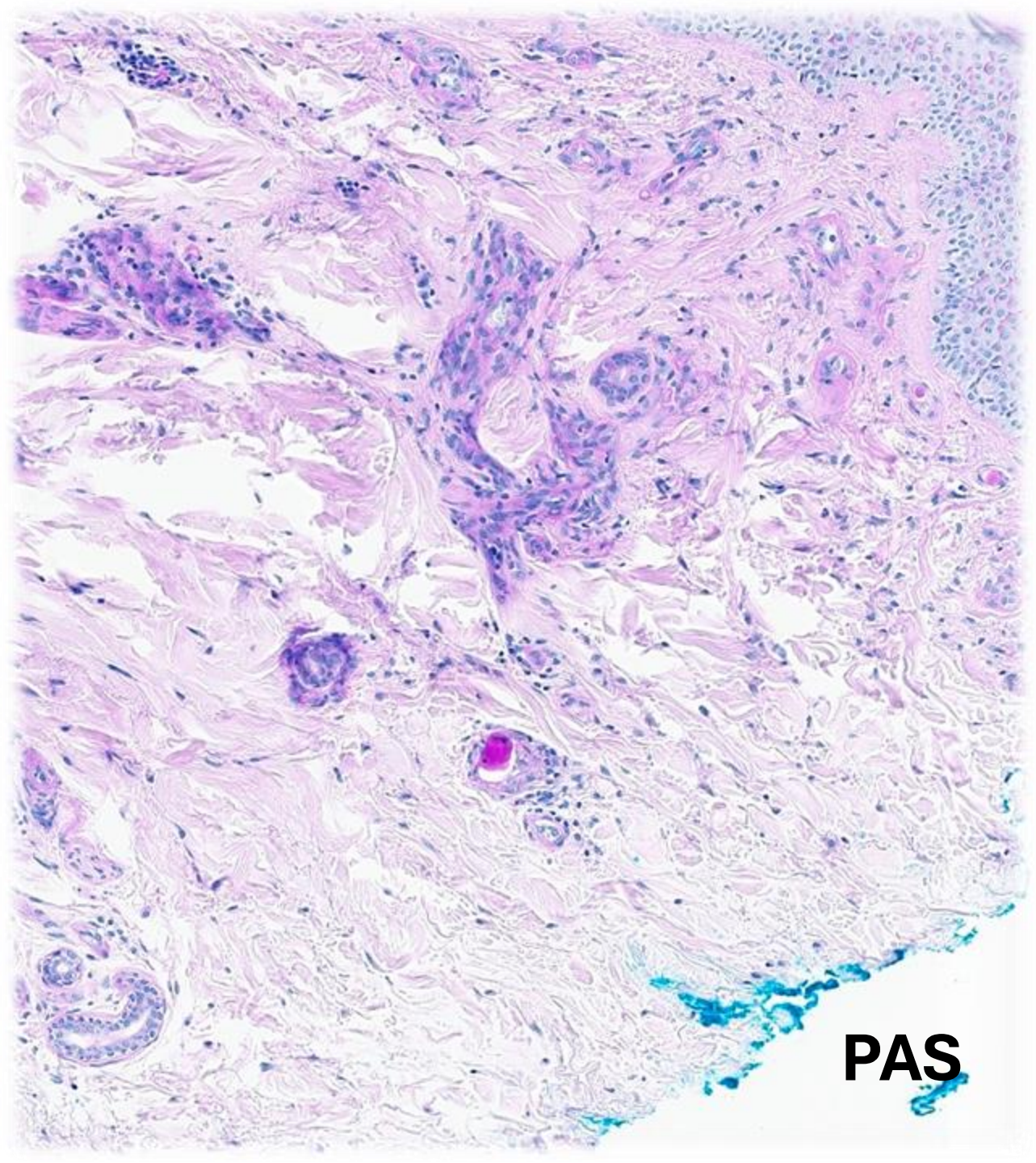
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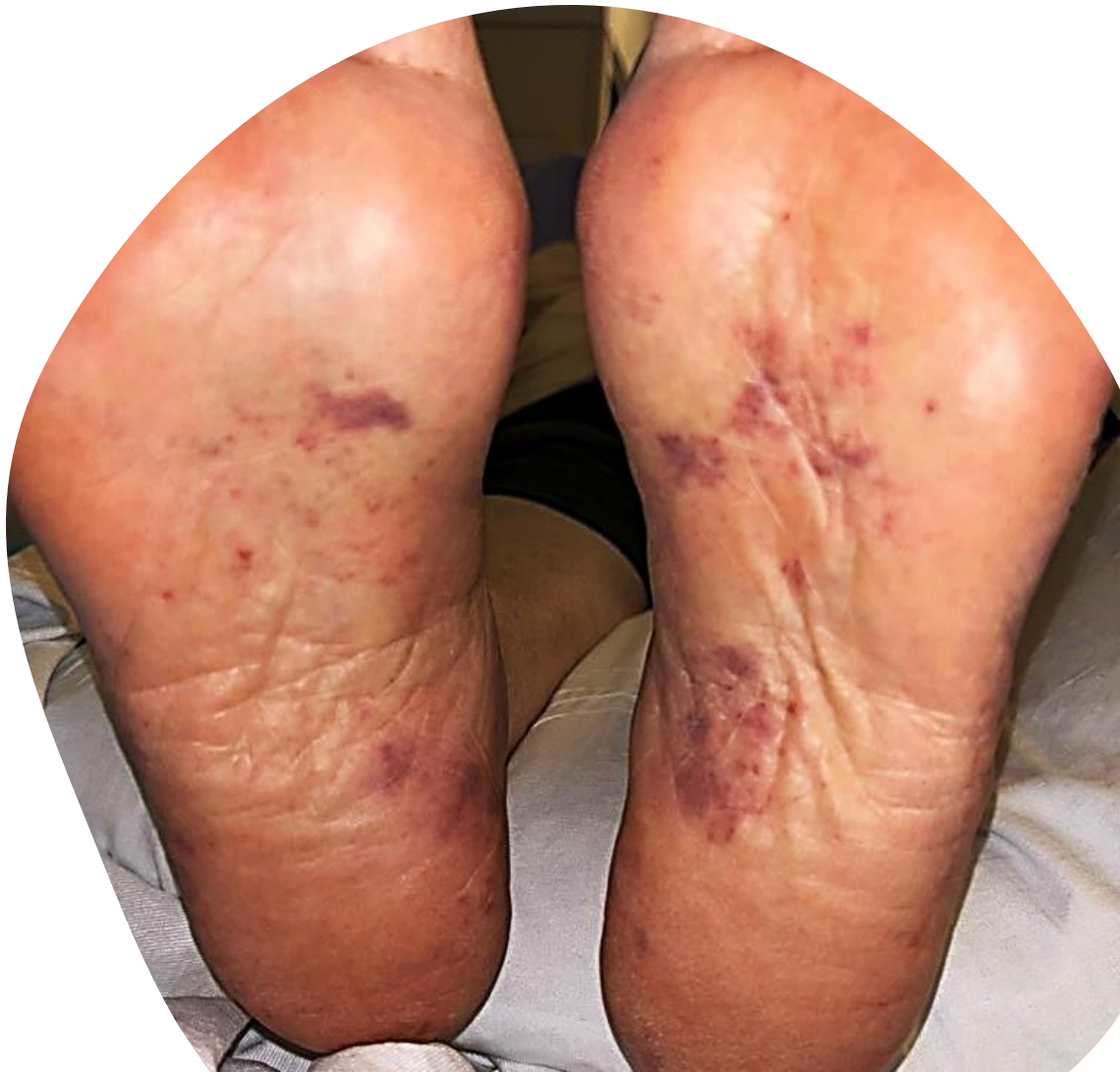

Case 144. 71F Left foot, recent bilateral purpuric macules, joint pain, right great toe infection. What is your diagnosis?

A. IgA Vasculitis (Henoch-Schönlein Purpura)

B. Septic emboli

C. Leukocytoclastic vasculitis in systemic lupus erythematosus

D. Cryoglobulinemia, Type I (Monoclonal)

E. Mixed Cryoglobulinemia (Types II & III)

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Summary: Cryoglobulinemia, Type I (Monoclonal)

Clinical Snapshot

- Cryoglobulinemia is a systemic vasculitis caused by cold-precipitating immunoglobulins ("cryoglobulins"). The classic presentation is **Meltzer's Triad: purpura, arthralgia, and weakness**. It is strongly associated with **Hepatitis C virus infection**.

Classification & Associations:

- **Type I (Monoclonal):** Associated with **lymphoproliferative disorders** (e.g., myeloma, Waldenström's). Presents with severe vascular occlusion (purpura, infarction).
- **Type II/III (Mixed):** Composed of monoclonal/polyclonal IgM + polyclonal IgG. Function as immune complexes. Primarily associated with **Hepatitis C**.

Histopathology:

Type I (Monoclonal):

- **Pattern: Thrombotic Vasculopathy**.
- **Key Feature:** Dermal vessels are plugged by **PAS-positive, hyaline (glass-like) thrombi** without significant inflammation.

Type II/III (Mixed):

- **Pattern: Leukocytoclastic Vasculitis (LCV)**.
- **Key Features:** Fibrinoid necrosis of post-capillary venules, neutrophilic infiltrate with **leukocytoclasis** (nuclear dust), red blood cell extravasation.
- **Immunofluorescence:** Vessel walls show deposits of **IgG, IgM, and C3**.

Summary: Cryoglobulinemia, Type I (Monoclonal)

Histologic Differential Diagnosis

For Type I (Thrombotic Vasculopathy):

- **Other Microangiopathies:** Thrombotic Thrombocytopenic Purpura (TTP), Disseminated Intravascular Coagulation (DIC), warfarin-induced skin necrosis.

