Derm Meets Gyn:
Daily Challenges in Vulvar Pathology

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NO RELEVANT DISCLOSURES

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Vulvar/anogenital disease—at the intersection of gyn, GU, GI, derm

Vulvar/anogenital disease

Vulvar/anogenital pathology requires a team effort

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BENIGN VULVAR/ANOGENITAL SKIN PATHOLOGY :

1) “ULCER”
2) “IRRITATION”
3) “RULE OUT CONDYLOMA”

* Some slides include clinical photos of vulvar lesions

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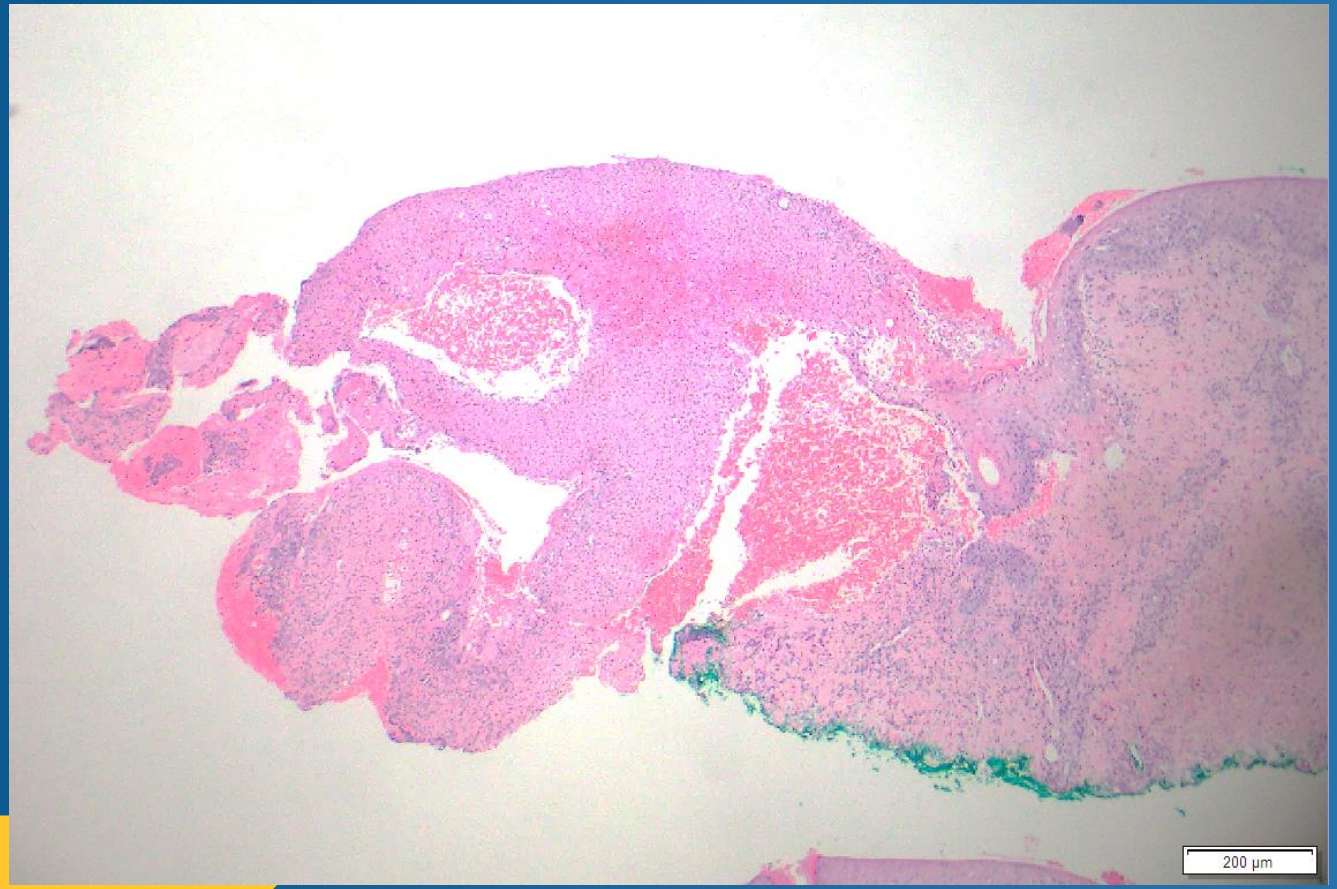
Case 1: “Ulcer”

Reference:

UCLA

Case 1-1: Vulvar ulcer in a 11 year old girl --Rapid onset of bilateral vulvar ulcers



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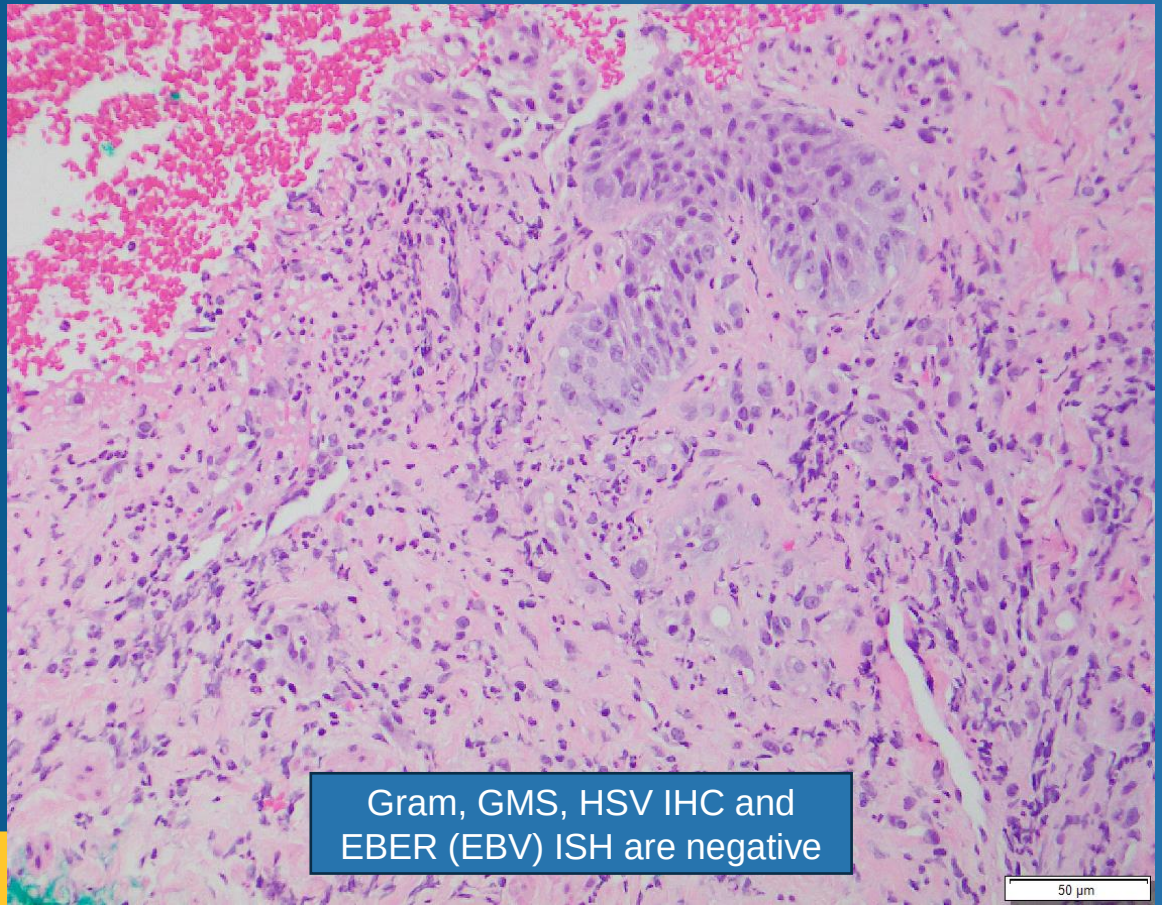

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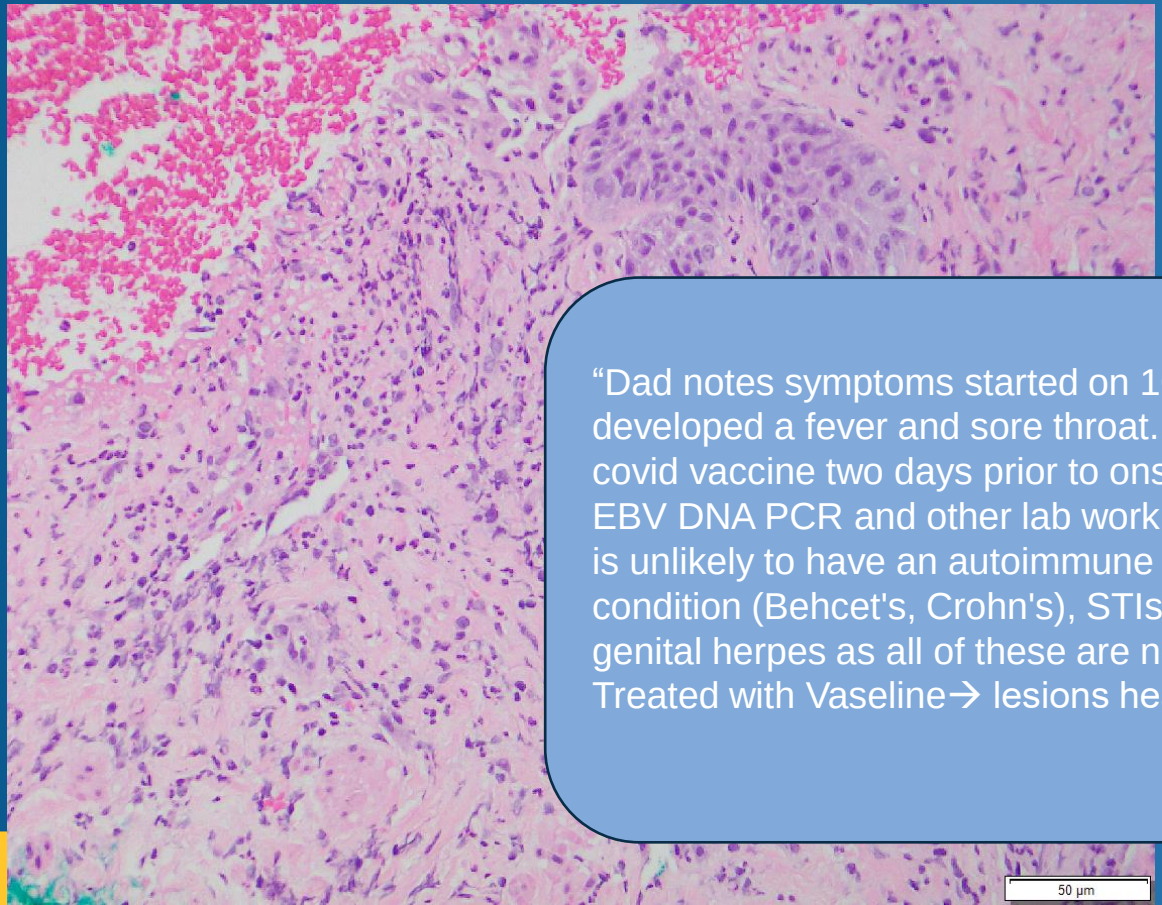
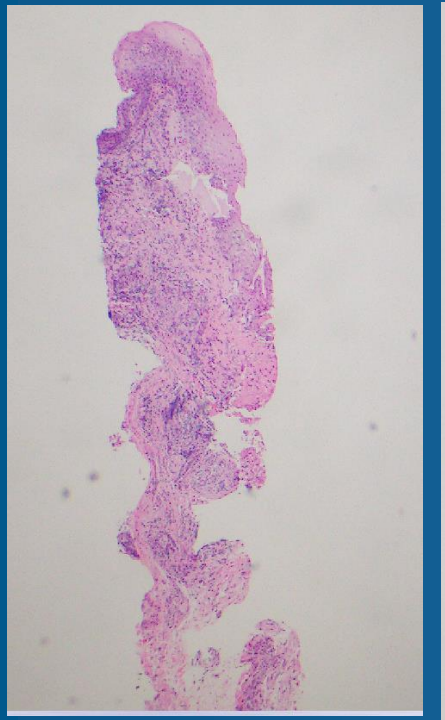
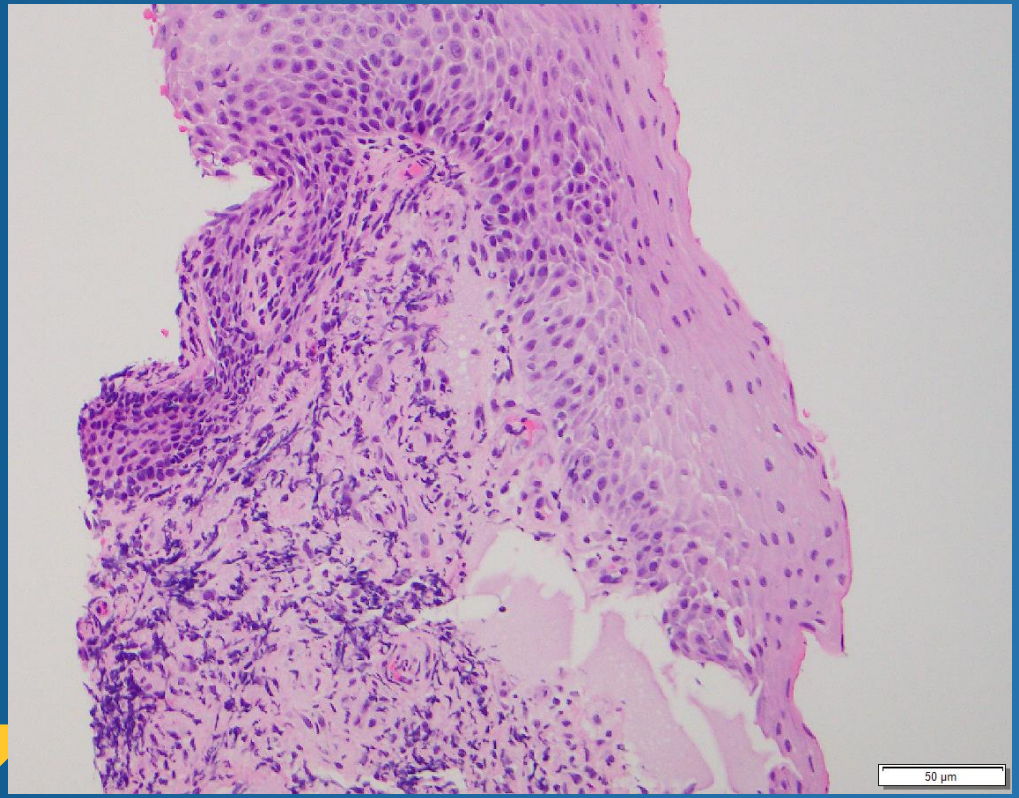


"Dad notes symptoms started on 10/22/22 after she developed a fever and sore throat. She received a covid vaccine two days prior to onset of symptoms. EBV DNA PCR and other lab work is negative. She is unlikely to have an autoimmune associated condition (Behcet's, Crohn's), STIs (syphilis, HIV), or genital herpes as all of these are negative.
Treated with Vaseline→ lesions healed on follow up"

Reference:
UCLA

Case 1-2: Vulvar ulcer in a 47 year old woman





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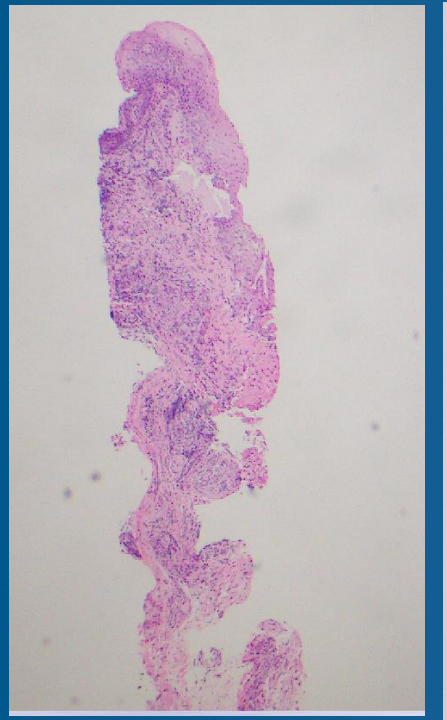

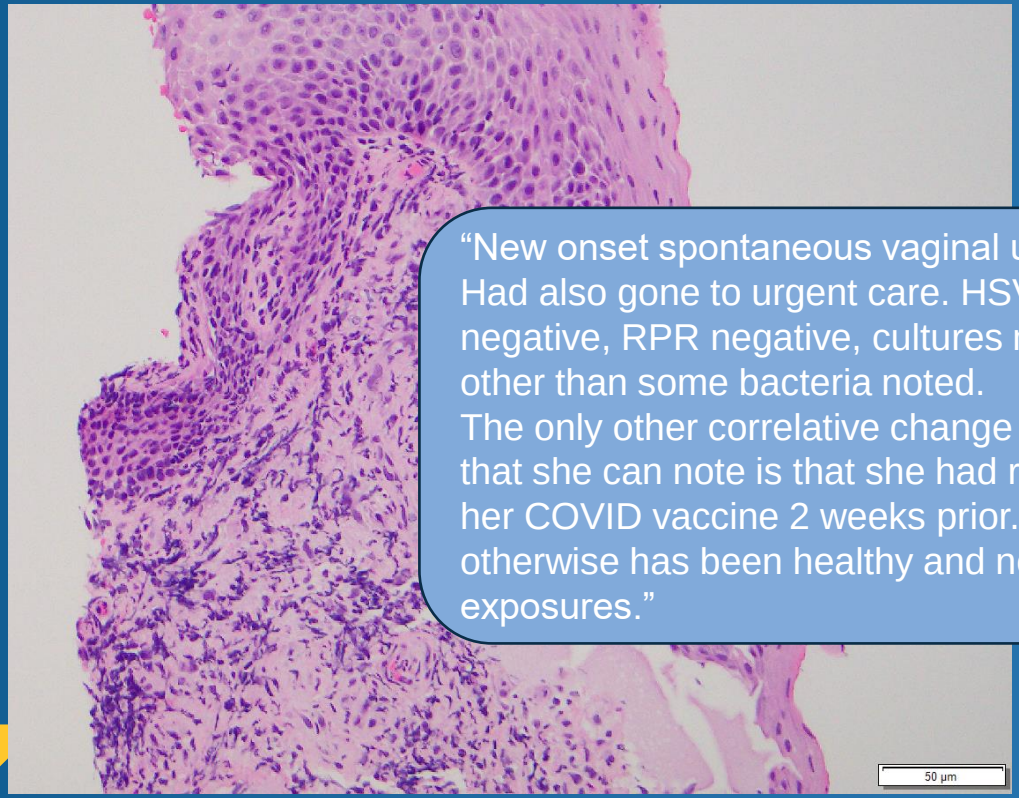

"New onset spontaneous vaginal ulcers. Had also gone to urgent care. HSV negative, RPR negative, cultures negative other than some bacteria noted.
The only other correlative change in health that she can note is that she had received her COVID vaccine 2 weeks prior. She otherwise has been healthy and no new exposures."

“Ulcer”

BENIGN ANOGENITAL ULCER DDX

- Infection (HSV, bacterial/fungal, syphilis etc)
- Systemic disease: Behçet disease (history of painful orogenital ulceration and ocular involvement), Crohn disease
- Drug (medication)-related eruption
- **Acute genital ulceration (Lipschütz Ulcer)**

Reference:

Case 1: Lipschütz Ulcer (acute genital ulceration)

- **Diagnosis of exclusion--sexually transmitted infections, Behc¸et's syndrome, extra-genital Crohn's disease, drugs eruption must be ruled out**.
- Initially described in 1913 by Benjamin Lipschütz--it was thought to be a rare and likely underdiagnosed condition, but a recent studies report that it may account for up to 30% of vulvar ulcerations encountered in a clinic[1].
- Demographics: Commonly seen in younger age groups (mean age of 29 in one study[1]), but reported in a wide age range including children.
- Pathogenesis? Not well studied—hypotheses include: immune complex deposition and formation of microthrombi secondary to bacterial or viral infection (EBV, mycoplasma, CMV, influenza, etc.), leading to ulcers[2].

Reference:
1. Vieira-Baptista P, et al. PMID 26297242
2. Moise et al. PMID: 30510669

Case 1: Lipschütz Ulcer (acute genital ulceration)

- **Clinical presentation:** In vulva, the lesions were more frequently found on the labia minora/vestibule.
- **History:** Patients commonly report non-gynecological symptoms (such as fever, respiratory symptoms) prior to presenting with the vulvar lesions, supporting possibility of association with possible infectious agents.*
- **Treatment:** The lesions are self-limiting and heal within several weeks, and only conservative measures are taken.

Reference: *Vieira-Baptista P, et al. PMID 26297242

Case 1: Lipschütz Ulcer—COVID-19 link?

- Cases of Lipschütz ulcers are reported in association with COVID-19 infection (n=18) or vaccinations (n=33)[1]. Several different types of vaccines implicated
- Vulvar ulcer usually occurs within 48–72 h following the vaccination and resolved 2-3 weeks later[2].

Reference:
1. Vismara et al. PMID: 37358748
2. Merlino, et al. PMID: 37754317

Case 1: Lipschütz Ulcer

Microscopic findings of LU:

- Non-specific superficial ulceration with granulation tissue, fibrin deposition, and a mixed inflammatory cell infiltrate.
- Vasculitis, including lymphocytic arteritis and leukocytoclastic vasculitis, have been reported.
- In EBV-associated cases, EBV may be detected by ISH or PCR.

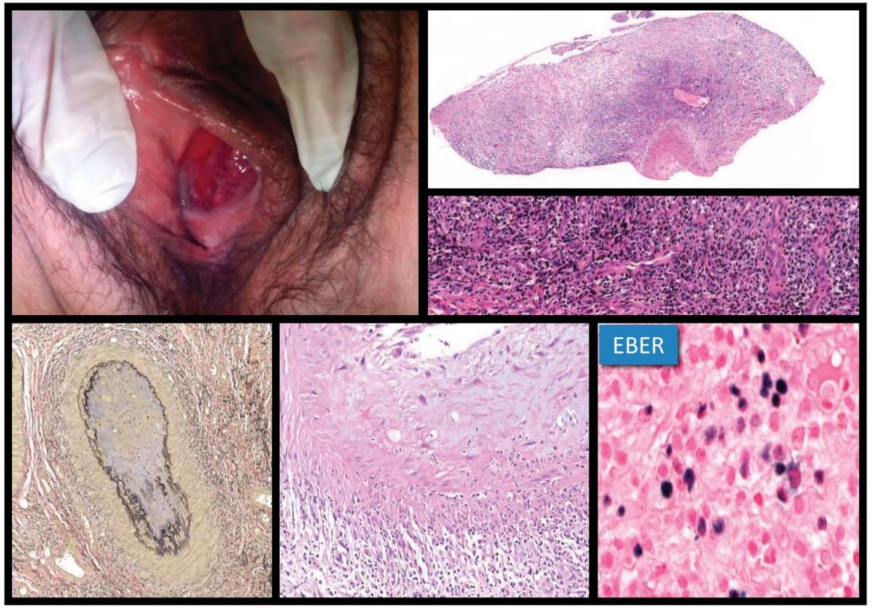

FIGURE 4. Endarteritis obliterans, chronic active arteritis, and ulcerated mucosal lymphoid hyperplasia associated with EBV early mRNA (EBER) expression. A 40-year-old woman and RTR presented with 4-month history of a persistent painful ulcer. She has a history of anogenital ulcers that improve with acyclovir therapy, unlike the present ulcer which was resistant to acyclovir therapy. Incisional biopsy of the ulcer showed a diffuse, dense lymphocytic infiltrate with coexisting fibrosis (top right and mid-panels). Scattered lymphocytes, less than 5%, expressed EBER by in situ hybridization. At the ulcer base and throughout the sampled tissue could be found arteries with panmural inflammation and fibrointimal hyperplasia (bottom mid panel) or arteries with complete occlusion of their lumens (endarteritis obliterans) (bottom left panel, elastic tissue stain). EBV-positive mucocutaneous ulcer is in the differential diagnosis[29,30]; the absence of a polymorphous infiltrate with atypical large lymphocytes (immunoblasts), Reed–Sternberg-like cells, and plasmacytoid apoptotic cells exclude this closely related entity showing persistent ulceration that is associated with chronic active EBV infection and immunosuppression.

Figure: Barrett, Mary M et al. "Lymphocytic Arteritis in Epstein-Barr Virus Vulvar Ulceration (Lipschütz Disease): A Report of 7 Cases." *The American Journal of dermatopathology* vol. 37,9 (2015): 691-8.

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Case Reports > Am J Mens Health. 2023 Jul-Aug;17(4):15579883231184683. doi: 10.1177/15579883231184683.

Genital Ulcer as a Complication of COVID-19 Infection: A Case Report

Rayka Sharifian [1], Ali Mohammad Mirjalili [2], Arshia Zamani Hajiabadi [3]

Affiliations + expand

PMID: 37421309 PMCID: PMC10331107 DOI: 10.1177/

Case Reports > Int J STD AIDS. 2022 May;33(6):622-624. doi: 10.1177/09564624221085726. Epub 2022 Mar 25.

A case of COVID-19-related acute genital ulceration in a male

Abdurrahman Kaya [1], Sibel Yıldız Kaya [2]

Affiliations + expand

PMID: 35337226 PMCID: PMC8960746 DOI: 10.1177/09564624221085726

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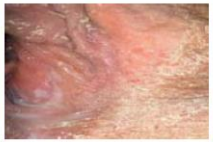
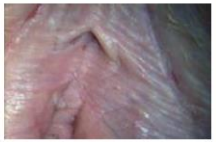
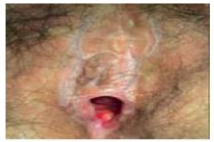
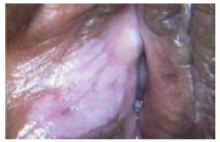
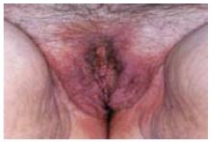
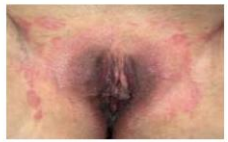
Case 2: “Irritation”

Reference:
UCLA

TABLE

Characteristic conditions*

	Candidiasis	Lichen sclerosus	Lichen planus	VIN (vulvar intraepithelial neoplasia)	Eczema	Psoriasis
Clinical presentation						
Frequency (prevalence)	10–20%	0.1–3%	0.1–0.8%	Exact prevalence unknown, incidence Approx. 3/100 000 women in Germany	0.5–10%	2%
Morphological features	Red and white plaques, erosions, ulcers	– Early form: erythema, erosions – Late form: white, firm plaques, bleeding into skin, scarring, atrophy, fissures, exaggerated skin markings	– Early form: charact. whitish reticulate (Wickham) striae – Late form/erosive form: erosive erythema, scarring, extragenital involvement (e.g. oral)	Skin-colored papules and nodules, white and red plaques, acetowhite lesions (after application of 5% acetic acid), erosions (especially with differentiated VIN)	Poorly marginated erythematous lesions on the labia majora and labia minora, edema (acute), lichenification (chronic)	Well-demarcated, slightly scaly, erythematous red plaques, accompanying fissures and rhagades
Signs & symptoms	Pruritus, erythema, increased vaginal discharge (white, curd-like, no odor)	Pruritus, burning, dyspareunia	– Early form: pruritus, burning, pain – Late form: dyspareunia, burning, vaginal stenosis	Pruritus, burning, soreness, often asymptomatic	Pruritus, soreness	Pruritus
Diagnosis	pH value: normal (< 4.0) Lactobacilli: yes Leukocytes: increased Clue cells: none Microscopy: Pseudomycelium & blastospores	History, clinical examination, typical figure-of-8 pattern surrounding the vulva and anus; histological confirmation by biopsy, if required	History, clinical examination, characteristic Wickham striae, vaginal involvement, histological confirmation by biopsy	Vulvoscopy, histological confirmation by biopsy	History, clinical examination; if necessary, patch test	Typical involvement of labia majora, characteristic non-involvement of labia minora
Management	– Acute: Antifungal agent (e.g. oral fluconazole or topical clotrimazole preparations) – Chronic: Following the initial treatment, fluconazole 150 mg orally 1 x/week for at least 6 months after loading dose	– Initially ultrapotent glucocorticoids (GC) (topical) – Life-long GC maintenance dose in reduced dose, lipid replenishment – Second-line therapy: calcineurin inhibitors (off-label)	– Initially ultrapotent glucocorticoids (GC) (topical) – Life-long GC maintenance dose in reduced dose, lipid replenishment –Second-line therapy: calcineurin inhibitors (off-label)	– Laser vaporization (standard with usual-type VIN) – Surgical excision rather with differentiated VIN (Warning: occult carcinoma) – Imiquimod 5%, topical for usual-type VIN (off-label)	– Avoidance of trigger factors – Glucocorticoids (topical)	– Avoidance of mechanical stress and trigger factors – Topical treatment as for extragenital psoriasis (typically GC/calcineurin inhibitors)

Compiled based on (e41–e45); VIN, vulvar intraepithelial neoplasia

* Photographs courtesy of Prof. Dr. Linn Woelber and Prof. Dr. Werner Mendling

Woelber et al, PMID: 32181734

Causes of “vulvar irritation”

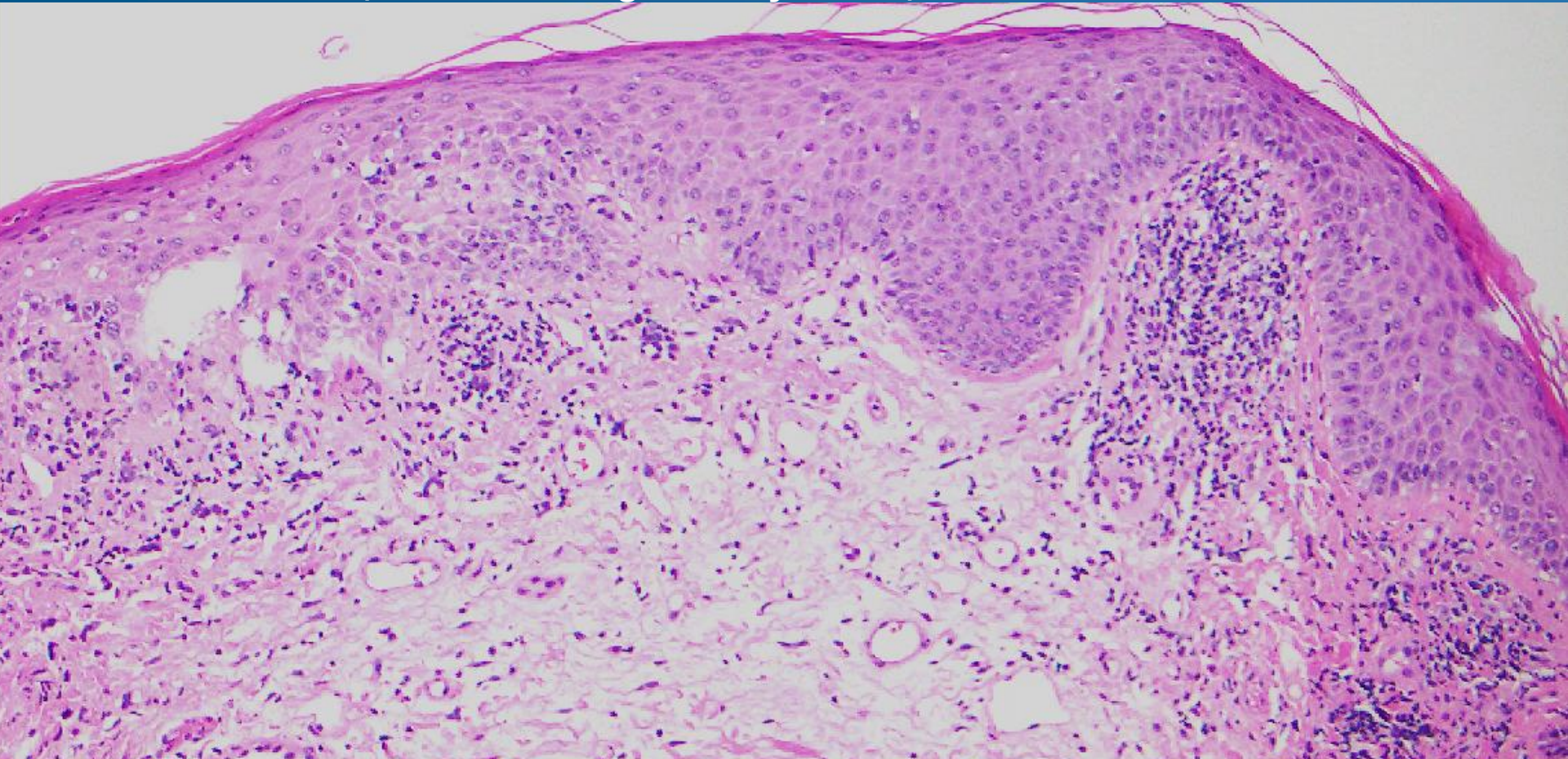
ONCE DYSPLASIA/MALIGNANCY IS RULED OUT…

1) **BUGS? FUNGAL (CANDIDA/TINEA), HSV, MOLLUSCUM, ETC**
2) **IS IT LICHEN SCLEROSUS (LS)?**
3) **ECZEMATOUS/CONTACT DERMATITIS OR PSORIASIS?**