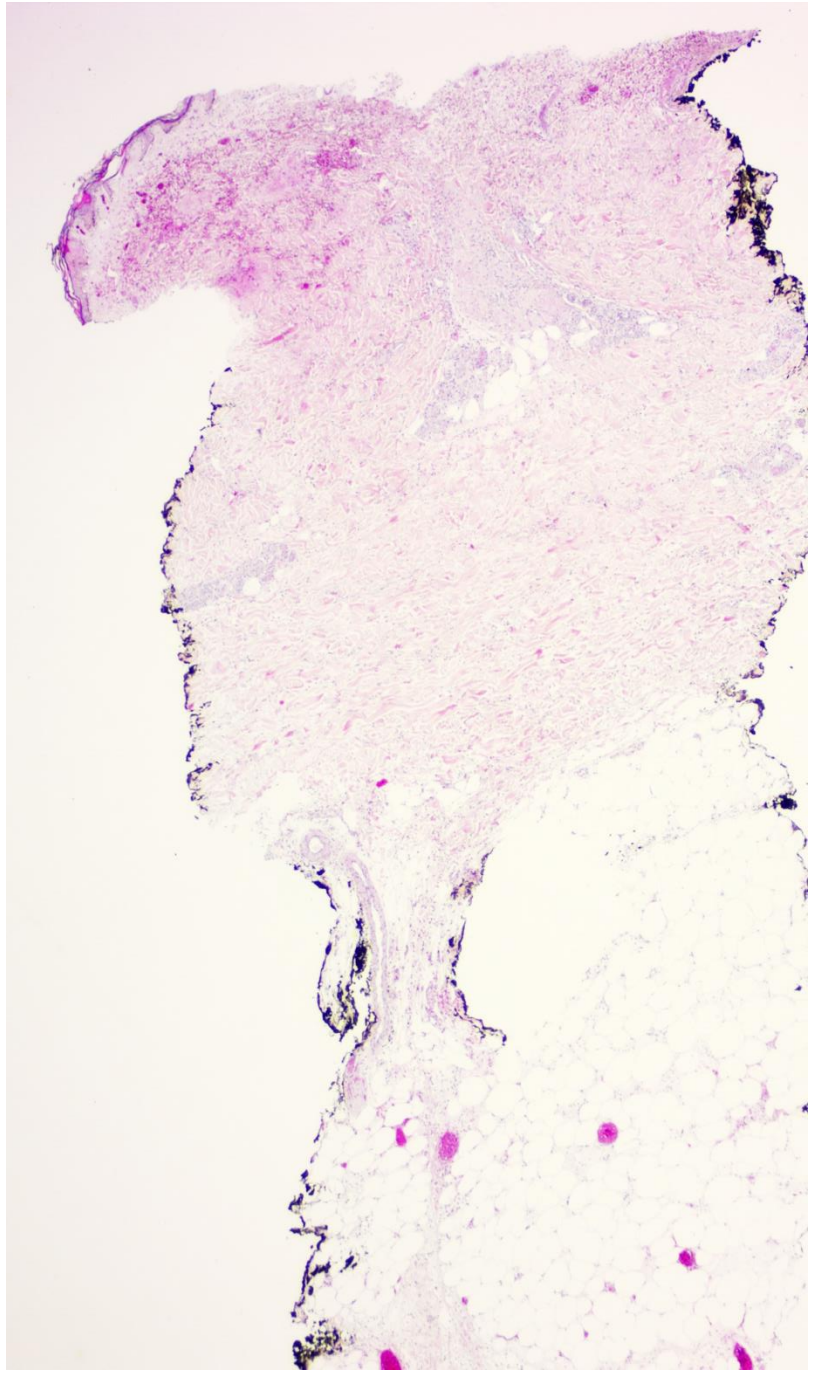
- **Differentiator:** The **hyaline quality** of the thrombi is a clue, but **serum cryoglobulin testing is essential for definitive diagnosis**.

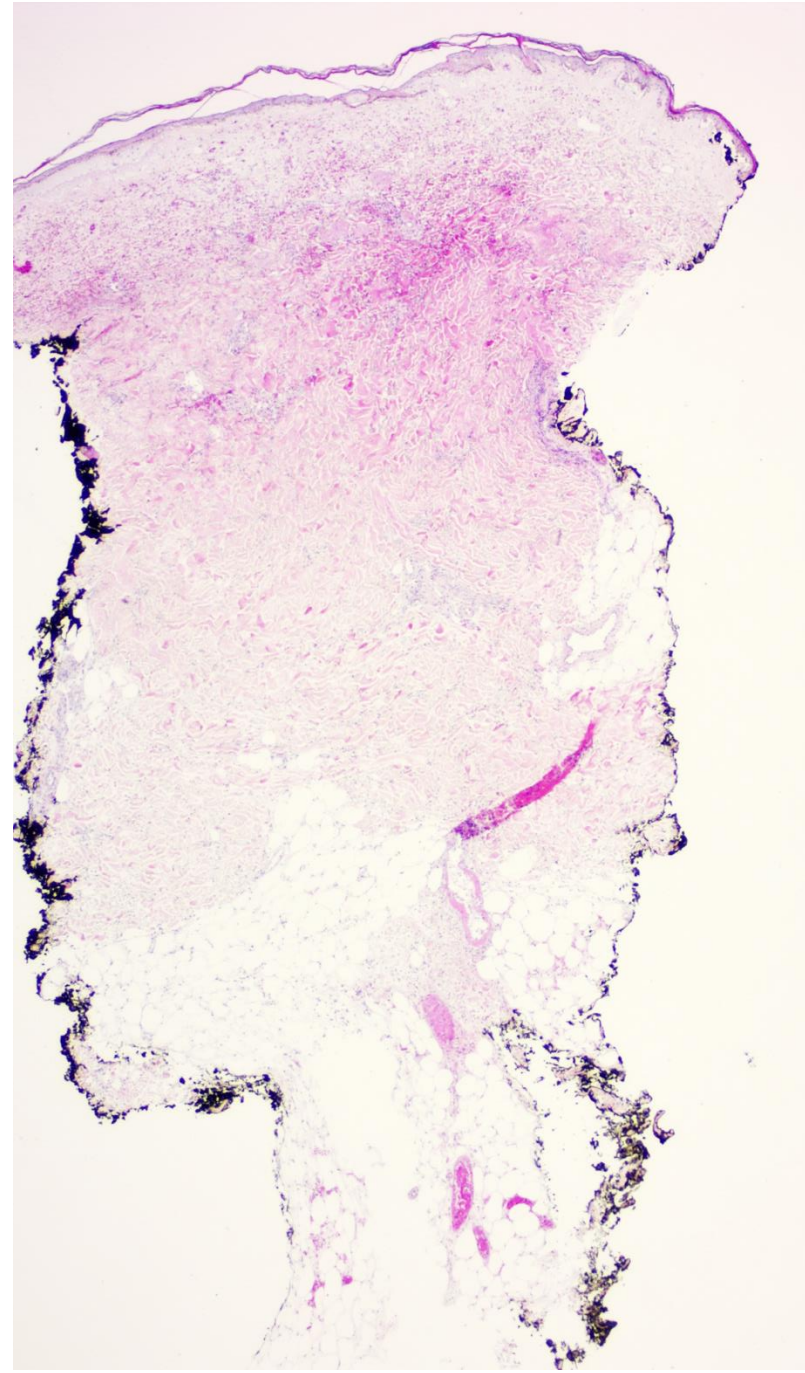
For Type II/III (Leukocytoclastic Vasculitis):

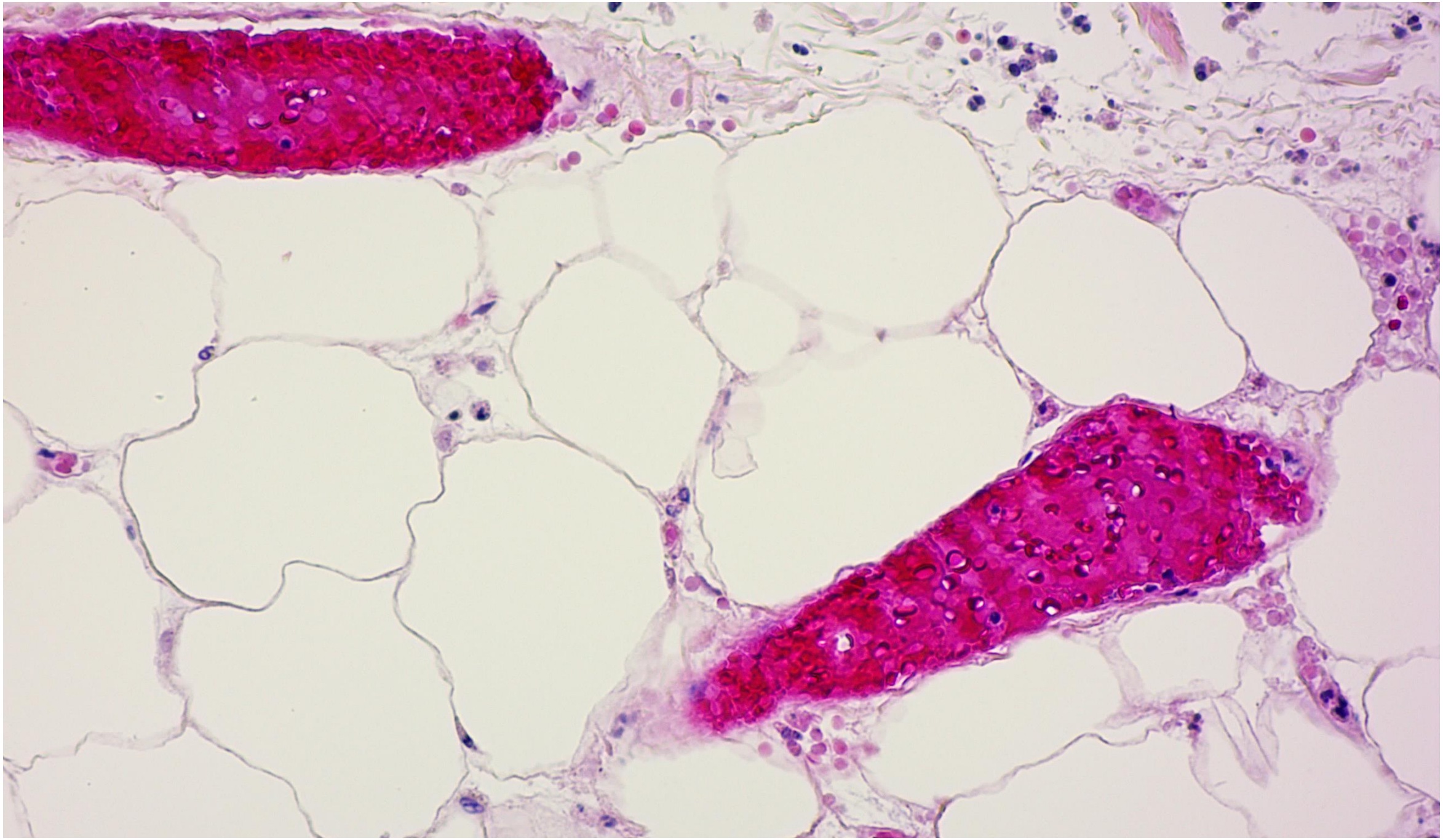
- **IgA Vasculitis (Henoch-Schönlein Purpura):** Histologically identical. Differentiated by **dominant IgA deposition** on immunofluorescence.