Reference:

Reference:
UCLA

Case 2: 70F, vulvar itching and erythema, rule out lichen sclerosus



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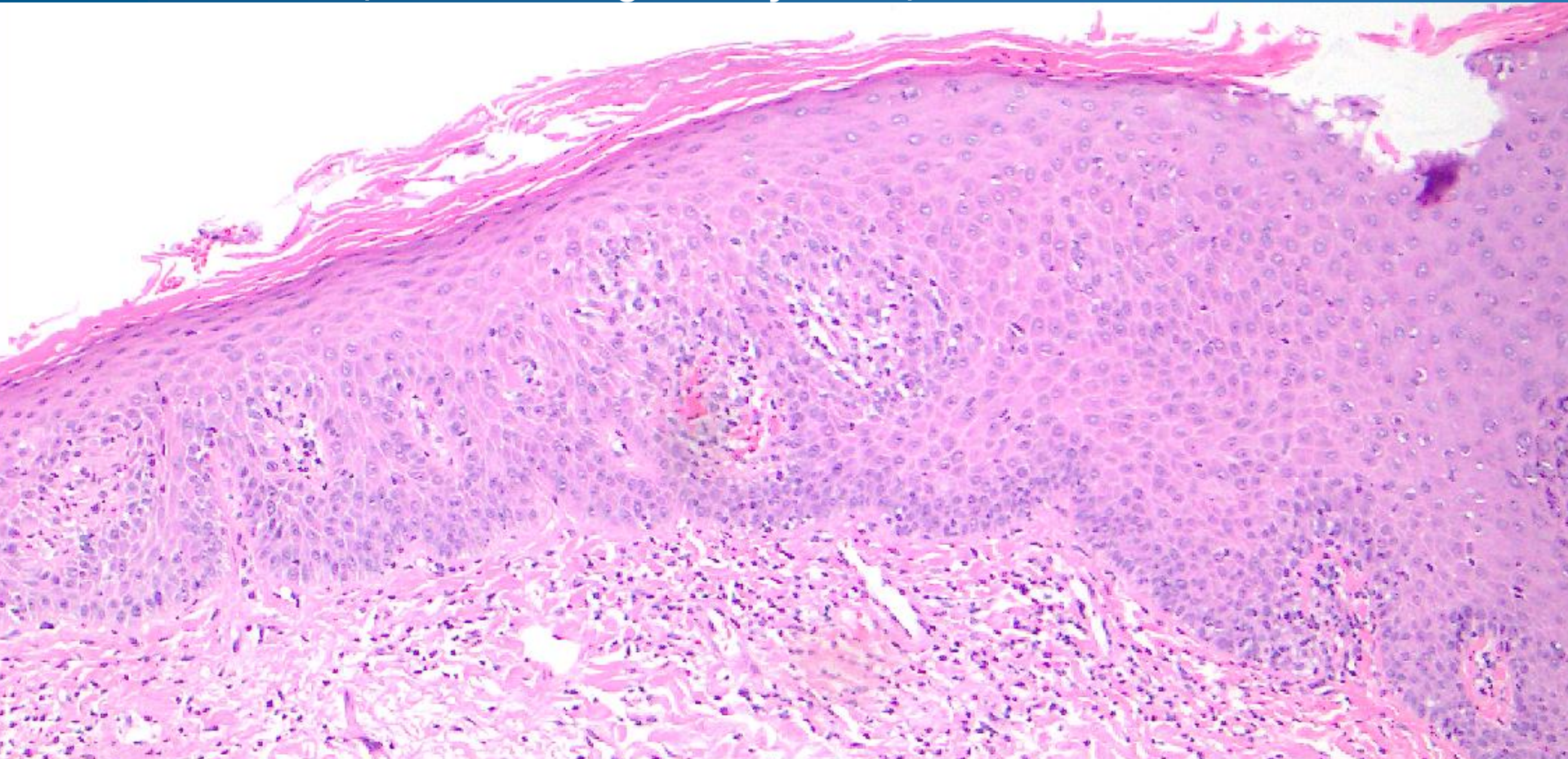

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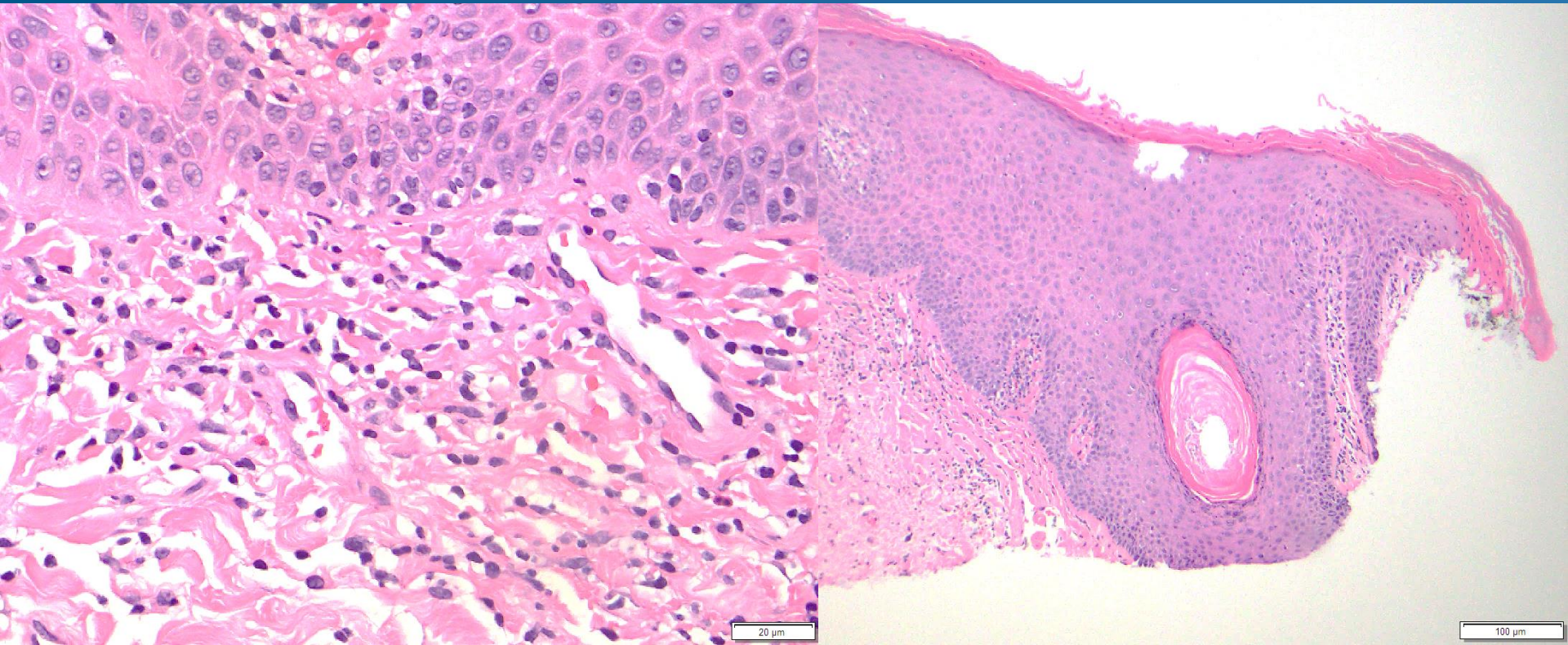

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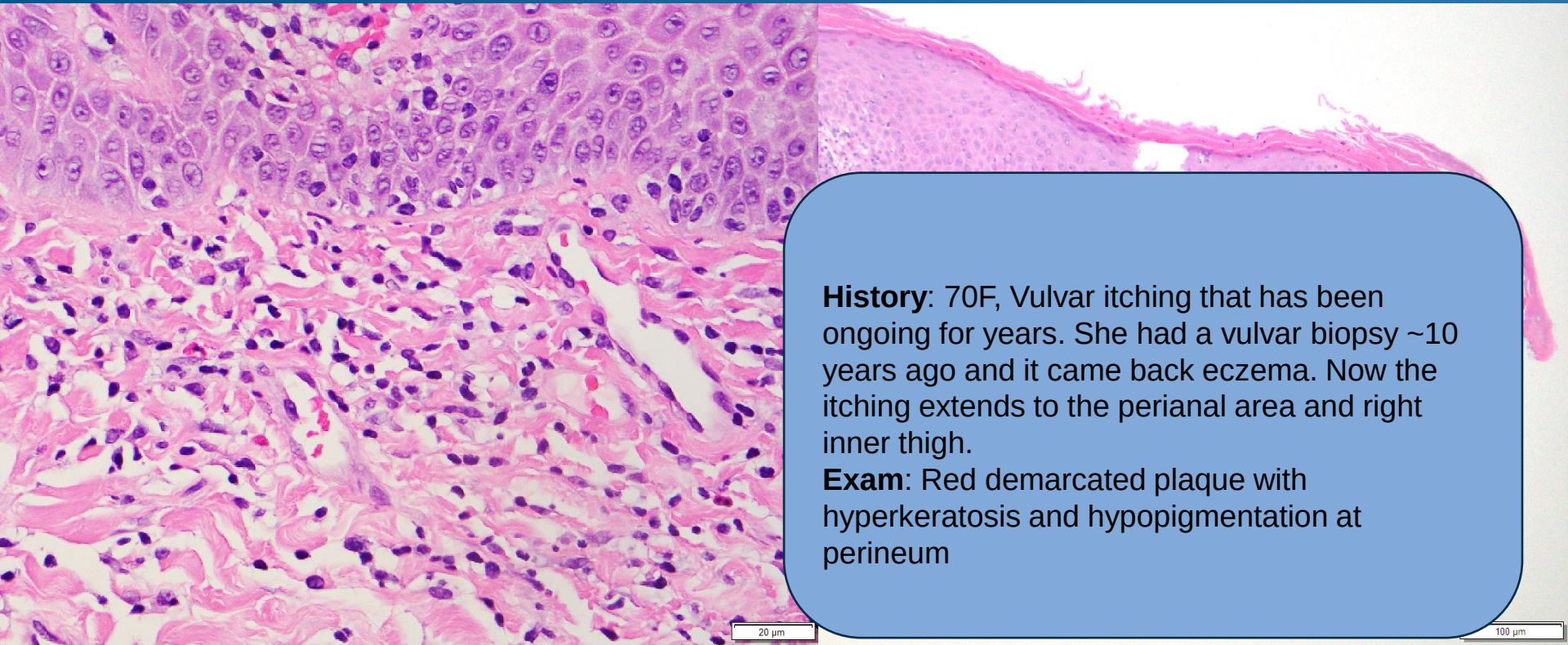


History: 70F, Vulvar itching that has been ongoing for years. She had a vulvar biopsy ~10 years ago and it came back eczema. Now the itching extends to the perianal area and right inner thigh.
Exam: Red demarcated plaque with hyperkeratosis and hypopigmentation at perineum

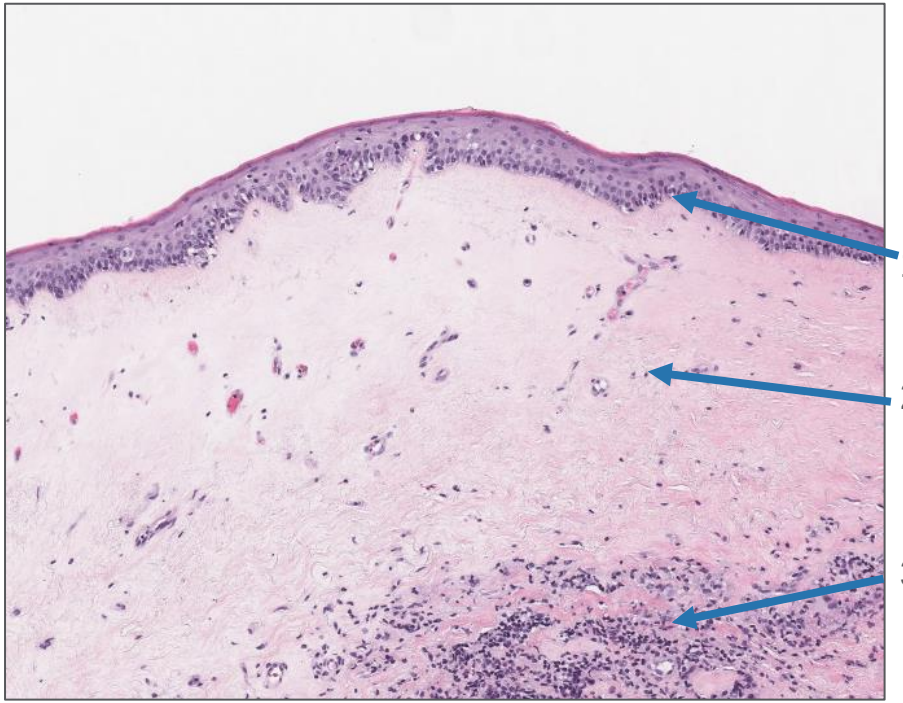
Causes of “vulvar irritation”

ONCE DYSPLASIA/MALIGNANCY IS RULED OUT…

1) **BUGS? FUNGAL (CANDIDA/TINEA), HSV, MOLLUSCUM, ETC**
2) **LICHEN SCLEROSUS?**
3) **ECZEMATOUS/CONTACT DERMATITIS OR PSORIASIS?**

Reference:

LS histopathology—classic features



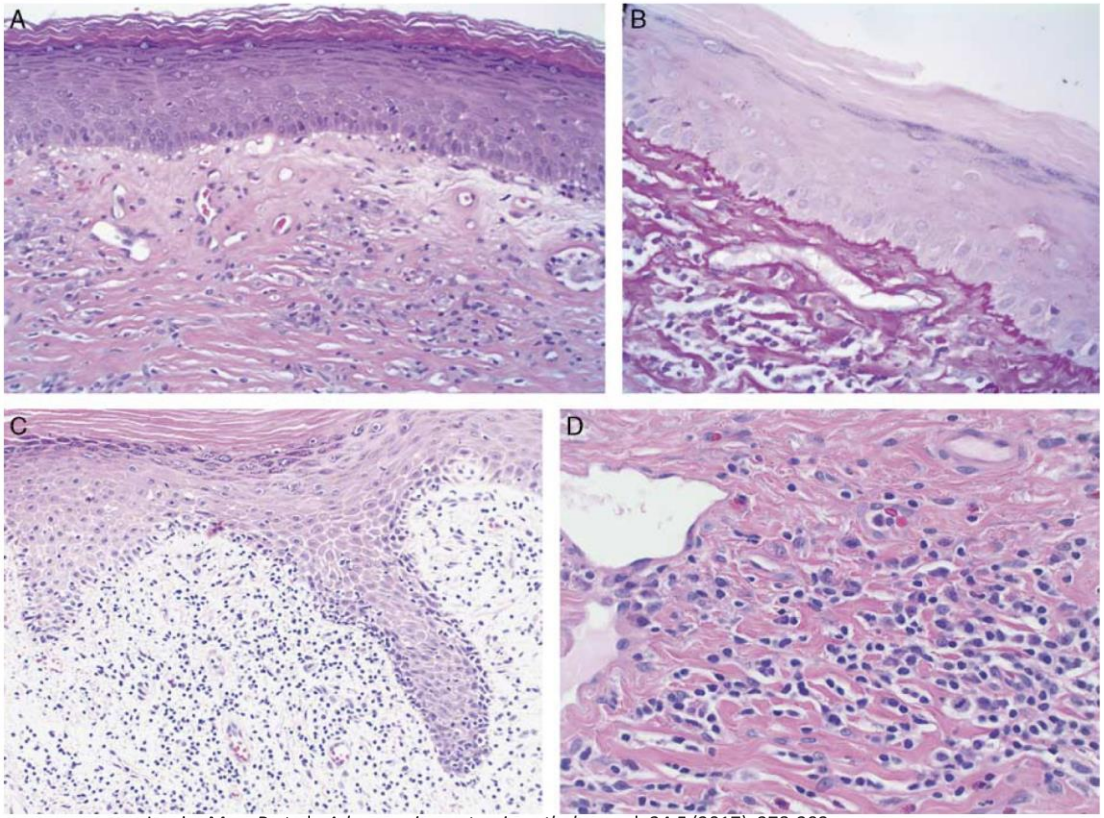
1) Interface changes in the basal layer

2) Superficial dermal edema, sclerosis and hyalinization

3) Lichenoid inflammation=Band of lymphocyte-predominant inflammation below the sclerosis

Reference:

LS histopathology—when things are less classic…



Lewin, Marc R et al. *Advances in anatomic pathology* vol. 24,5 (2017): 278-293.

CLUES TO THE DIAGNOSIS OF LS

A) Early superficial hyalinization

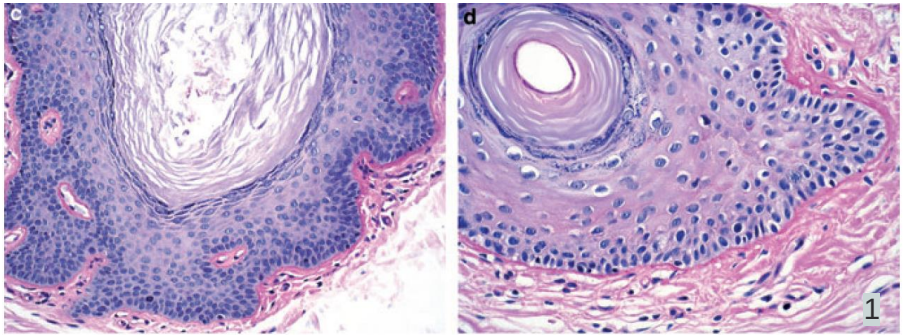
B) PAS stain highlighting early deposition of hyalinized material underneath the basement membrane and around vessels in the superficial dermis.

C) Lymphocytes lining up along the basal layer

D) Entrapment of lymphocytes in wiry collagen

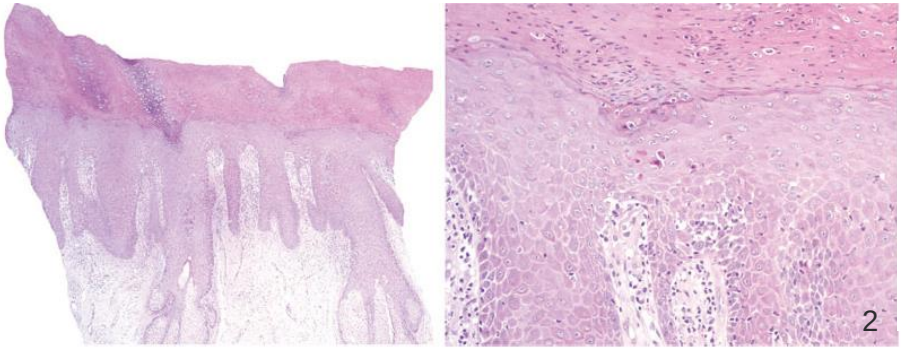
* Telangiectasia is often prominent and associated purpura (dermal red blood cell extravasation) and hemosiderin may be present.

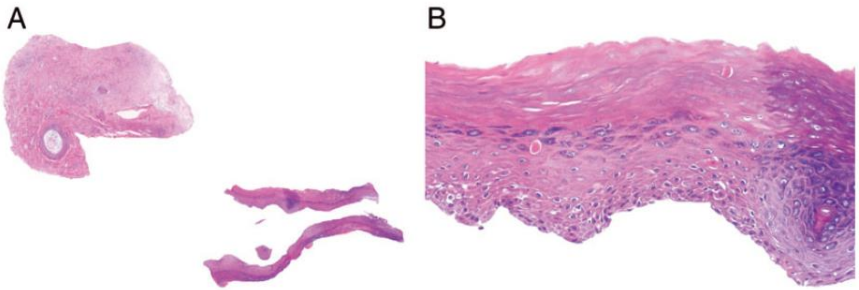
LS histopathology—when things are less classic…



OTHER CLUES

- Follicular changes:
  - perifollicular basement membrane thickening
  - follicular plugging/ hyperkeratosis
- Vertical columns of parakeratosis [2]
- Detached epidermis [2]





References: 1 Regauer S, et al. Histopathology. 2005;47(4):340-347. 2. Weyers W. J Cutan Pathol. 2015;42(2)

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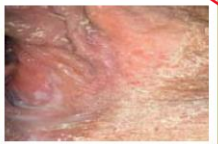
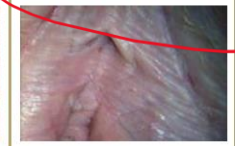
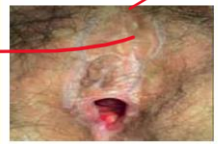
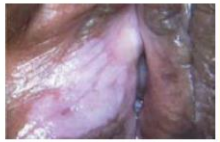
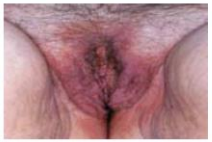
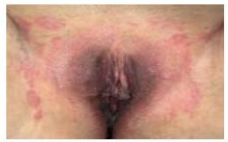
Clinical presentation						
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Diagnosis	pH value: normal (< 4.0) Lactobacilli: yes Leukocytes: increased Clue cells: none Microscopy: Pseudomycelium & blastospores	History, clinical examination, typical figure-of-8 pattern surrounding the vulva and anus; histological confirmation by biopsy, if required	History, clinical examination, characteristic Wickham striae, vaginal involvement, histological confirmation by biopsy	Vulvoscopy, histological confirmation by biopsy	History, clinical examination; if necessary, patch test	Typical involvement of labia majora, characteristic non-involvement of labia minora
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Compiled based on (e41–e45); VIN, vulvar intraepithelial neoplasia

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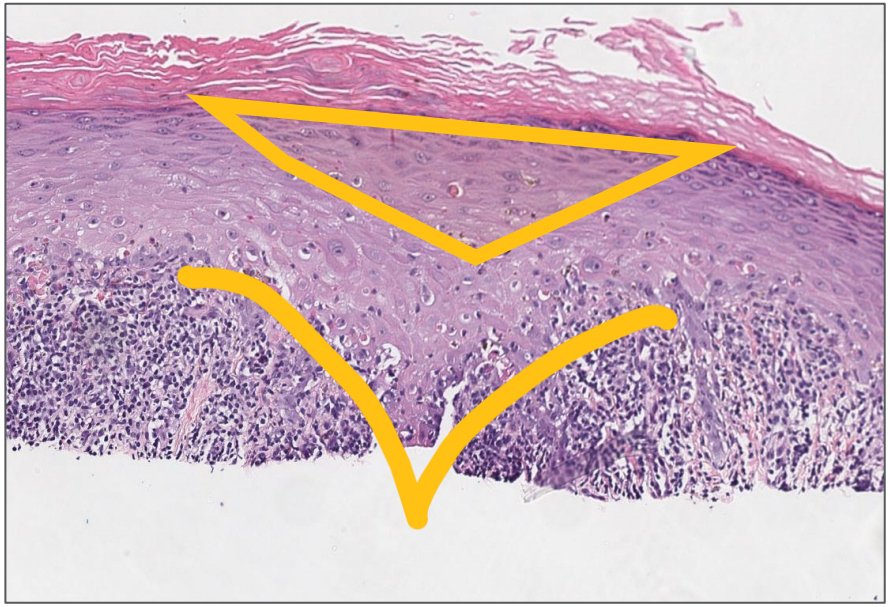
Woelber et al, PMID: 32181734

LP histopathology



- Hyperkeratosis and wedge-shaped Hypergranulosis
- Saw-toothing/serrated epidermis (pointed rete)
- Lichenoid (band-like) lymphocyte-predominant inflammation in the superficial dermis, obscuring the basal epidermis + many necrotic keratinocytes
- Subepidermal clefting may be present

Lichen sclerosus (LS)—clinical clues

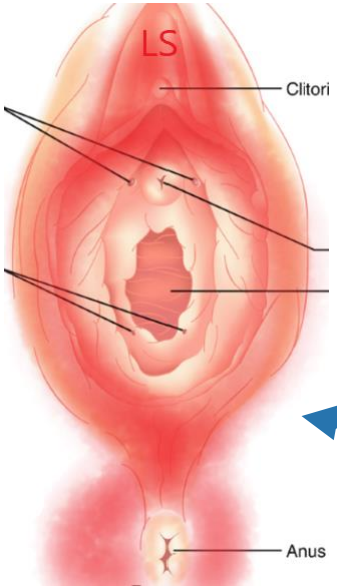


Fig. 5. Clinical presentation of hypertrop... sclerosus. Thick waxy plaques overlying both inner labia majora, complete reso... labia minora, complete clitoral phimosis, and perianal involvement are seen.

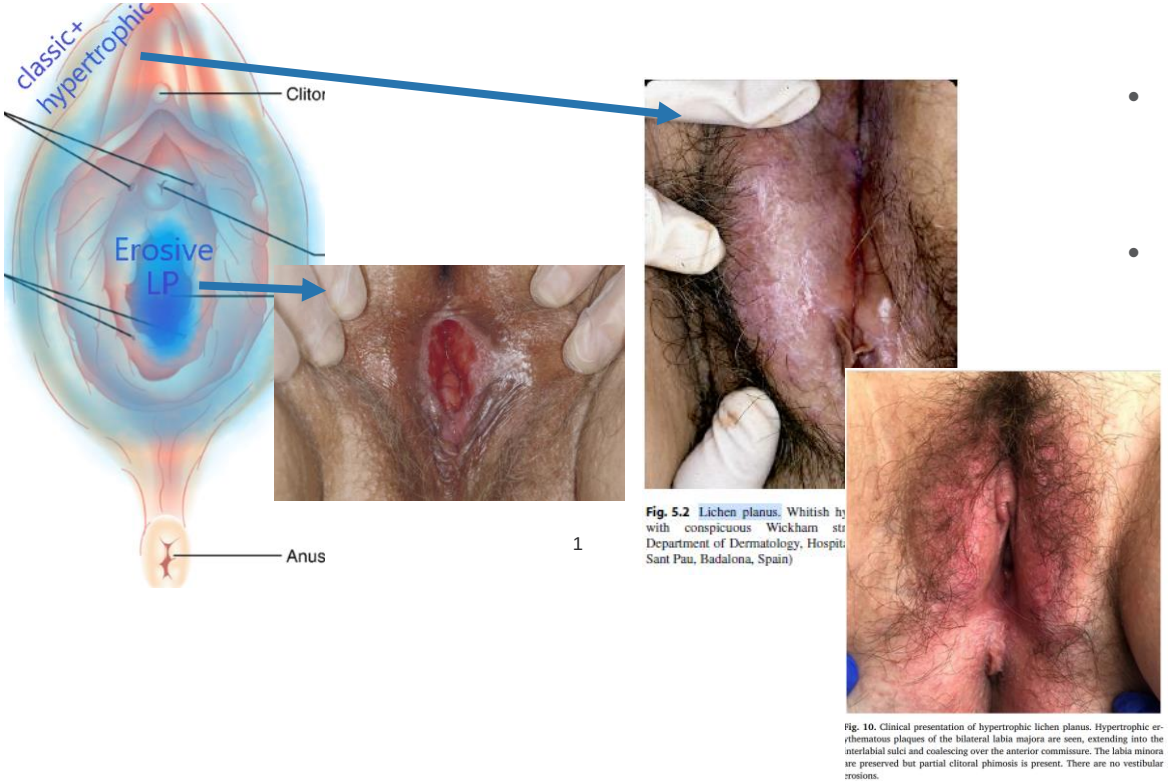
CLINICAL EXAM

- Female genital LS affects vulva, perineum, anus, genitocrural folds, buttocks and thighs.
- Lichenified, white/porcelain atrophic skin with hemorrhage and architectural changes
- **"Figure of eight"** involvement of vulva and anus is a common distribution. Mucosal involvement of vagina is not a typical feature (in contrast to LP).

Usually involves clitoris→ labia minora/majora→ perineum → perianal skin (vaginal mucosal involvement is rare)

Images: [L] Modified: http://www.emdocs.net/em3am-bartholins-abscess/ [R] Shalin, S st al. Seminars in diagnostic pathology vol. 38,1 (2021): 3-18..

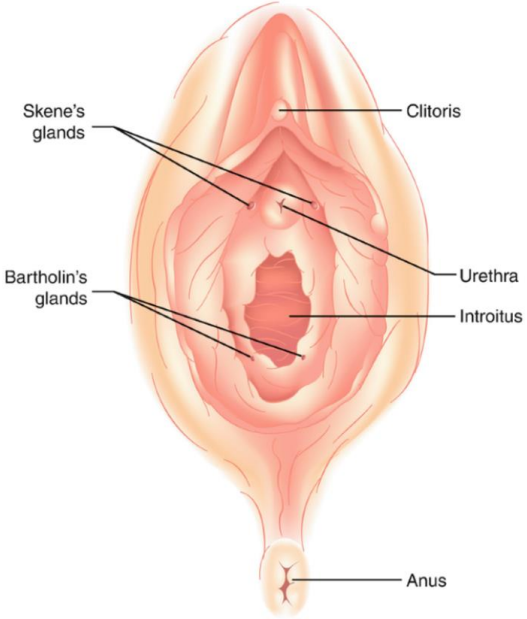
Lichen planus—clinical clues

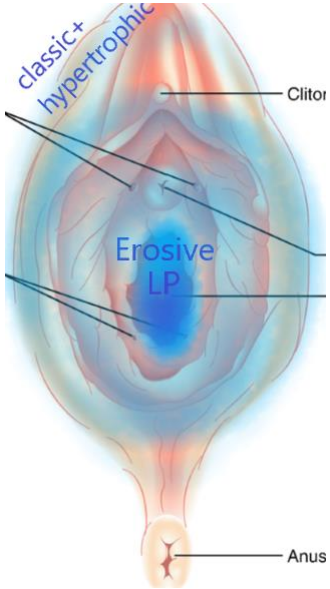


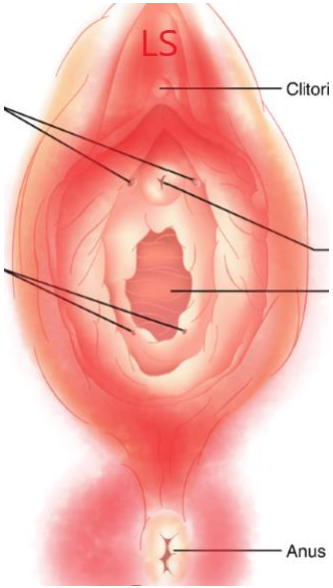
- Check for clinical history of LP: patients with vulvar LP frequently have a history of LP involving other parts of the body (i.e. oral)
- Several subtypes of LP exist (classic/hypertrophic, and erosive)
  - Erosive LP involves the vagina and may result in scarring/stricture if left untreated.

Images, left→right
Modified: http://www.emdocs.net/em3am-bartholins-abscess
Sand FL, Thomsen SF. J Obstet Gynaecol. 2018 Feb;38(2):149-160.
[Hoang, M. and Selim, M. (2015) Vulvar Pathology. New York: Springer.
Shalin, S st al. *Seminars in diagnostic pathology* vol. 38,1 (2021): 3-18.