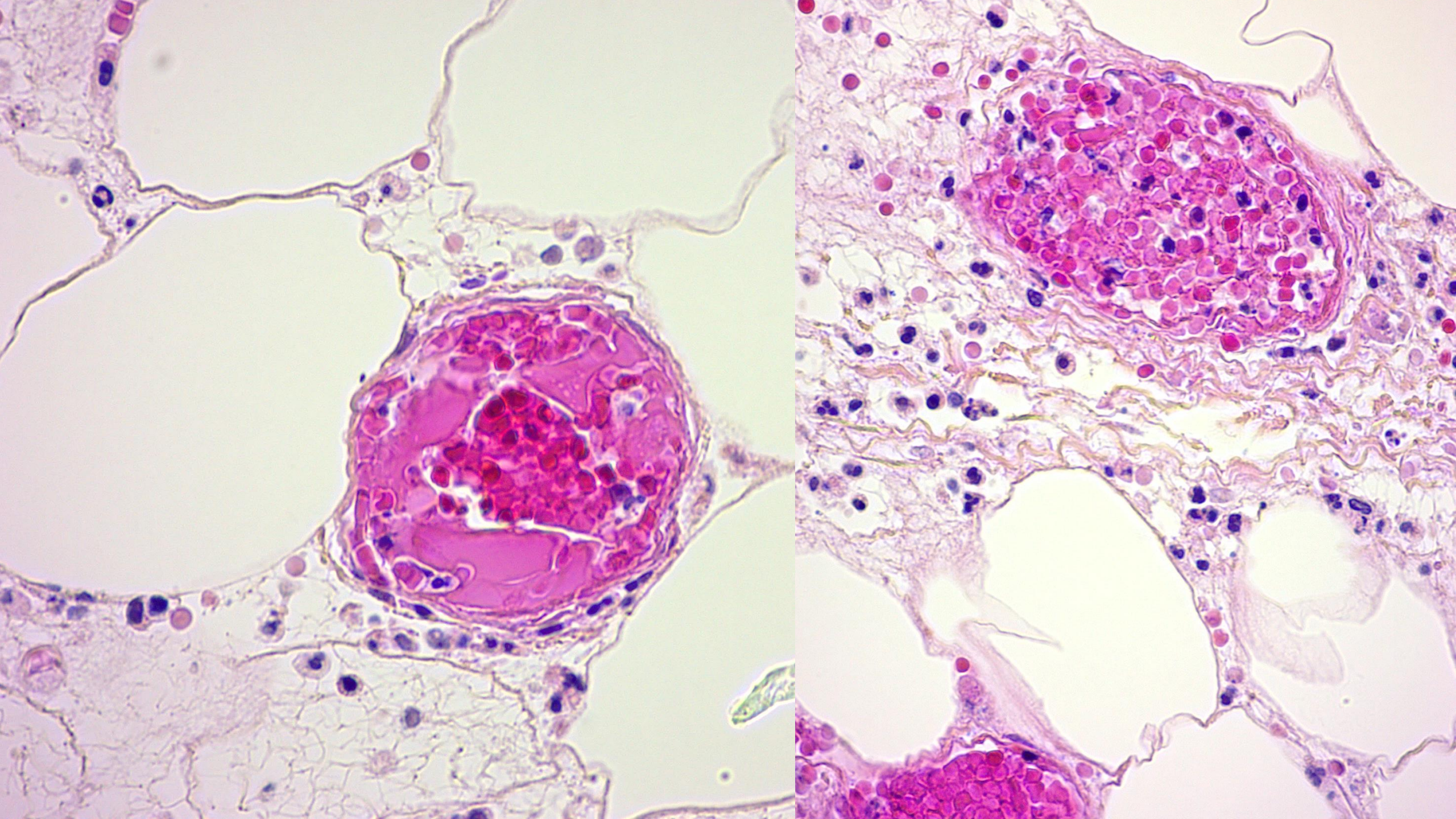
- **ANCA-Associated Vasculitis** (e.g., Granulomatosis with Polyangiitis): Differentiated by positive **ANCA serology** (MPO/PR3) and often a more pauci-immune pattern on biopsy.

- **Hypersensitivity Vasculitis:** Triggered by drugs or infection. A diagnosis of exclusion; requires a thorough clinical history and lacks the specific lab findings of cryoglobulinemia (negative cryocrit, normal C4).









Case 145. 67M, history of factor IX deficiency (Hemophillia B) with extensive ecchymoses on bilateral lower legs. What is your diagnosis?

A. Leukocytoclastic vasculitis

B. Cholesterol embolism

C. Atrophie blanche

D. Purpura fulminans/disseminated intravascular coagulation

E. Cryoglobulinemia

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Summary: Purpura fulminans/disseminated intravascular coagulation

Clinical Snapshot

- Purpura Fulminans is a **life-threatening hematologic emergency** characterized by the rapid onset of progressive cutaneous hemorrhage and necrosis due to widespread microvascular thrombosis. It is the cutaneous manifestation of severe Disseminated Intravascular Coagulation (DIC).
- **Trigger:** Often a catastrophic event: **Severe infection (most common, e.g., meningococcemia), trauma, obstetric calamities, or malignancy.**

Key Symptoms:

Skin: Rapidly expanding, painful **ecchymoses and purpura** that evolve into **hemorrhagic bullae and well-demarcated gangrene**.

Systemic: Shock, fever, organ failure (kidneys, lungs, adrenal glands).

Pathogenesis: Dysregulated systemic activation of the coagulation cascade, leading to **microthrombi** that consume platelets and clotting factors, resulting in simultaneous **thrombosis and hemorrhage**.

Summary: Purpura fulminans/disseminated intravascular coagulation

Histopathology

Primary Pattern: Thrombotic Vasculopathy (Non-inflammatory).

Key Features:

Microthrombi: Fibrin thrombi within dermal and subcutaneous vessels.

Hemorrhage: Extensive extravasation of red blood cells.

Necrosis: Coagulative necrosis of the epidermis, dermis, and subcutaneous fat.

Lack of Inflammation: Notably **absent leukocytoclastic vasculitis**; the process is primarily thrombotic, not inflammatory.

Histologic Differential Diagnosis:

Coumarin (Warfarin) Necrosis: Also shows dermal microthrombi. Differentiated by history of **recent warfarin initiation** (often in protein C/S deficient patients) and location (typically fat-rich areas like breasts, buttocks).

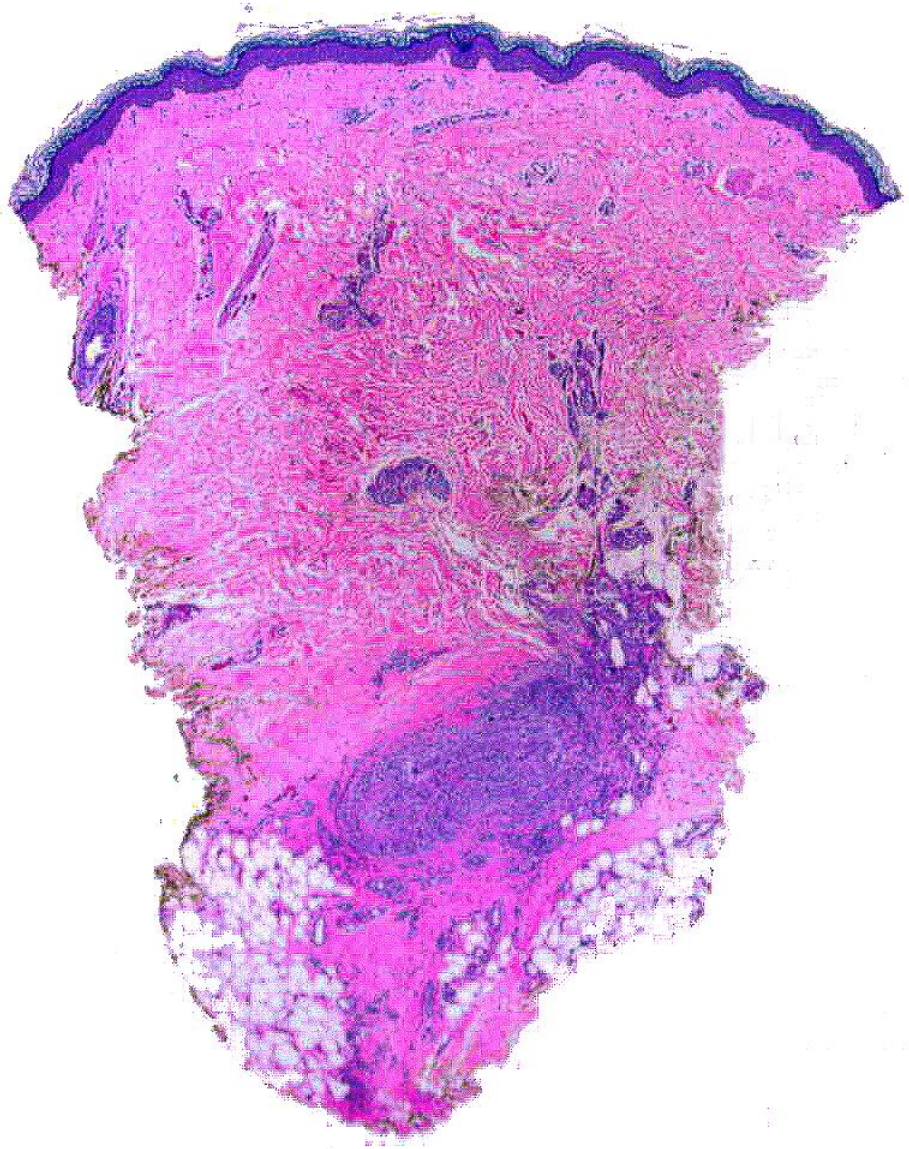
Histologic Differential Diagnosis

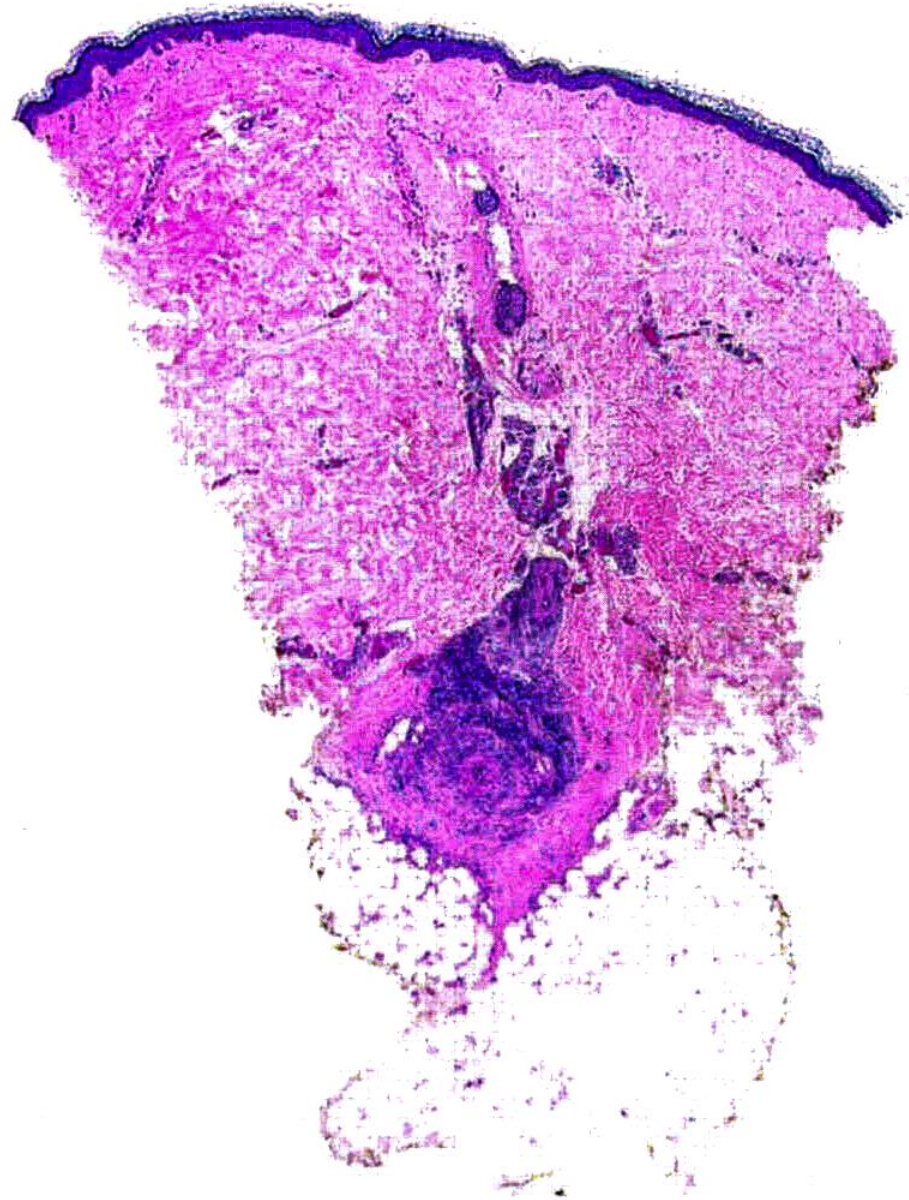
Heparin-Induced Thrombocytopenia (HIT): Causes thrombotic complications. Differentiated by **thrombocytopenia occurring 5-10 days after heparin exposure** and positive anti-PF4 antibodies.