CRITERIA		LICHEN PLANUS	LICHEN SCLEROSUS
CLINICAL	Vaginal involvement	**Frequent** in erosive LP	Extremely rare
	Oral involvement	**Frequent**	Extremely rare
	Perianal involvement	Rare	**Frequent**







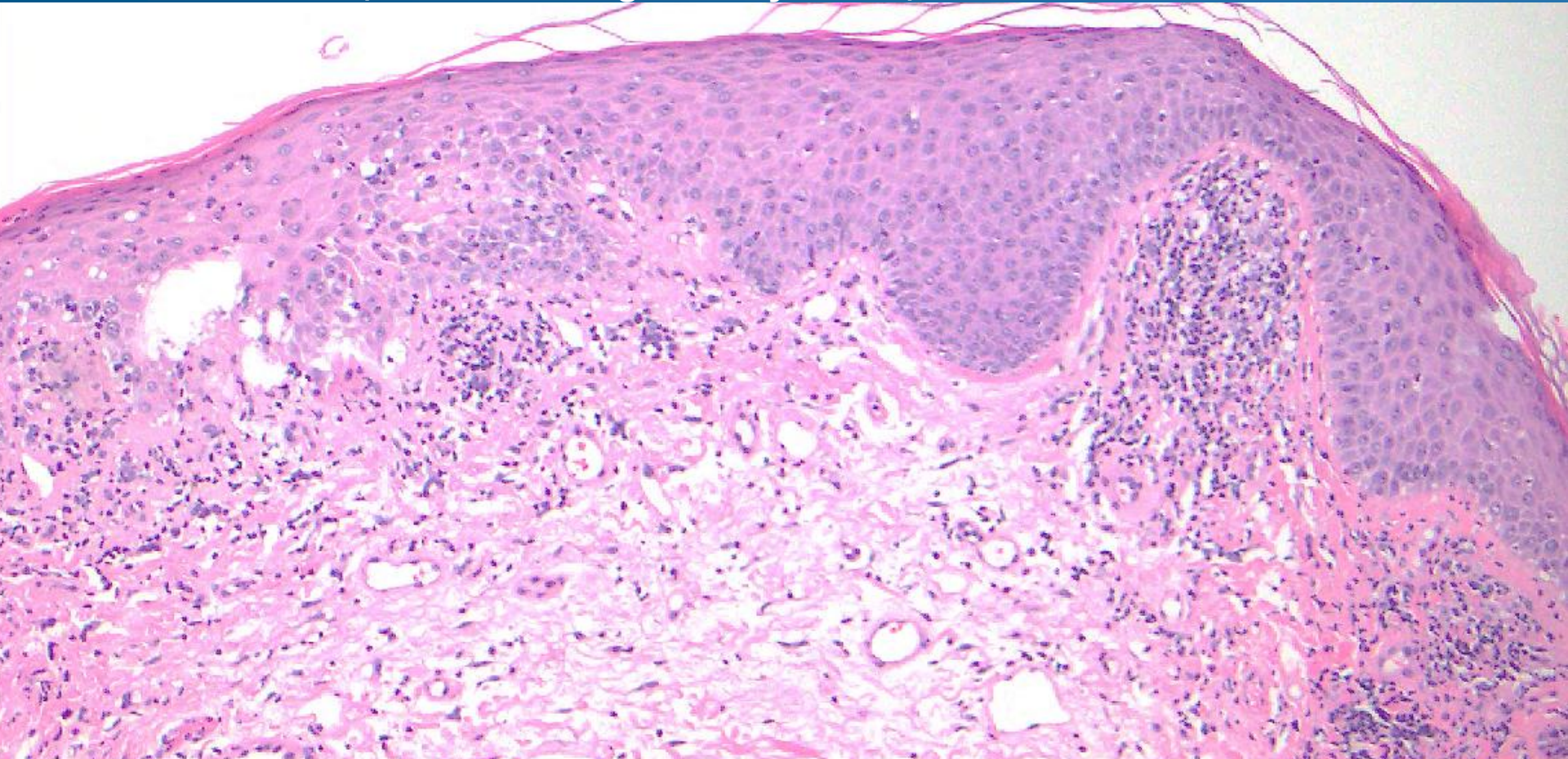
Reference:

Modified: http://www.emdocs.net/em3am-bartholins-abscess

CRITERIA		LICHEN PLANUS	LICHEN SCLEROSUS
CLINICAL	Vaginal involvement	**Frequent** in erosive LP	Extremely rare
	Oral involvement	**Frequent**	Extremely rare
	Perianal involvement	Rare	**Frequent**
HISTOLOGIC	Serrated epidermis/sawtoothing	**Frequent**	Rare
	Wedge-shaped hypergranulosis	**Frequent**	Rare
	Necrotic keratinocytes/Colloid bodies	**Numerous**	Not as numerous as LP
	Thickening of the basement membrane	Rare	**Frequent**
	Collagen hyalinization	Rare	**Frequent**
	Hemorrhage or siderophages	Rare	**Frequent**
	Lymphocyte entrapment by wiry fibrosis	Rare	**Frequent**

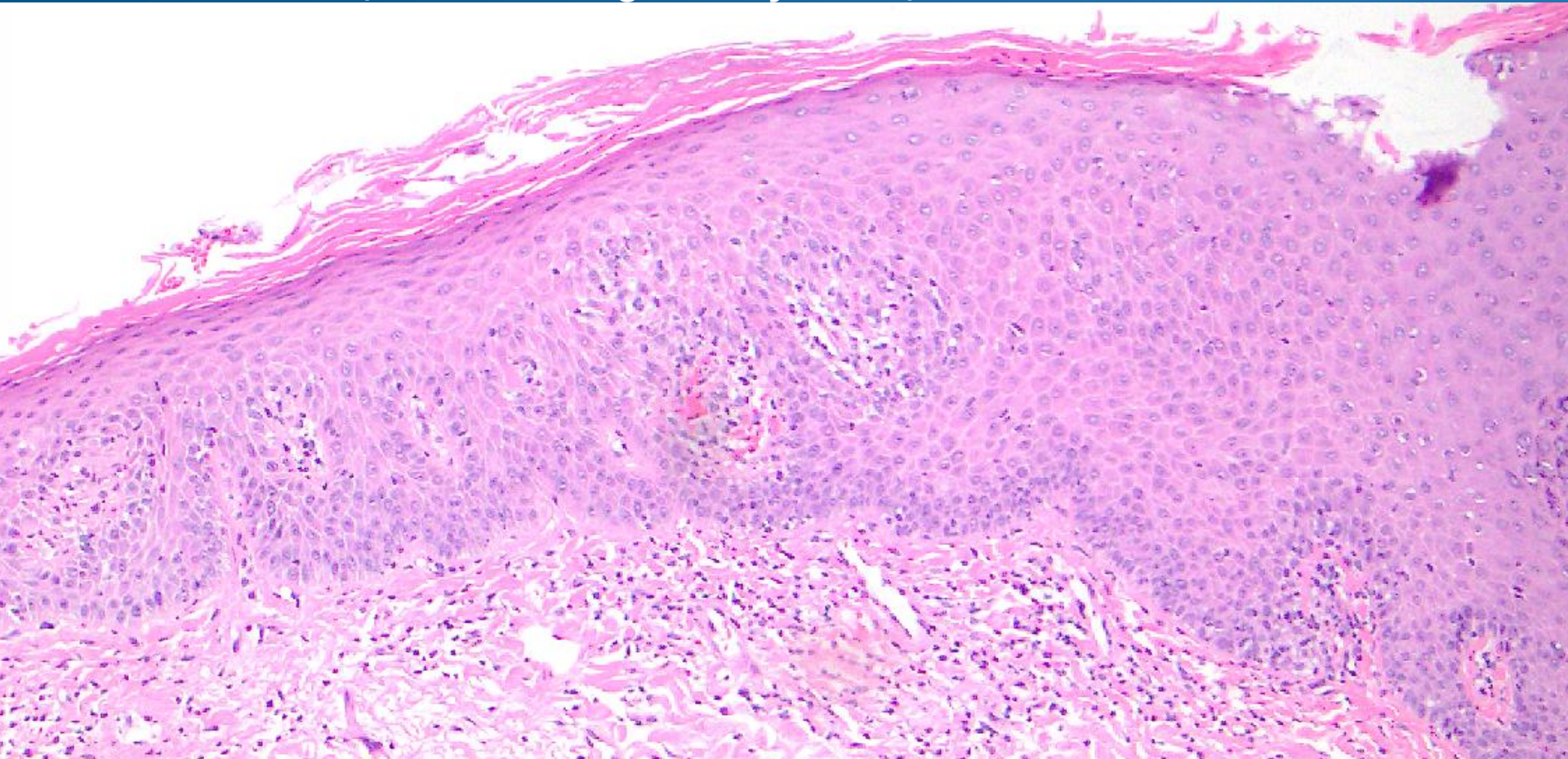
Reference:
UCLA

Case 2: 70F, vulvar itching and erythema, rule out lichen sclerosus



Reference:
UCLA

Case 2: 70F, vulvar itching and erythema, rule out lichen sclerosus



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UCLA

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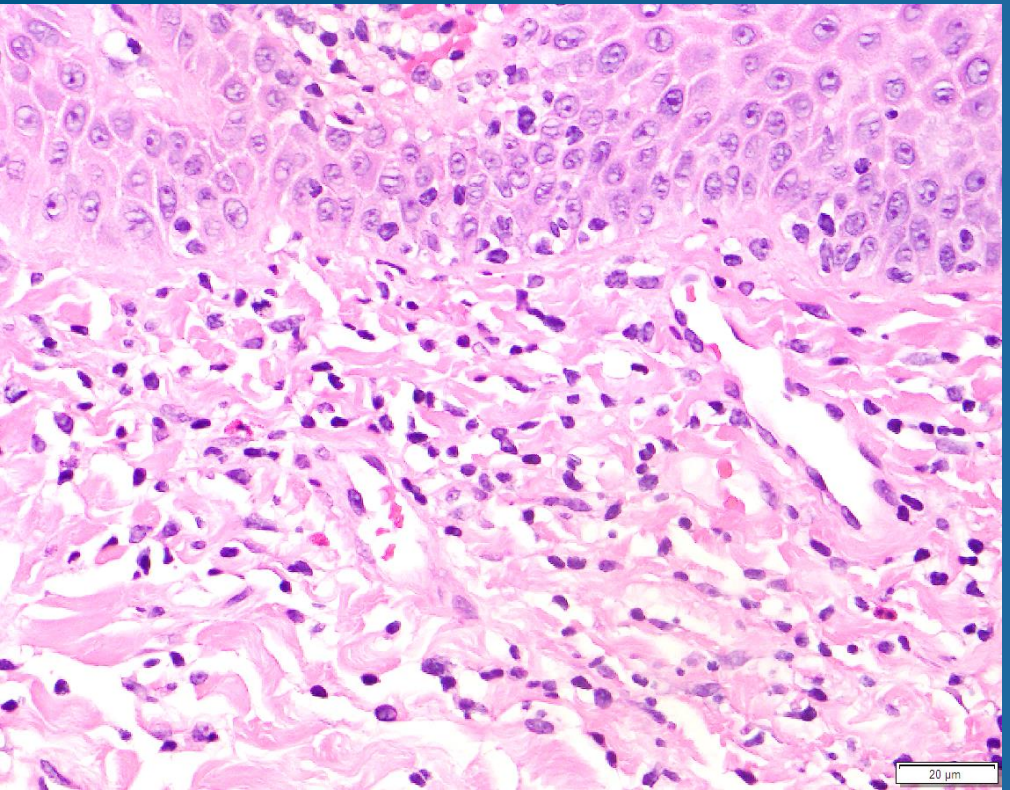

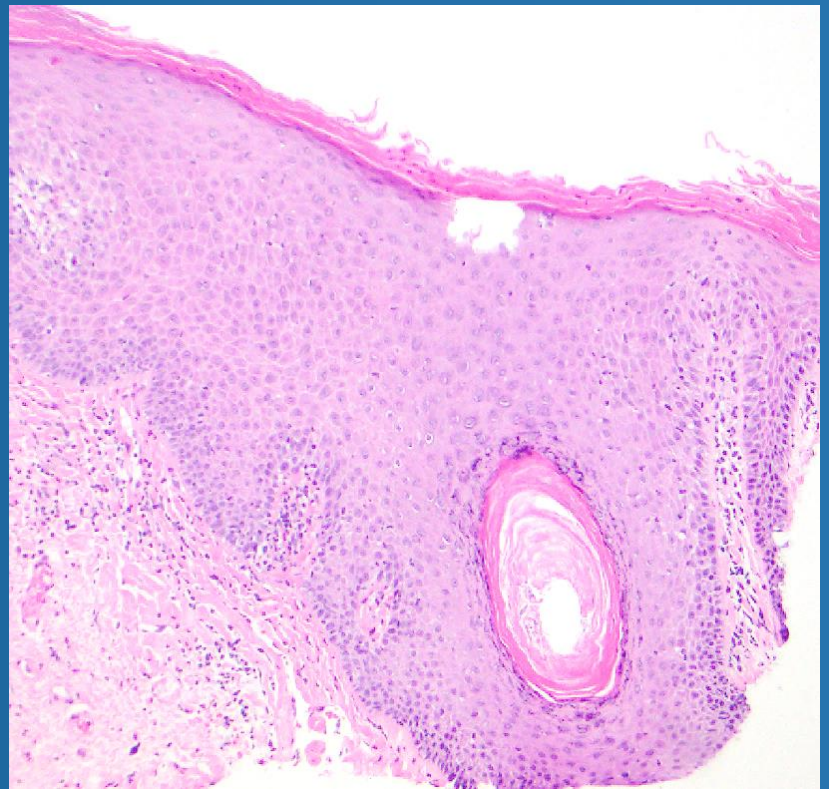

Reference:
UCLA

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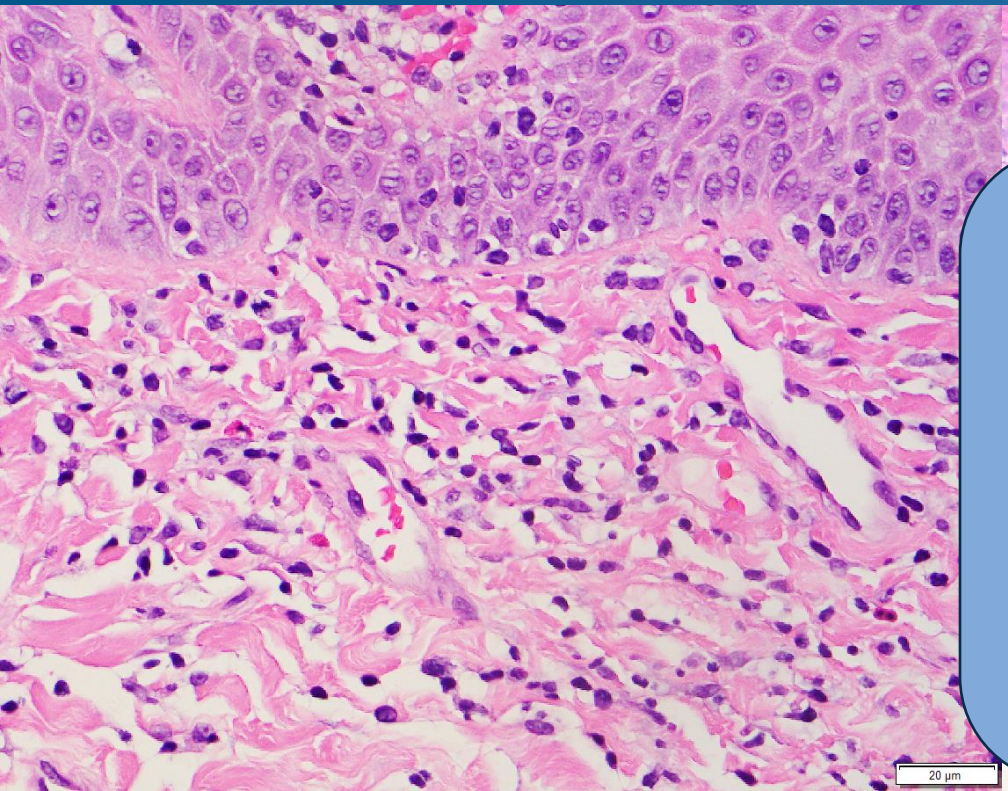
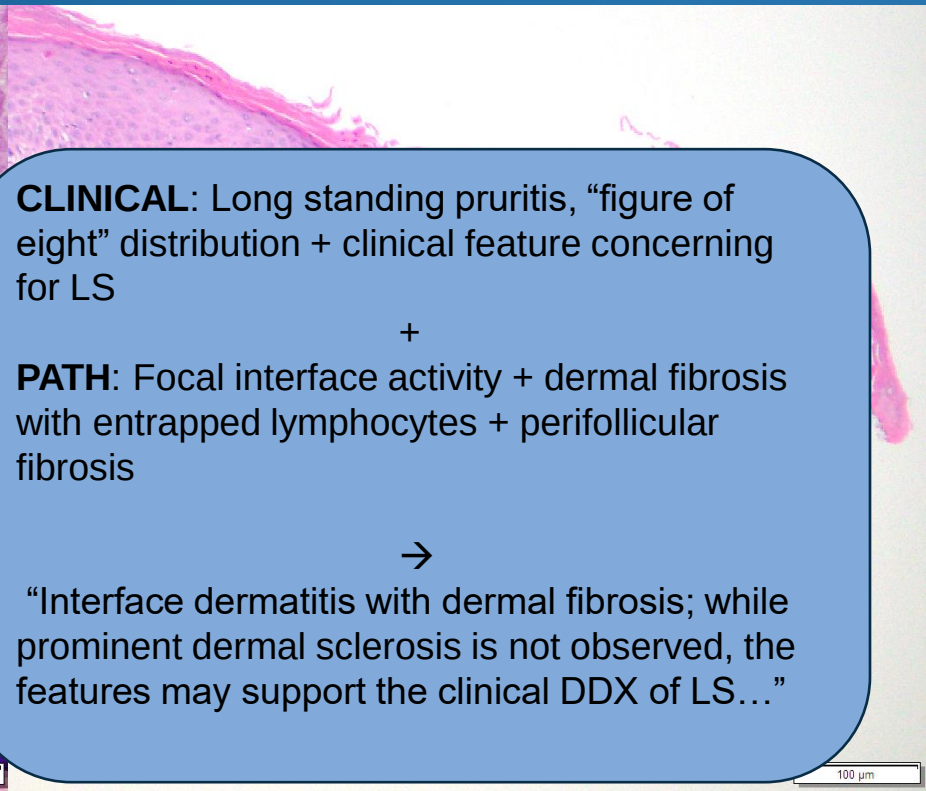




CLINICAL: Long standing pruritis, “figure of eight” distribution + clinical feature concerning for LS

+

PATH: Focal interface activity + dermal fibrosis with entrapped lymphocytes + perifollicular fibrosis

→

“Interface dermatitis with dermal fibrosis; while prominent dermal sclerosis is not observed, the features may support the clinical DDX of LS…”

Clinical significance of LS

- LS has been considered to carry an increased risk of vulvar squamous cell carcinoma (SCC)—lifetime risk of 2-6% for untreated/inadequately treated

With intervention, these complications may be prevented*

Therefore, use clinical and pathologic clues, and if LS is in the microscopic DDX, keep it in the DDX

Reference:

UCLA

“Atchoum, as you may have figured out, is a cat "

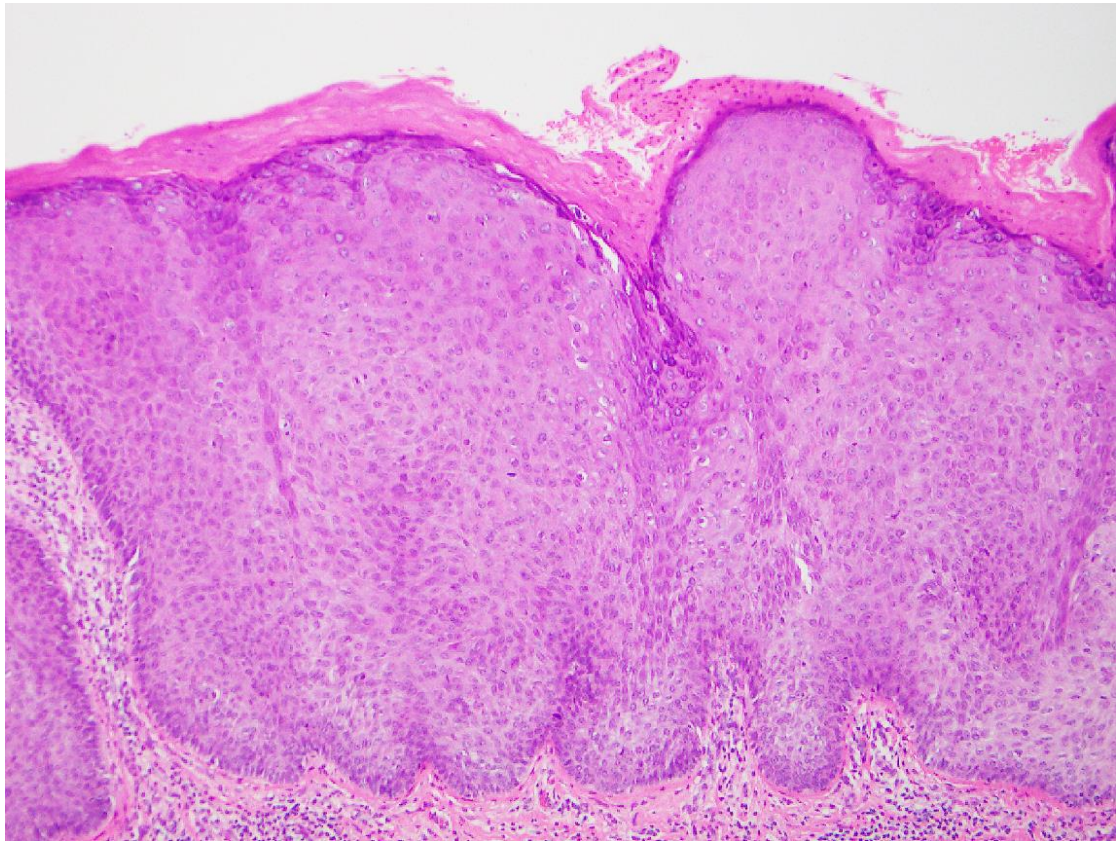
https://www.cnet.com/culture/pet-cat-dog-atchoum-instagram-hypertricosis/

UCLA

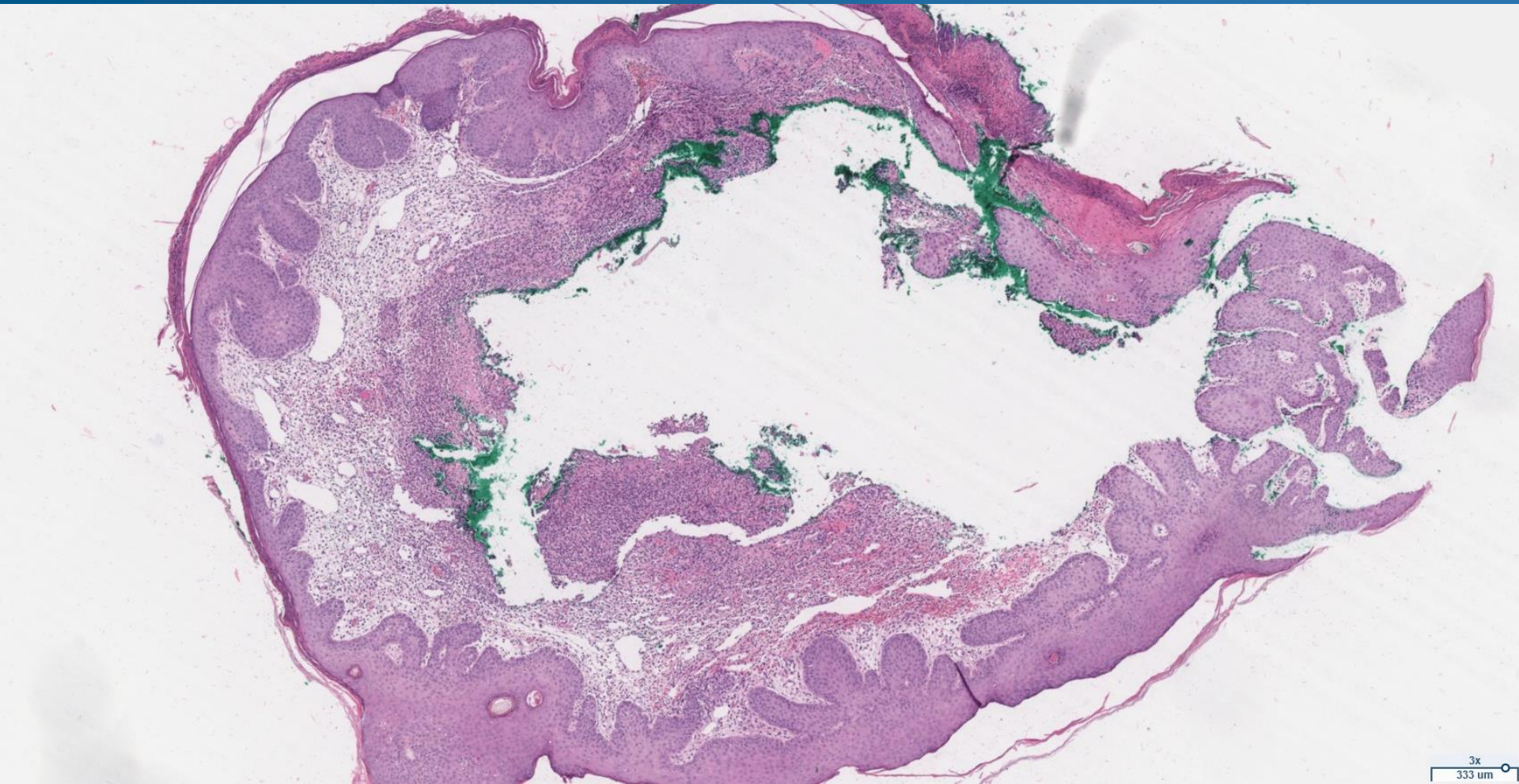
Case 3: “Rule out condyloma”