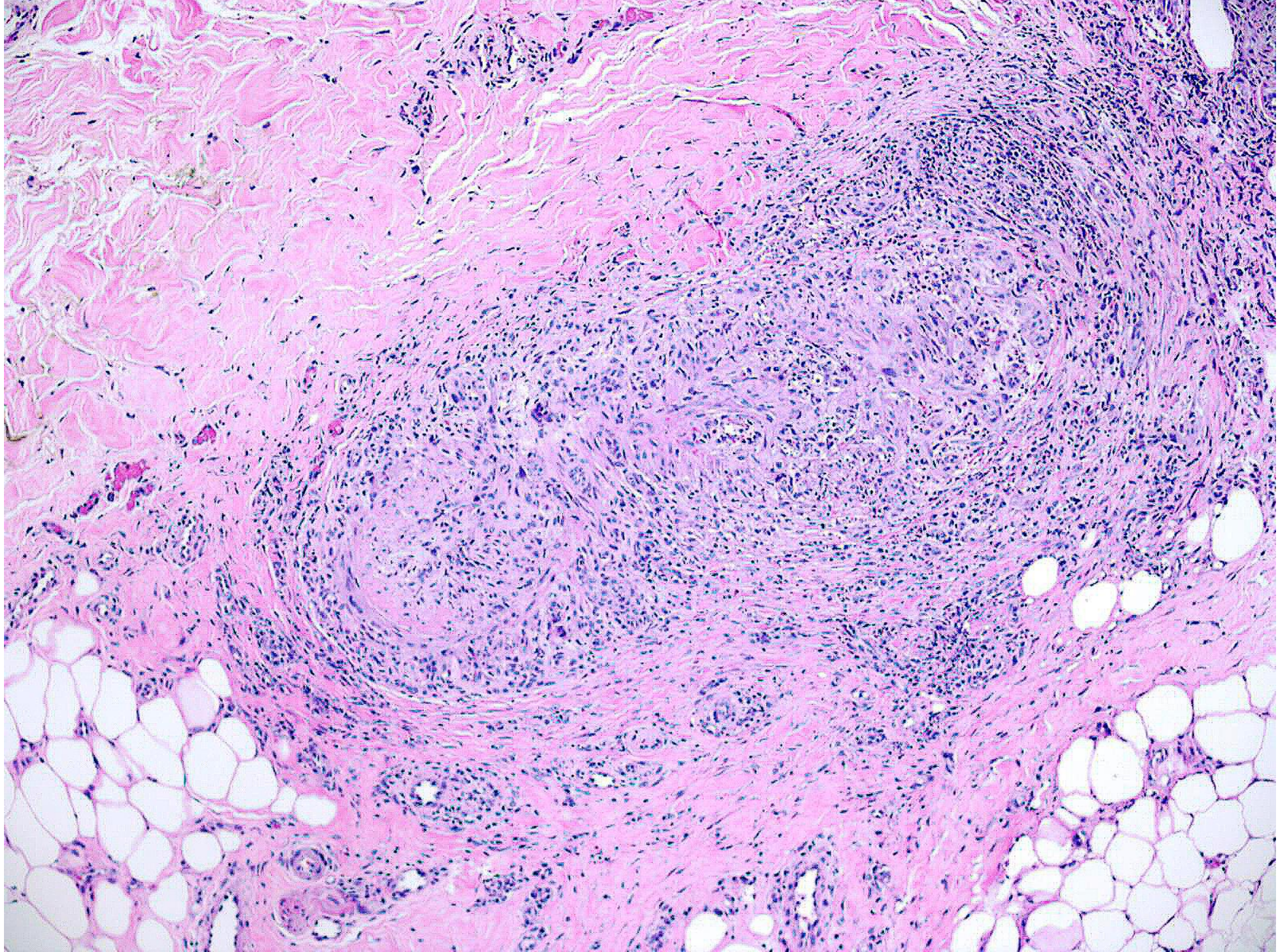
Calciphylaxis: Shows **calcification of medial layer of small vessels** and intimal hyperplasia, which are not features of purpura fulminans.

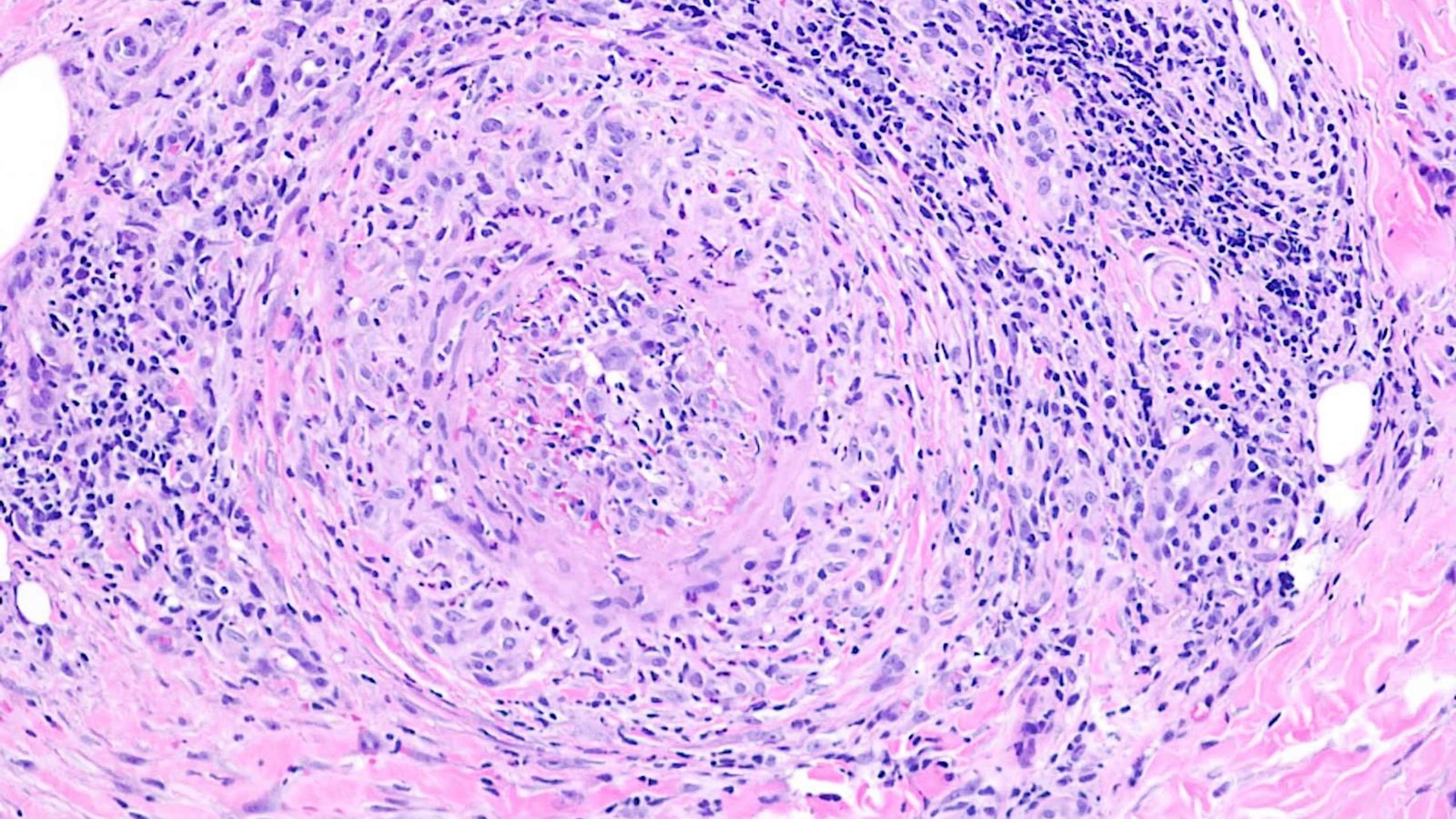
Cryoglobulinemia (Type I): Features **hyaline (PAS-positive) thrombi** composed of immunoglobulins, not fibrin. Clinical history and cryoglobulin test are definitive.

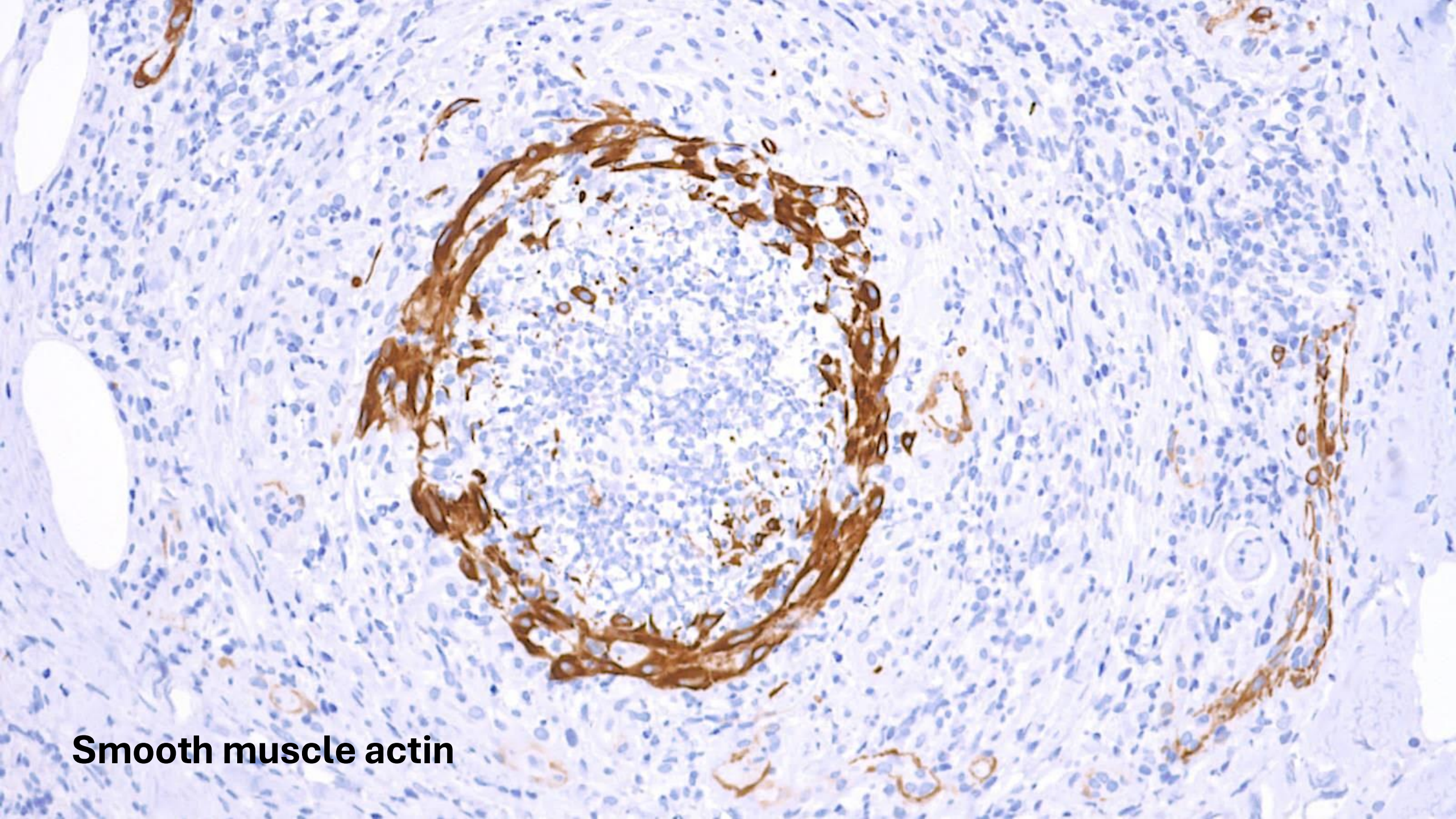
Leukocytoclastic Vasculitis (e.g., IgA Vasculitis): An **inflammatory vasculitis** with neutrophil infiltration, nuclear dust, and fibrinoid necrosis of the vessel wall. Purpura Fulminans lacks this inflammation.










Smooth muscle actin

Case 146. 64F, biopsy of left arm subcutaneous nodule; history of necrobiosis lipoidica (biopsy results of right leg subcutaneous nodule). What is your diagnosis?

A. ANCA-Associated Vasculitis (Microscopic Polyangiitis, Granulomatosis with Polyangiitis)

B. Cholesterol embolism

C. Polyarteritis nodosa

D. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss)

E. Leukocytoclastic Vasculitis

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Summary: Polyarteritis nodosa

Clinical Snapshot

Polyarteritis Nodosa (PAN) is a rare, systemic **necrotizing vasculitis** affecting **medium-sized muscular arteries**. It does not involve small vessels (capillaries, venules) or glomerulonephritis.

Key Symptoms: Constitutes a "**medium-vessel vasculitis**" syndrome.

- **Systemic:** Fever, weight loss, malaise, myalgia/arthralgia.
- **Cutaneous:** Livedo racemosa, subcutaneous nodules (along vascular tracts), ulcers, gangrene, and palpable purpura (if small vessel involvement occurs secondarily).

Key Symptoms:

Neurological: Mononeuritis multiplex (most characteristic finding).

Renal: Renal artery vasculitis leading to hypertension, infarction, and renal failure (not glomerulonephritis).

Gastrointestinal: Mesenteric artery involvement causing abdominal pain, bleeding, bowel infarction ("**gut infarction**").

Associations: Strongly linked to **Hepatitis B virus** infection.

Summary: Polyarteritis nodosa

Histopathology

The pathology is characterized by transmural, inflammatory destruction of muscular arteries.

Primary Pattern: Acute Necrotizing Vasculitis of medium-sized arteries at the dermal-subcutaneous junction.

Key Features:

- **Transmural Inflammation:** Inflammatory infiltrate (neutrophils, lymphocytes, histiocytes) throughout all layers of the arterial wall.
- **Fibrinoid Necrosis:** The hallmark finding. **Brightly eosinophilic, smudgy necrosis** of the vessel wall.
- **Elastic Lamina Disruption:** Fragmentation of the internal elastic lamina (highlighted by an **elastic stain**).
- **Staging:** Lesions of different stages (acute, healing, healed) often coexist.

Histologic Differential Diagnosis

ANCA-Associated Vasculitis:
Differentiator: AAV primarily affects **small vessels** (capillaries, venules, arterioles) causing leukocytoclastic vasculitis and **necrotizing glomerulonephritis**. **c-ANCA (PR3)** or **p-ANCA (MPO)** positivity is typical. PAN is ANCA-negative.

Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss):
Differentiator: Features **eosinophil-rich** granulomatous inflammation, asthma, and peripheral eosinophilia. PAN lacks significant tissue eosinophilia.

Buerger's Disease (Thromboangiitis Obliterans):
Differentiator: Affects medium *and* small arteries of extremities in heavy smokers. Shows highly **cellular, inflammatory thrombus** but **preservation of the internal elastic lamina** and no fibrinoid necrosis.

Leukocytoclastic Vasculitis:
Differentiator: LCV is a **small-vessel vasculitis** affecting post-capillary venules in the superficial dermis. PAN affects deeper, medium-sized arteries.

Case 147. Is there a clinical or pathogenetic relationship between Polyarteritis Nodosa (PAN) and Necrobiosis Lipoidica (NL)?

A. No, they are unrelated

B. Yes, there is clinical association; but no pathogenetic

C. Yes, both clinical and pathogenetic

D. Yes, there is pathogenetic association; but no clinical

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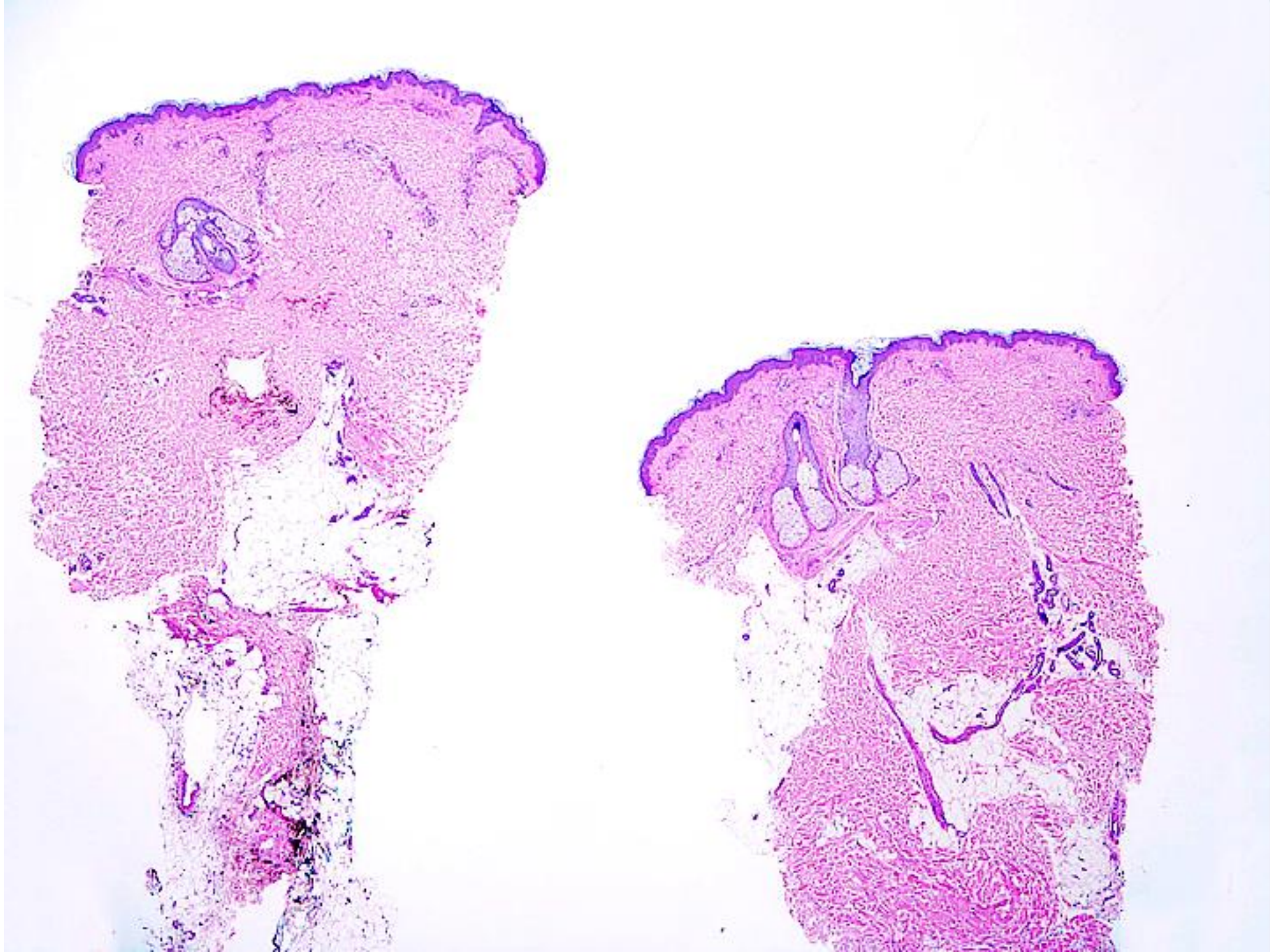
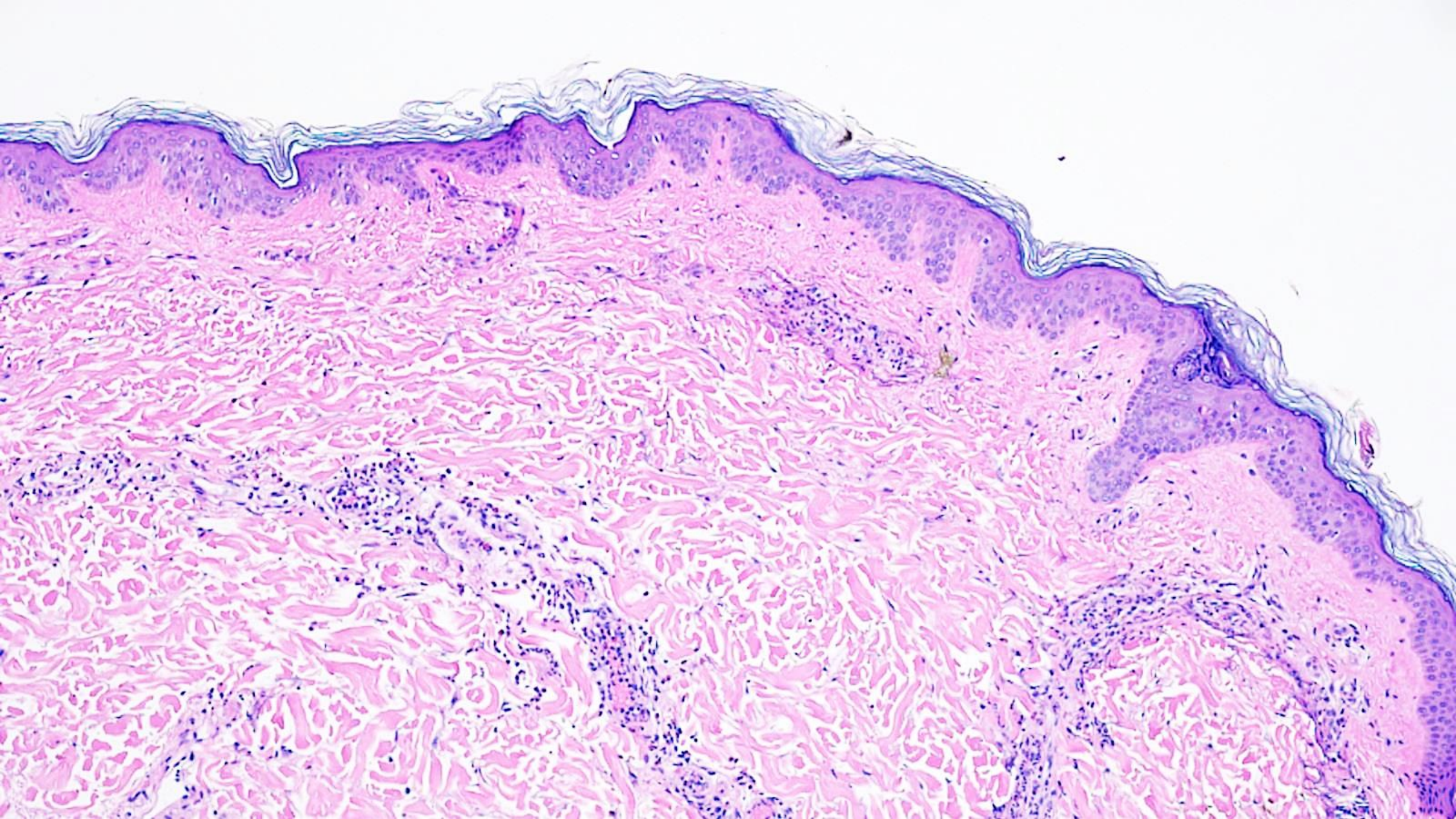
Summary: Polyarteritis nodosa vs. Necrobiosis lipoidica

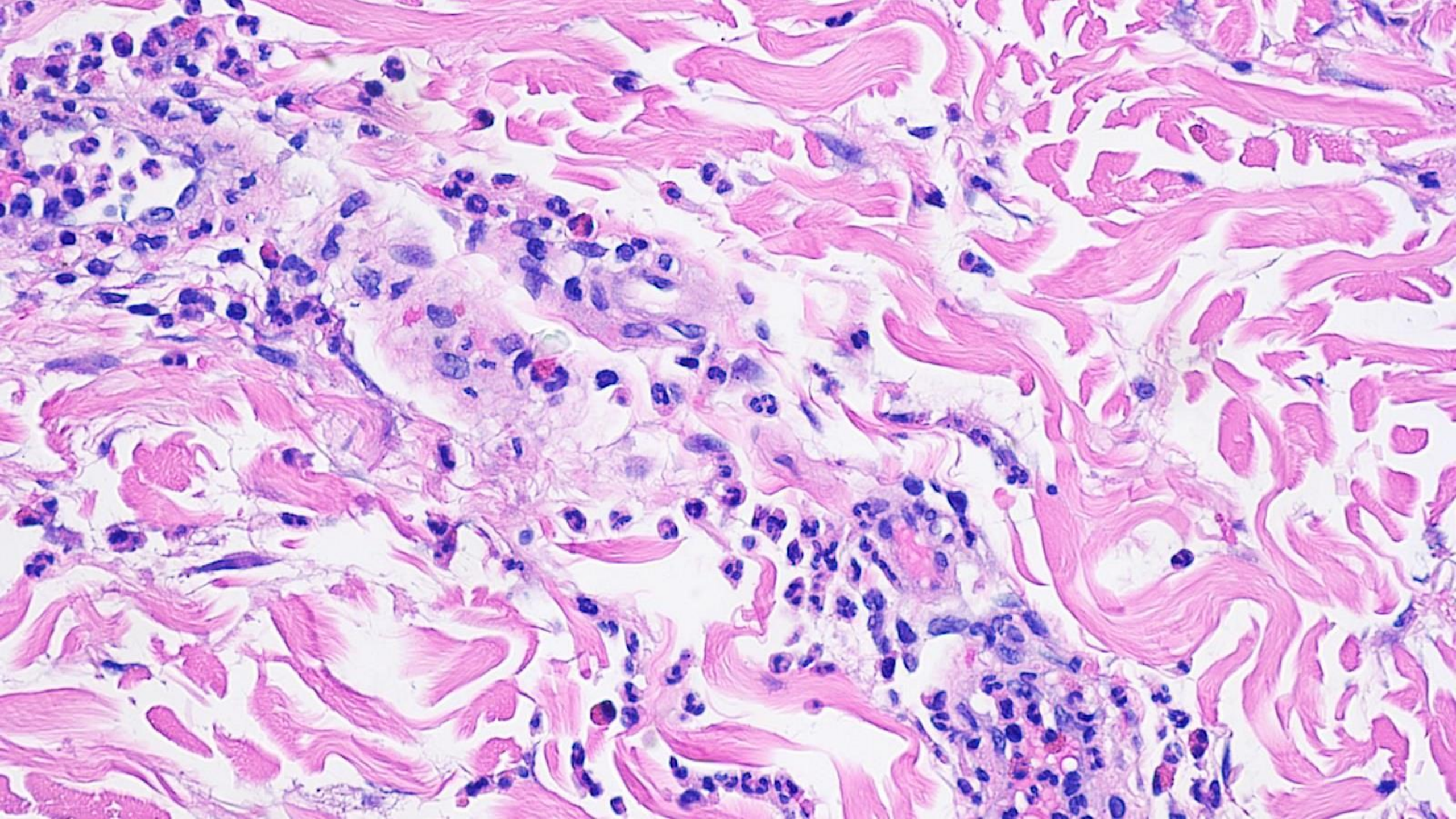
- **Core Relationship:** Necrobiosis Lipoidica is considered a **cutaneous marker of underlying systemic disease**, with a well-known association with diabetes mellitus. In a smaller subset of patients, it can also be a marker for **occult systemic vasculitis**, most commonly **PAN**.

- **Clinical Implication:** A diagnosis of NL, particularly if extensive, refractory, or ulcerated, should prompt clinicians to screen for underlying diabetes and, in the absence of diabetes, to consider and screen for systemic vasculitis like PAN.

- **Pathogenetic Link:** The link is not fully understood but is hypothesized to be related to **microvascular compromise and ischemia** in the skin, which can be caused by the vasculitic process of PAN.







Case 148. 34F, right thigh; febrile with diffuse painful wheals, papules, and areas of bruising. What is your diagnosis?

A. Simple urticaria

B. Neutrophilic urticarial dermatosis

C. Urticarial vasculitis

D. Erythema Marginatum (in Rheumatic Fever)

E. Leukocytoclastic Vasculitis

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Summary: Urticarial Vasculitis (UV)

Clinical Snapshot

Urticarial Vasculitis is a **small-vessel vasculitis** that presents with **urticaria-like wheals**, but the lesions differ from simple urticaria. It exists on a spectrum from a skin-limited disease to a systemic disorder.

Key Symptoms:

- **Skin: Wheals that are painful or burn** (rather than itch), last **>24 hours**, and **resolve with residual purpura, hyperpigmentation, or ecchymosis**. Individual lesions typically last 2-3 days.
- **Systemic:** Fever, angioedema, arthralgia/arthritis. In more severe cases, it can involve the kidneys (glomerulonephritis), lungs (pleuritis, obstructive disease), and gastrointestinal tract.

Subtypes & Associations:

- **Normocomplementemic UV:** Often limited to skin; milder course.
- **Hypocomplementemic UV (HUV):** More frequently associated with **systemic disease** (like SLE) and the **HUV Syndrome** (HUVS), which includes severe obstructive lung disease.

Summary: Urticarial Vasculitis (UV)

Histopathology

The biopsy must be taken from a **fresh lesion (<24-48 hours old)**. The pathology shows features of leukocytoclastic vasculitis superimposed on an urticarial background.

Primary Pattern: Leukocytoclastic Vasculitis (LCV) with urticarial features.

Key Features:

Vascular Damage: Fibrinoid necrosis and **fibrin deposition** within the walls of post-capillary venules.

Inflammatory Infiltrate: A **perivascular infiltrate of neutrophils** with **leukocytoclasis** (nuclear dust).

Urticarial Background: Concurrent **dermal edema** and a variable perivascular infiltrate of lymphocytes and eosinophils, resembling simple urticaria.

Hemorrhage: Extravasated red blood cells are a crucial finding that distinguishes it from simple urticaria.

Summary: Urticarial Vasculitis (UV)

Histologic Differential Diagnosis

The main challenge is distinguishing it from other conditions that can present with similar histologic or clinical features.

Simple Urticaria:

Differentiator: Shows **dermal edema** and a perivascular lymphocytic and eosinophilic infiltrate but **lacks** fibrinoid necrosis, leukocytoclasis, and significant red blood cell extravasation. *No true vasculitis*.

Leukocytoclastic Vasculitis (from other causes, e.g., IgA Vasculitis, Drug Reaction):

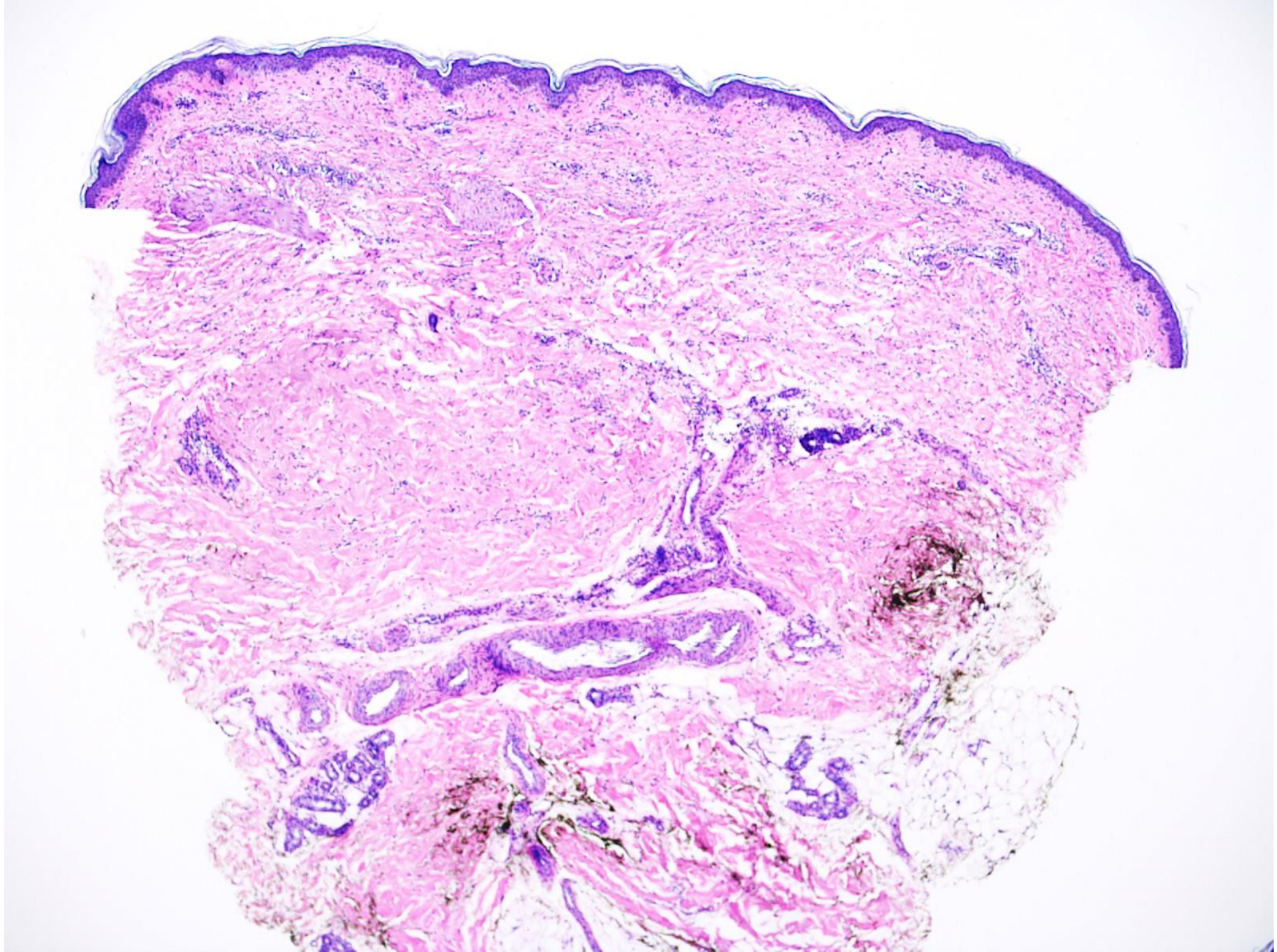
Differentiator: Histologically **identical**. Differentiation relies on **clinical history** (duration of lesions, associated symptoms), **immunofluorescence** (presence of IgA deposits suggests IgA Vasculitis), and **serology** (hypocomplementemia is a clue for HUV).

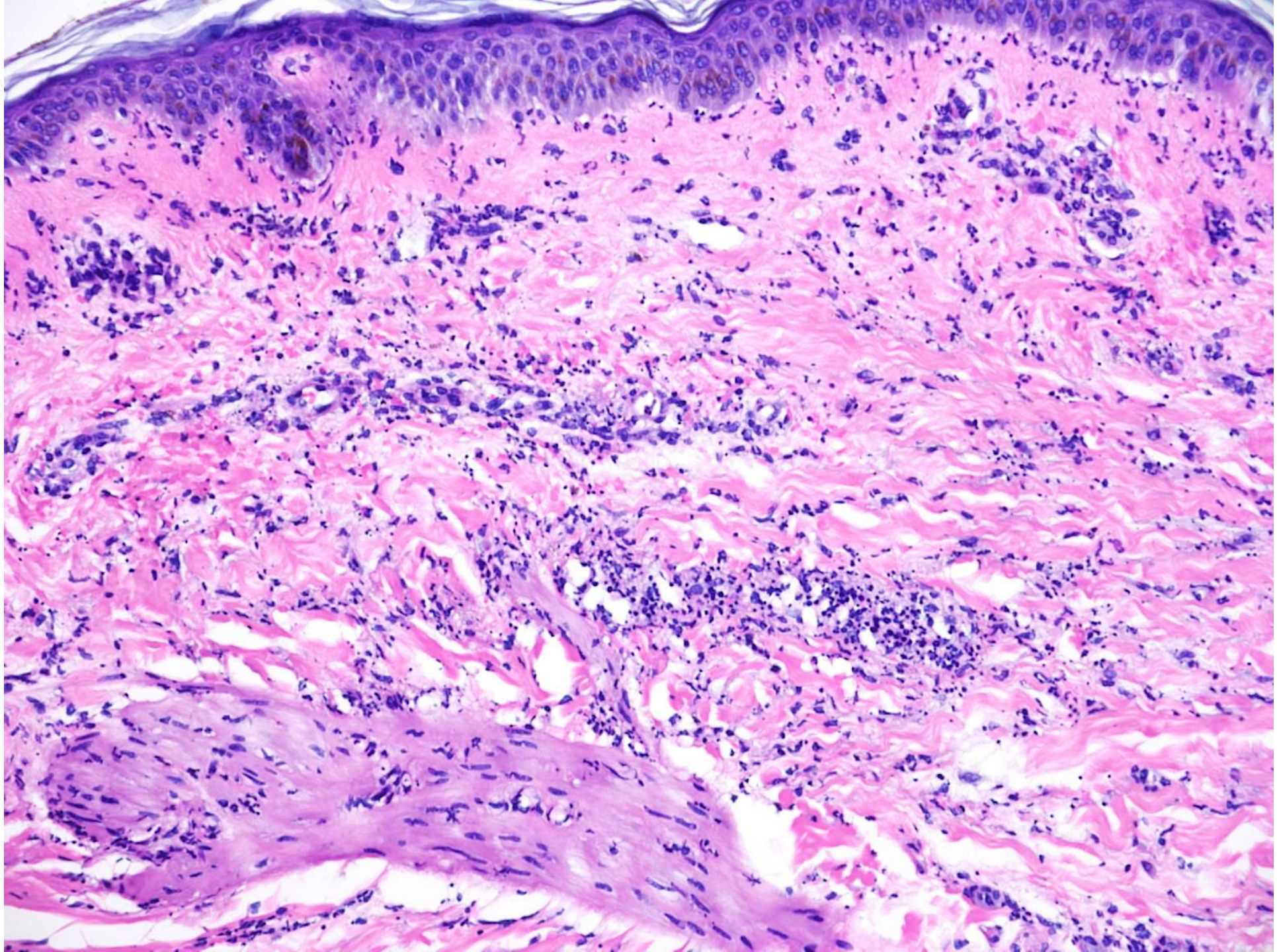
Neutrophilic Urticarial Dermatosis (NUD):

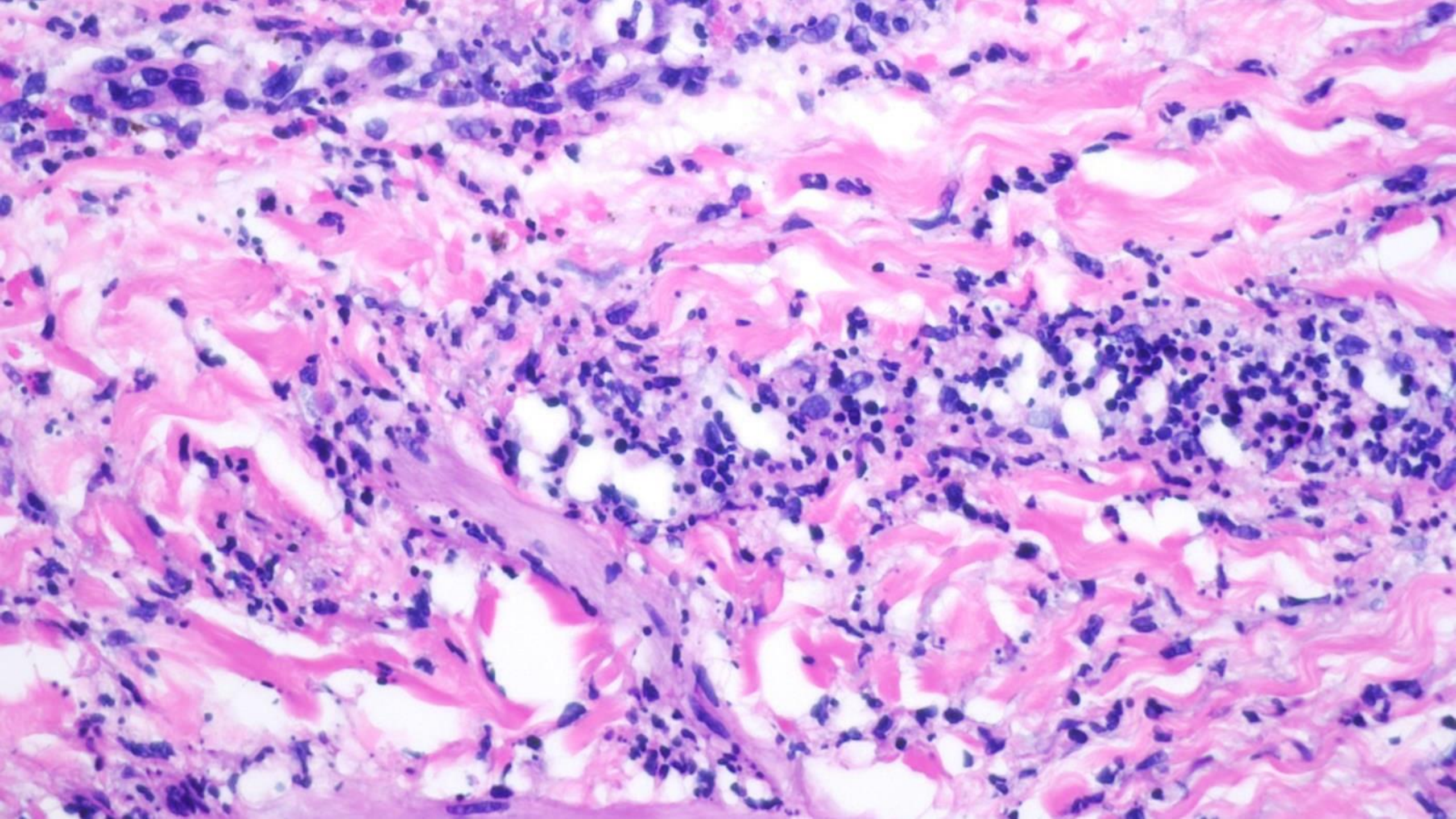
Differentiator: Often associated with autoinflammatory diseases like SLE. Shows a dense perivascular neutrophilic infiltrate **without** the fibrinoid necrosis, vessel wall damage, or significant RBC extravasation of true vasculitis.

Erythema Marginatum (in Rheumatic Fever):

Differentiator: Can show a perivascular neutrophilic infiltrate but **lacks** the features of vessel wall destruction (fibrinoid necrosis) seen in UV.







Case 149. 41F, Right thigh; New arcuate plaques, edematous papules on chest and back. What is your diagnosis?

A. Lupus vasculitis

B. IgA Vasculitis (Henoch-Schönlein Purpura)

C. Urticarial vasculitis

D. ANCA-Associated Vasculitis (Microscopic Polyangiitis, Granulomatosis with Polyangiitis)

E. Leukocytoclastic Vasculitis

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Summary: Lupus vasculitis

Patient history: systemic lupus erythematosus complicated by nephrotic syndrome and rheumatoid arthritis. She presents with recent acute onset of rash: arcuate plaques, edematous papules and plaques on the chest, back and lower extremities; and no malar rash.

Clinical Snapshot

- Lupus vasculitis is not a single entity but a manifestation of **Systemic Lupus Erythematosus (SLE)** where inflammation targets blood vessels. It represents a common and potentially serious complication of SLE.
- **Key Symptoms:**
  - **Cutaneous (Most Common): Palpable purpura** is the hallmark. Also includes urticaria-like lesions, digital ulcers, nodules, livedo reticularis, and splinter hemorrhages.
  - **Systemic:** Fever, arthritis, and neuropsychiatric symptoms.
  - **Organ Involvement:** Can affect the kidneys (lupus nephritis), lungs (pulmonary hemorrhage), gastrointestinal tract (abdominal pain, bleeding), and nervous system (mononeuritis multiplex).
- **Significance:** The presence of vasculitis often indicates **active systemic disease** and is associated with more severe SLE, including higher rates of renal and central nervous system involvement.

Summary: Lupus vasculitis

Histopathology

The histology depends on the size of the vessel affected, but small-vessel involvement is most frequent.

Primary Pattern: Leukocytoclastic Vasculitis (LCV) is the most common finding in skin biopsies.

Key Features:

- **Vascular Damage: Fibrinoid necrosis** of post-capillary venule walls.
- **Inflammatory Infiltrate:** A perivascular infiltrate of **neutrophils** with **leukocytoclasis** (nuclear dust).
- **Extravasated Erythrocytes.**
- **Additional Lupus-Specific Features:** The background skin may also show changes of **chronic cutaneous lupus**, such as epidermal atrophy, vacuolar interface dermatitis, and dermal mucin deposition.

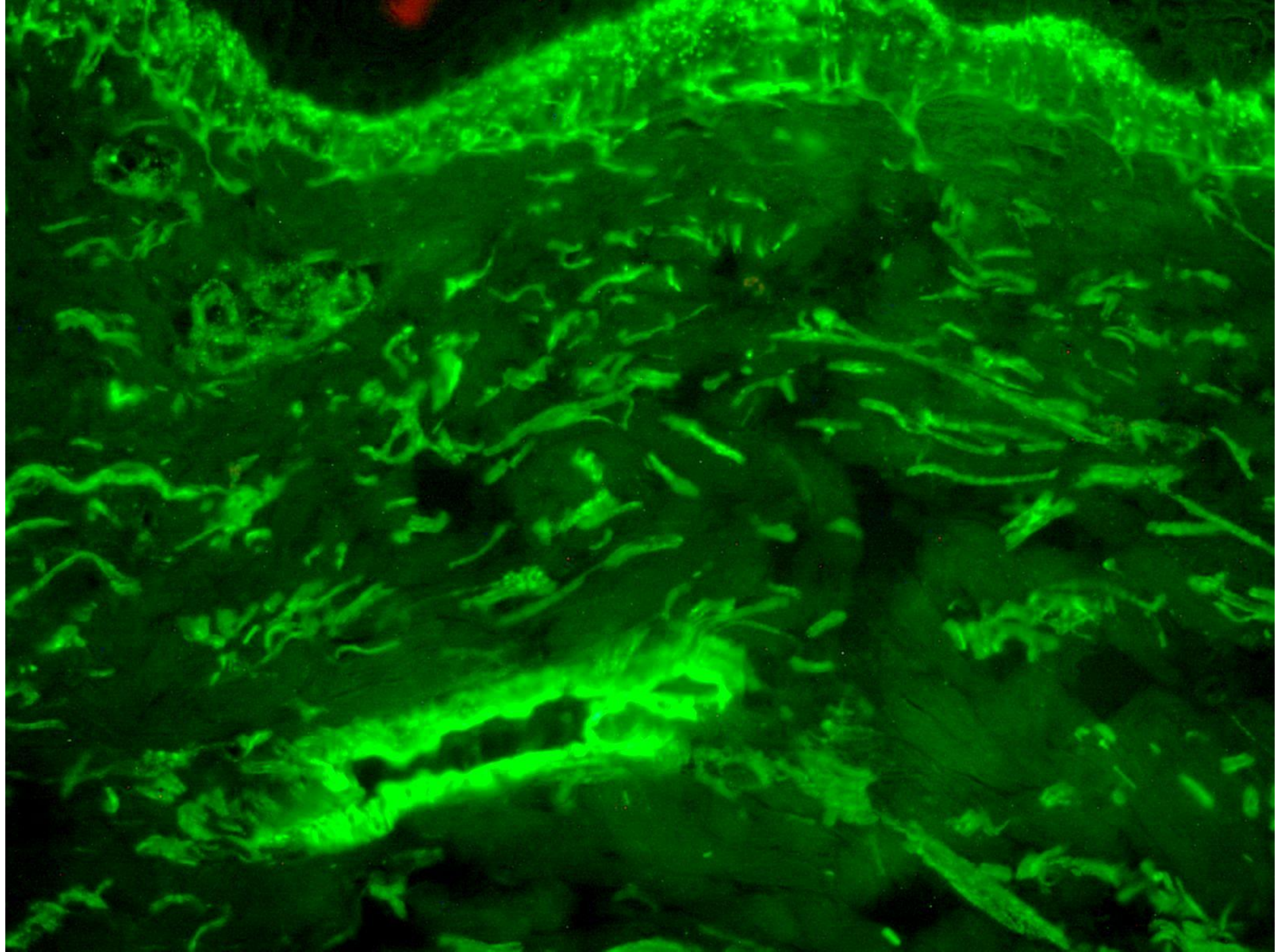
Direct Immunofluorescence (DIF) Findings: Lupus band test+ & vascular pattern

Pattern: Granular deposition of immunoreactants at the dermal-epidermal junction (DEJ).

Immunoreactants: Typically, a "**full house**" pattern, meaning positivity for **IgG, IgM, IgA, and C3** (positive Lupus band test).

Summary: Lupus vasculitis

- **Histologic Differential Diagnosis**
- The main challenge is distinguishing it from other forms of vasculitis, as the histology of LCV is often identical.
- **IgA Vasculitis (Henoch-Schönlein Purpura):**
  - **Differentiator:** Histologically identical. **DIF is definitive**, showing **dominant IgA deposits** in vessel walls. Lupus vasculitis shows a "full house" pattern at the DEJ, not dominant IgA.
- **ANCA-Associated Vasculitis (Microscopic Polyangiitis, Granulomatosis with Polyangiitis):**
  - **Differentiator:** Also presents with LCV. Differentiated by positive **ANCA serology** (MPO- or PR3-ANCA) and the absence of clinical and serologic criteria for SLE. DIF is typically negative or shows only scant deposits (**pauci-immune**).
- **Cryoglobulinemic Vasculitis:**
  - **Differentiator:** Shows LCV. Differentiated by a positive **cryoglobulin test**, low C4 levels, and association with Hepatitis C. DIF may show vascular deposits but lacks the specific "full house" DEJ pattern of lupus.
- **Hypersensitivity Vasculitis:**
  - **Differentiator:** A diagnosis of exclusion, often triggered by drugs or infection. Lacks the autoantibodies (ANA, anti-dsDNA) and hypocomplementemia of SLE. DIF is negative.



Case 150. What is the expected pattern for direct immunofluorescence (DIF) in lupus vasculitis?

A. Full-house granular IgG, IgA, IgM, & C3 reaction at the DEJ

B. Full-house granular IgG, IgA, IgM, & C3 reaction at the DEJ and vascular reaction

C. IgG, IgA, IgA, or C3 reaction in the vascular lumen

D. D. Linear subepidermal C3, IgG; in perilesional skin

E. Lace-like intraepidermal C3, IgG; in perilesional skin

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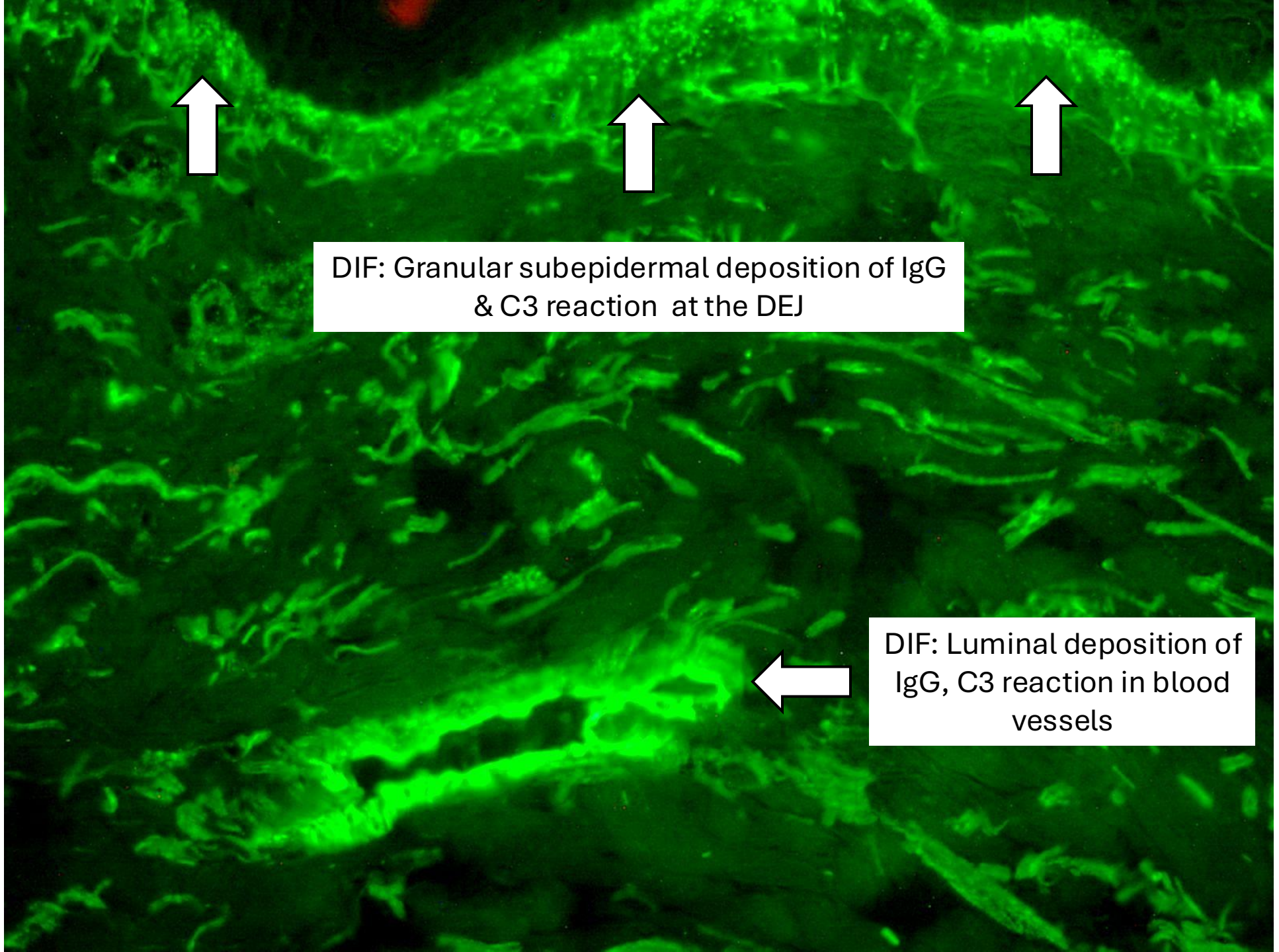
B. Full-house granular IgG, IgA, IgM, & C3 reaction at the DEJ and vascular reaction

C. IgG, IgA, IgA, or C3 reaction in the vascular lumen

D. D. Linear subepidermal C3, IgG; in perilesional skin

E. Lace-like intraepidermal C3, IgG; in perilesional skin


DIF: Granular subepidermal deposition of IgG & C3 reaction at the DEJ
DIF: Luminal deposition of IgG, C3 reaction in blood vessels

Summary: Lupus vasculitis

Direct Immunofluorescence (DIF) Findings

- DIF (lupus band test) is a critical diagnostic tool that provides strong supportive evidence for SLE.

Finding: Positive Lupus Band Test and Vascular Pattern

Pattern: Granular deposition of immunoreactants at the dermal-epidermal junction (DEJ).

Immunoreactants: Typically a "**full house**" pattern, meaning positivity for **IgG, IgM, IgA, and C3**. C1q is also commonly positive.

Significance: This finding is highly characteristic of lupus and helps distinguish lupus vasculitis from other causes of vasculitis, even in non-lesional skin.