UCLA

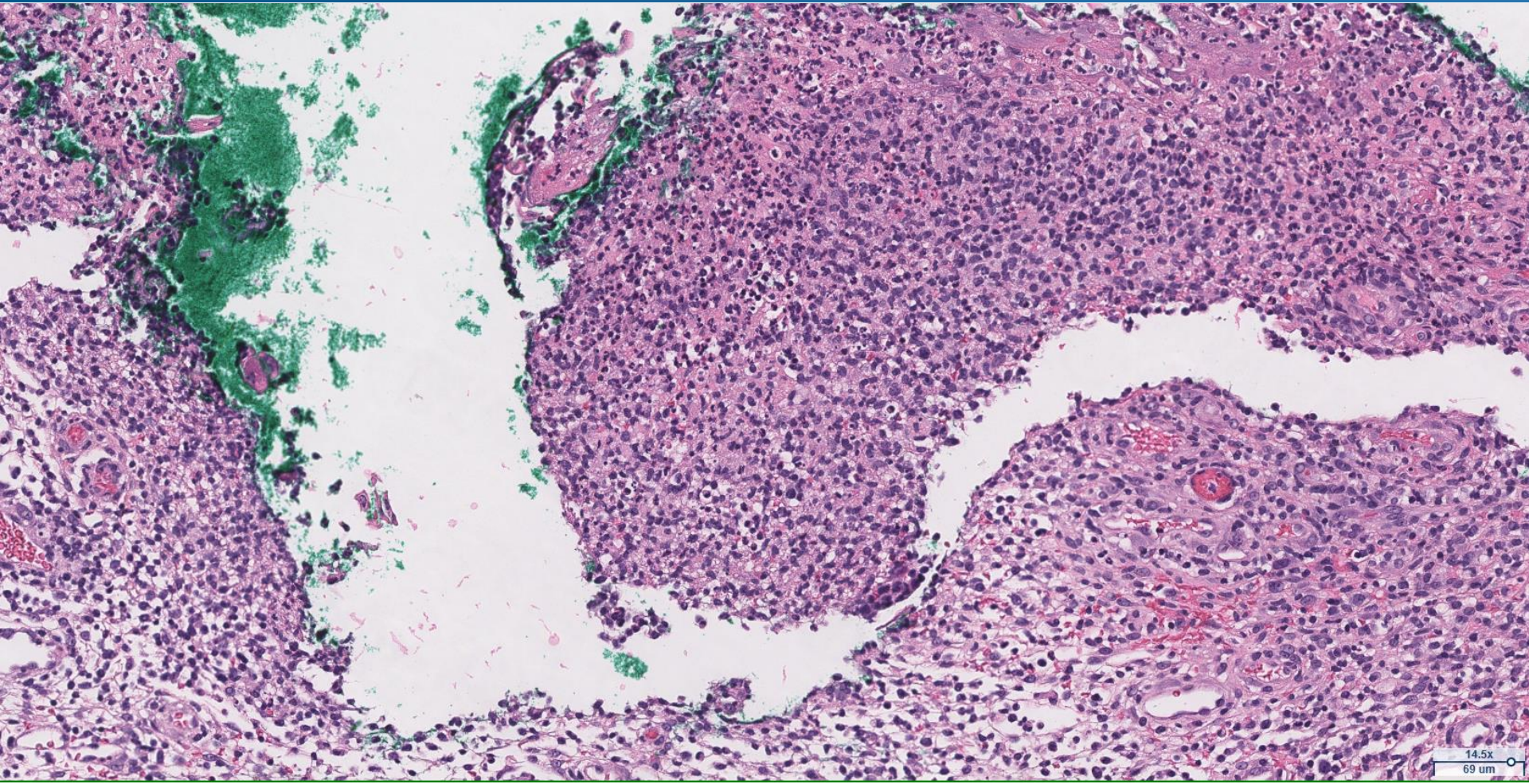
Low-grade SIL (LSIL)/VIN1



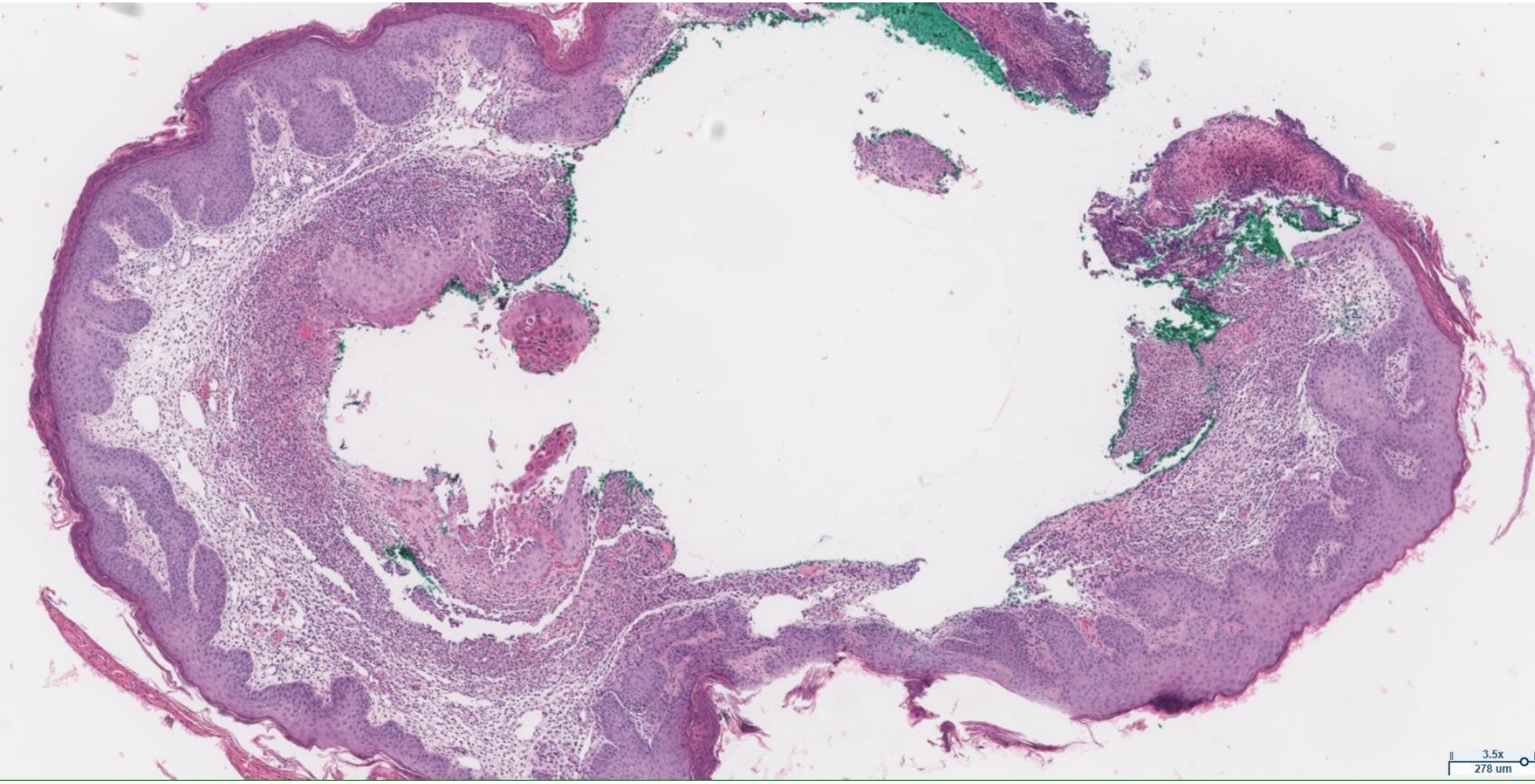
CASE 3-1



CASE 3-1

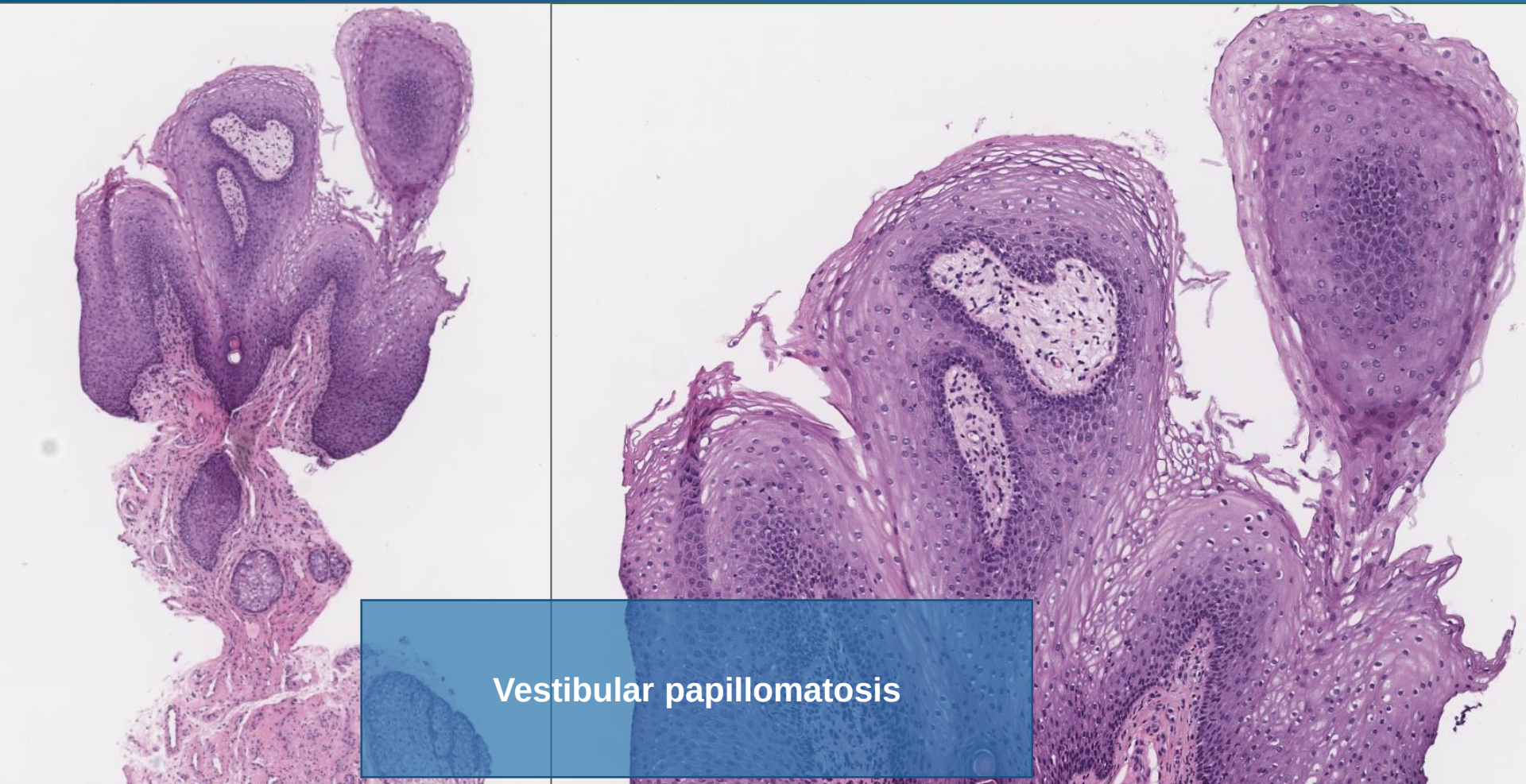


CASE 3-1



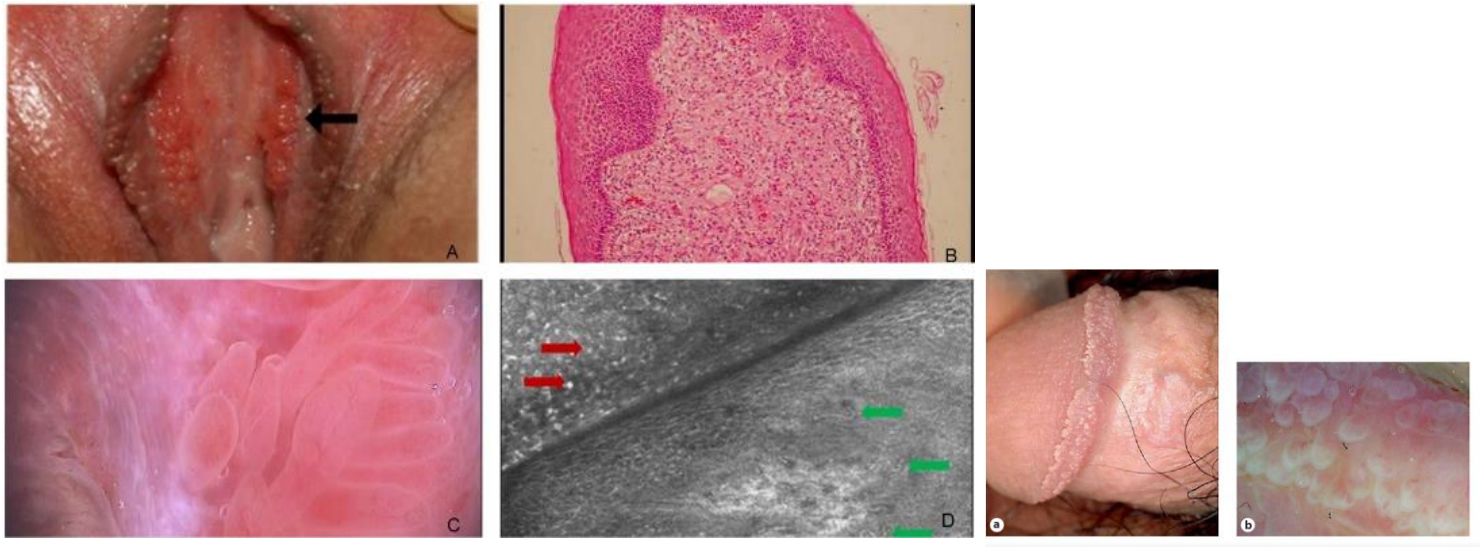

Molluscum contagiosum
12.5x
79 um

CASE 3-2: Labia minora/vestibular polypoid lesions, rule out condyloma



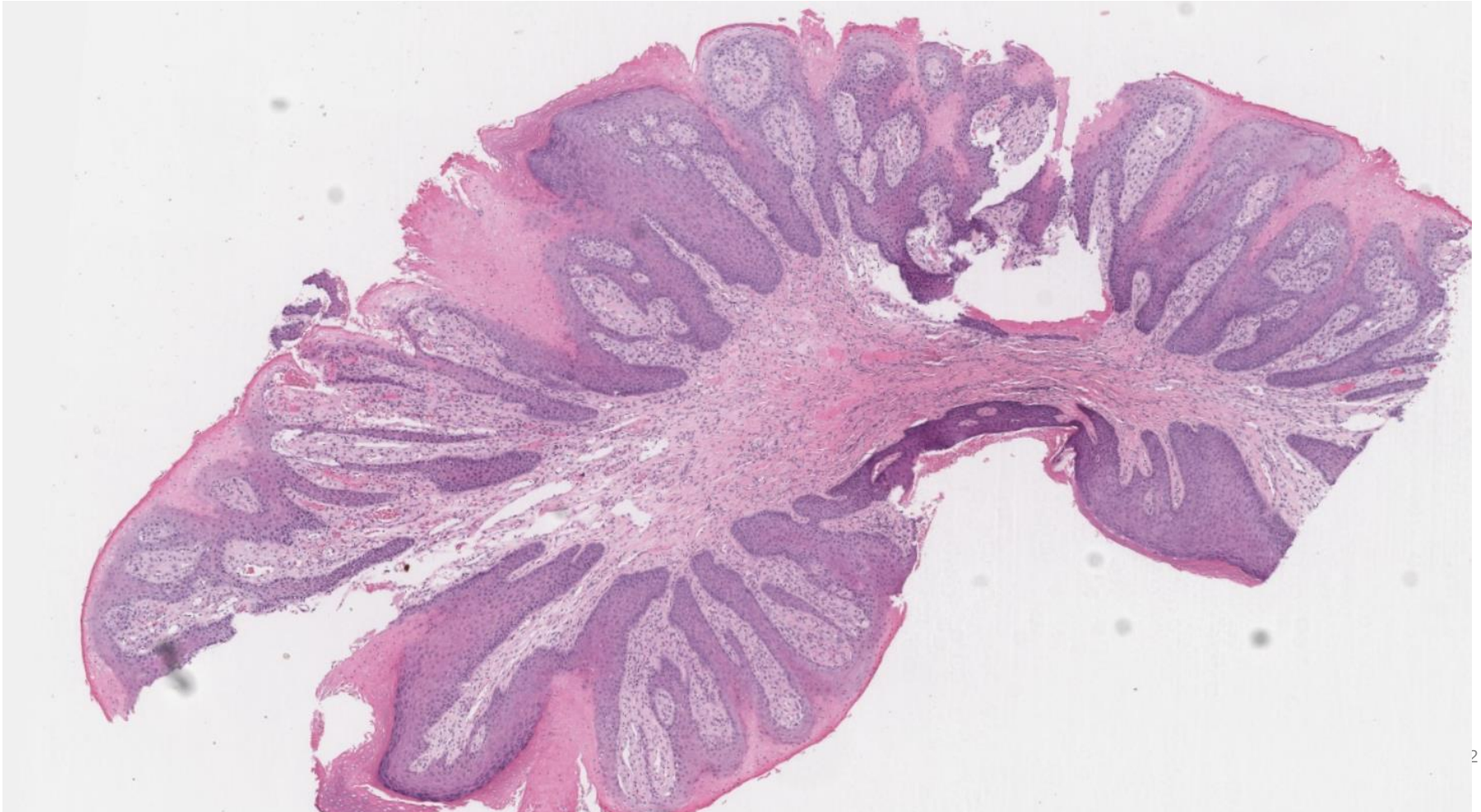
Vestibular papillomatosis

Vestibular papillomatosis

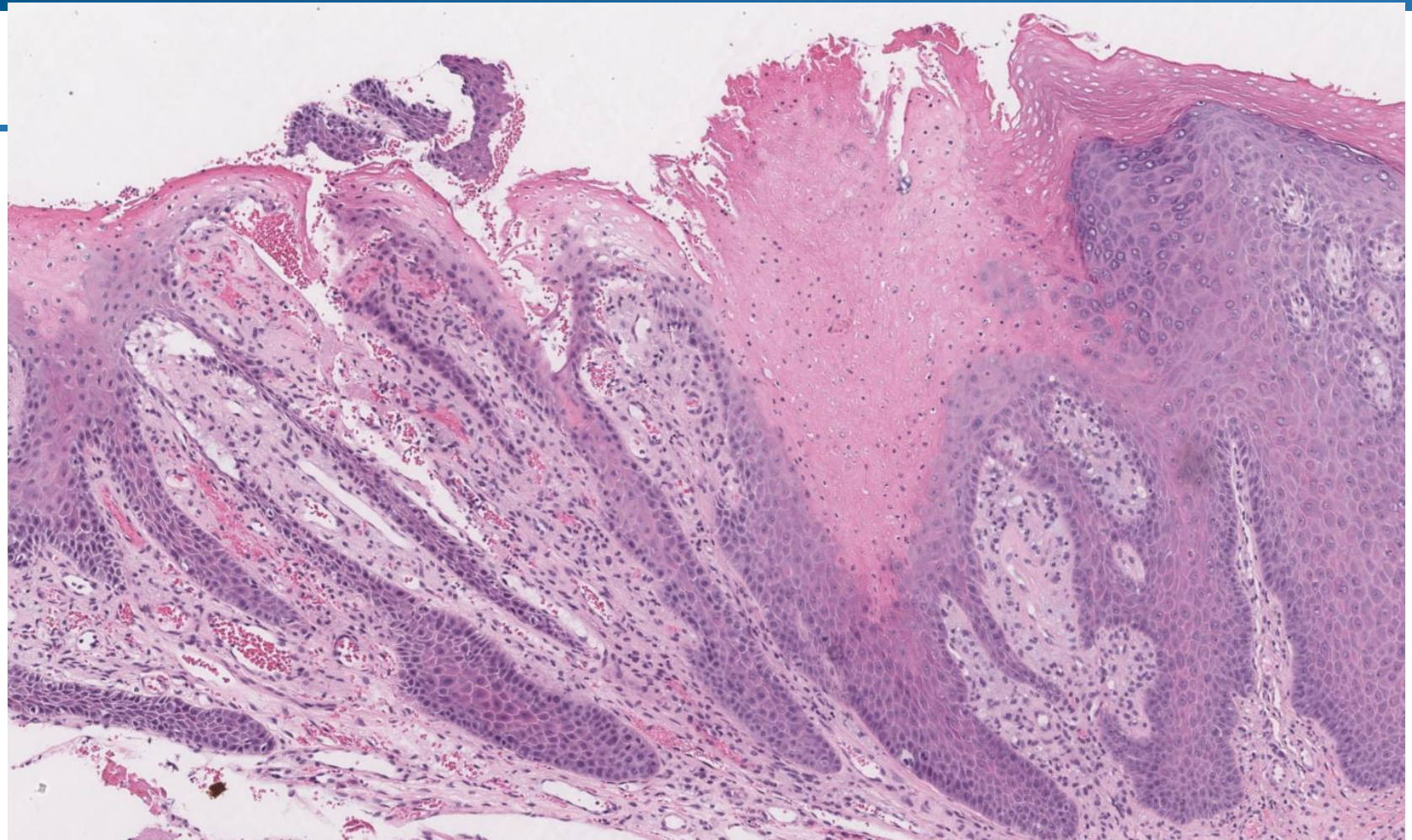


(L) Ozkur, et al. Dermatology online journal, 22(3) April 1, 2025 (R) Ozeki, M. et al. “Dermatology 217 (2008): 21 - 22.

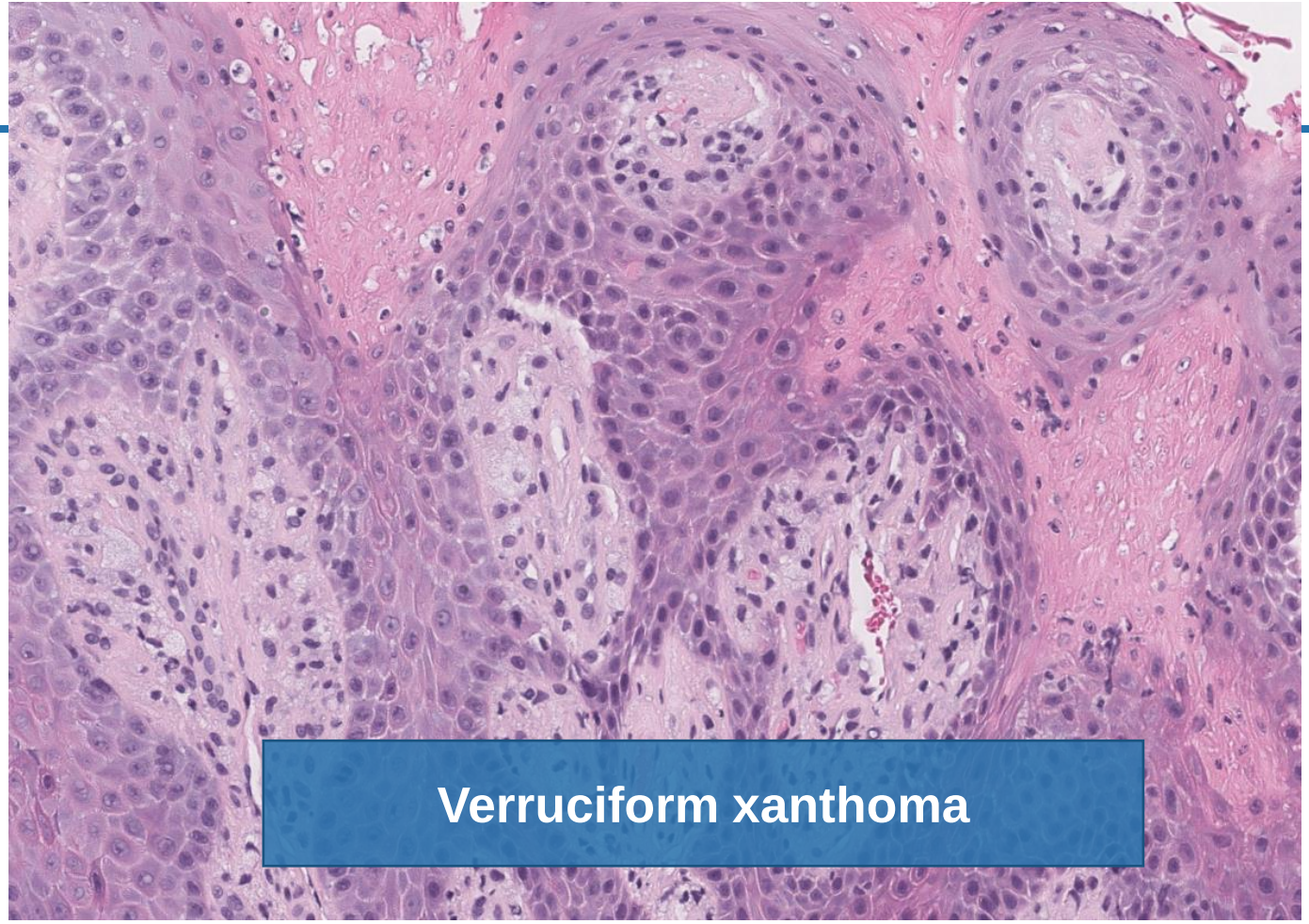
65F perineal mass, rule out condyloma



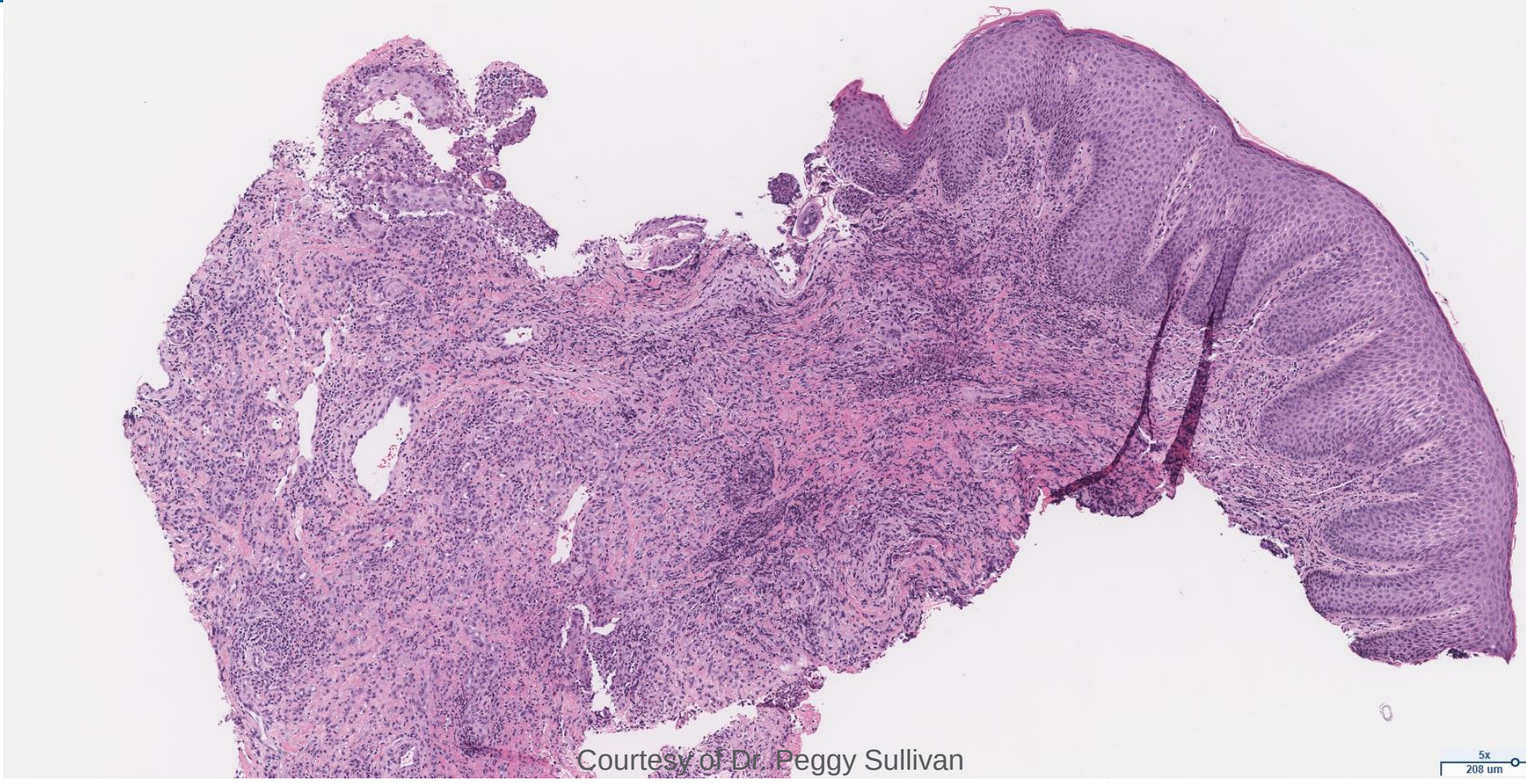
65F perineal mass, rule out condyloma



65F perineal mass, rule out condyloma

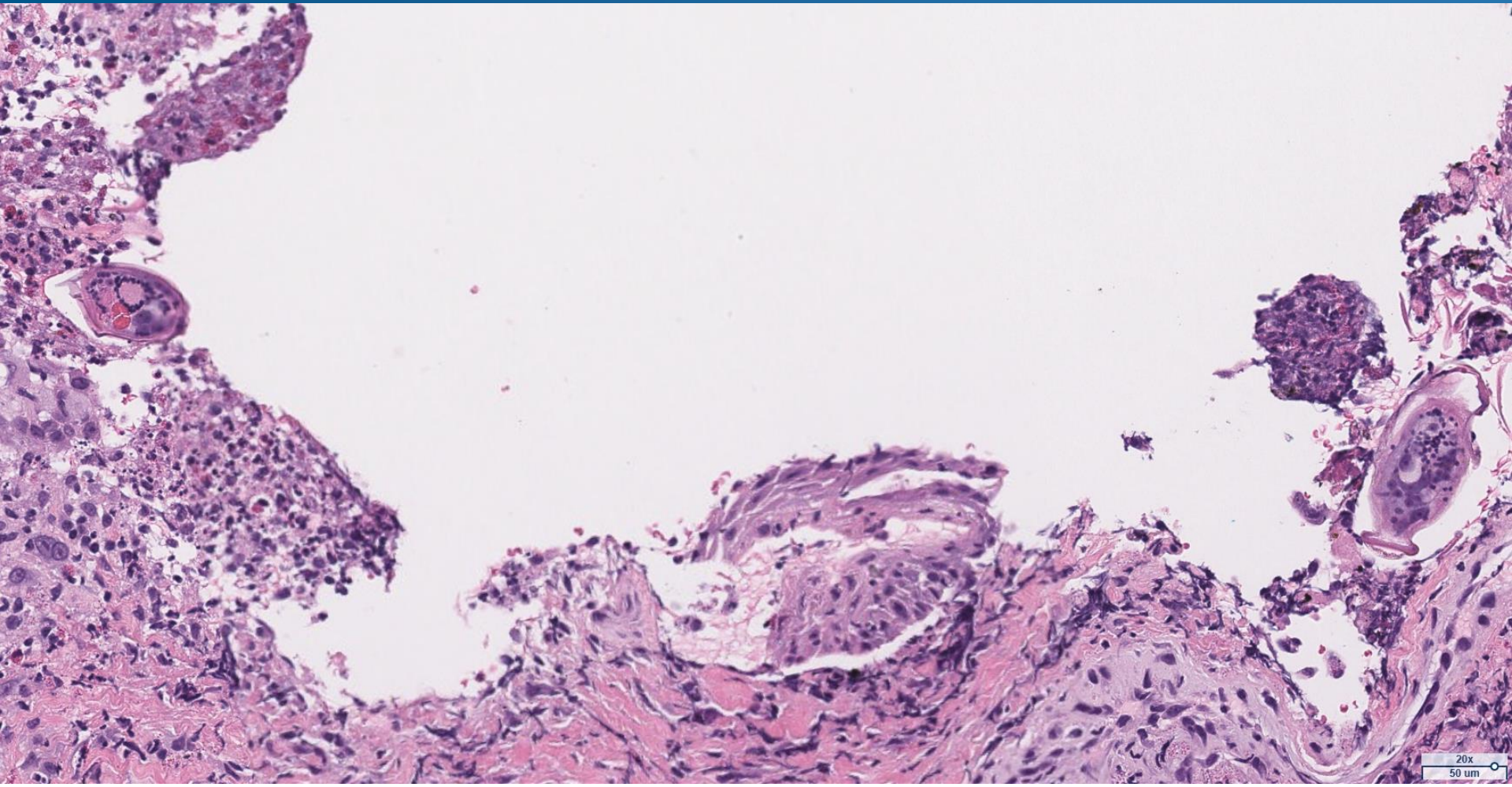


CASE 3-3: 2 cm vulvar mass, rule out condyloma

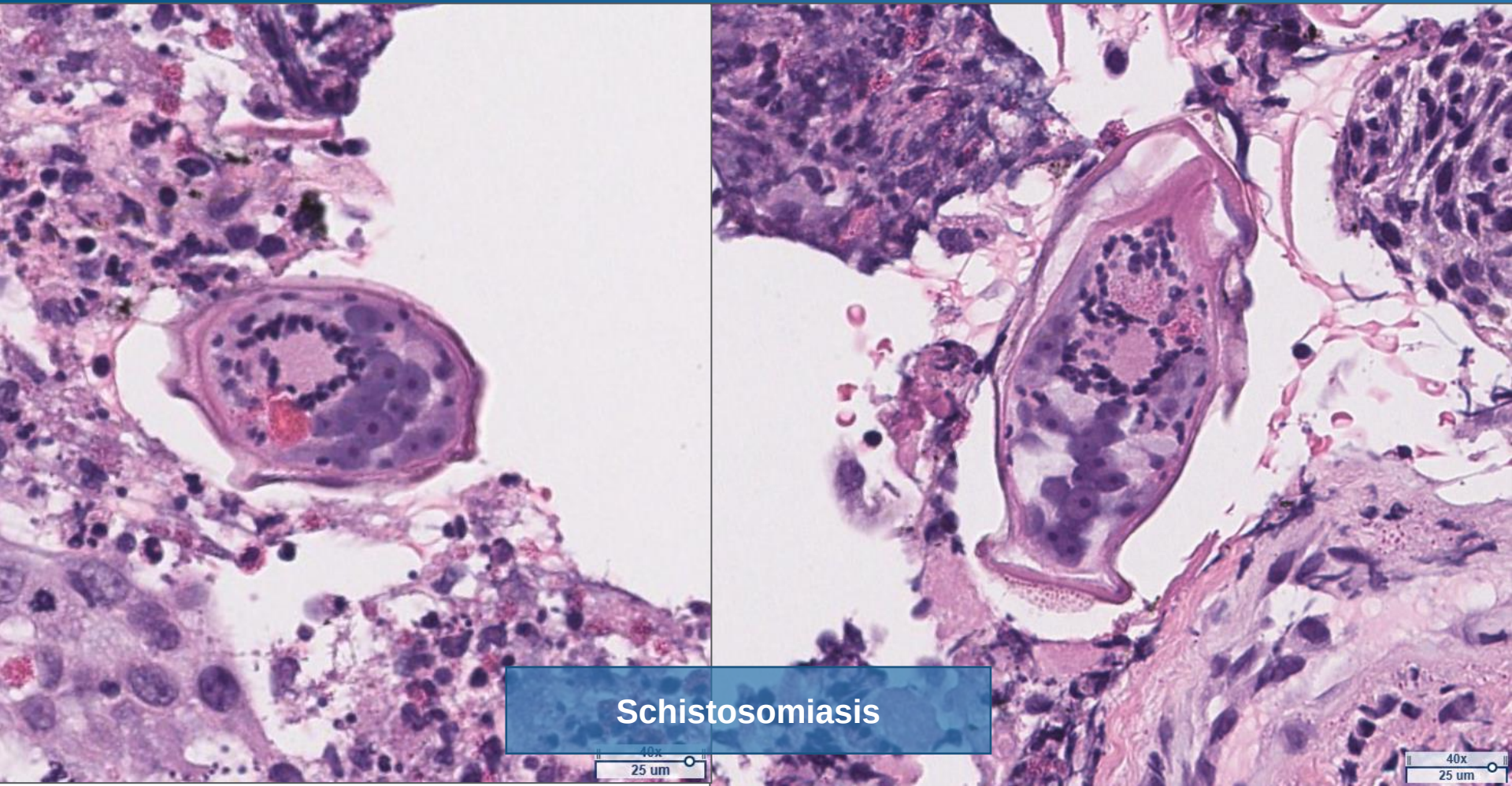


Courtesy of Dr. Peggy Sullivan

CASE 3-3: 2 cm vulvar mass, rule out condyloma



CASE 3-3: 2 cm vulvar mass, rule out condyloma



“Rule out condyloma”

BENIGN BUMPS DDX

- Folliculitis/epidermal inclusion cyst
- Molluscum
- Verruciform xanthoma
- Vestibular papillomatosis
- Angioma/ lymphangioma (circumscriptum)
- Sebaceous hyperplasia
- Other rare entities: parasites, cloacogenic remnants, etc.

Reference:

TAKE HOME POINTS

- **“ULCER” : Acute genital ulceration is a diagnosis of exclusion, and may occur following systemic infections (i.e. EBV, COVID) & COVID vaccine.**
- **“IRRITATION” : In “rule out LS” cases without prominent dermal sclerosis, it is helpful to correlate with site of involvement and look for the subtle clues of LS (superficial fibrosis, lymphocyte along the basal layer, follicular changes, entrapped lymphocytes in fibrotic dermis etc.)**
- **“RULE OUT CONDYLOMA”: Think about common anogenital “benign bumps”. Deeper sections may be necessary to find the diagnostic focus.**

Reference:

Reference: