Challenges in the Classification of Primary Cicatricial Alopecia

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CURTIS THOMPSON, MD & ASSOCIATES
SKIN, HAIR AND NAIL EXPERTS

SPECIAL REPORT

Summary of North American Hair Research Society (NAHRS)–sponsored Workshop on Cicatricial Alopecia, Duke University Medical Center, February 10 and 11, 2001

Elise A. Olsen, MD,[a] Wilma F. Bergfeld, MD,[b] George Cotsarelis, MD,[c] Vera H. Price, MD,[d] Jerry Shapiro, MD,[e] Rodney Sinclair, MD,[f] Alvin Solomon, MD,[g] Leonard Sperling, MD,[h] Kurt Stenn, MD,[i] David A. Whiting, MD,[j] and the members of the Workshop on Cicatricial Alopecia* *Durham, North Carolina; Cleveland, Ohio; Philadelphia, Pennsylvania; San Francisco, California; Vancouver, British Columbia; Melbourne, Australia; Atlanta, Georgia; Bethesda, Maryland; Skillman, New Jersey; and Dallas, Texas*

Year 2001

Proposed working classification of primary cicatricial alopecia

Lymphocytic

- Chronic cutaneous lupus erythematosus
- Lichen planopilaris (LPP)[4]
  - Classic LPP
  - Frontal fibrosing alopecia[5]
  - Graham-Little syndrome[3]
- Classic pseudopelade (Brocq)[6,7]
- Central centrifugal cicatricial alopecia[8]
- Alopecia mucinosa[3]
- Keratosis follicularis spinulosa decalvans[9]

Neutrophilic

- Folliculitis decalvans[3]
- Dissecting cellulitis/folliculitis[3] (*perifolliculitis abscedens et suffodiens*)

Mixed

- Folliculitis (acne) keloidalis[9]
- Folliculitis (acne) necrotica[3]
- Erosive pustular dermatosis[10]

Nonspecific

Probable changes to the current classification:

- Fibrosing alopecia in a pattern distribution (Added entity)
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Arch Dermatol. 1994 Jun;130(6):770-4.

Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution.

Kossard S[1].

Author information Papers

Erratum in
Arch Dermatol 1994 Nov;130(11):1407.

Abstract

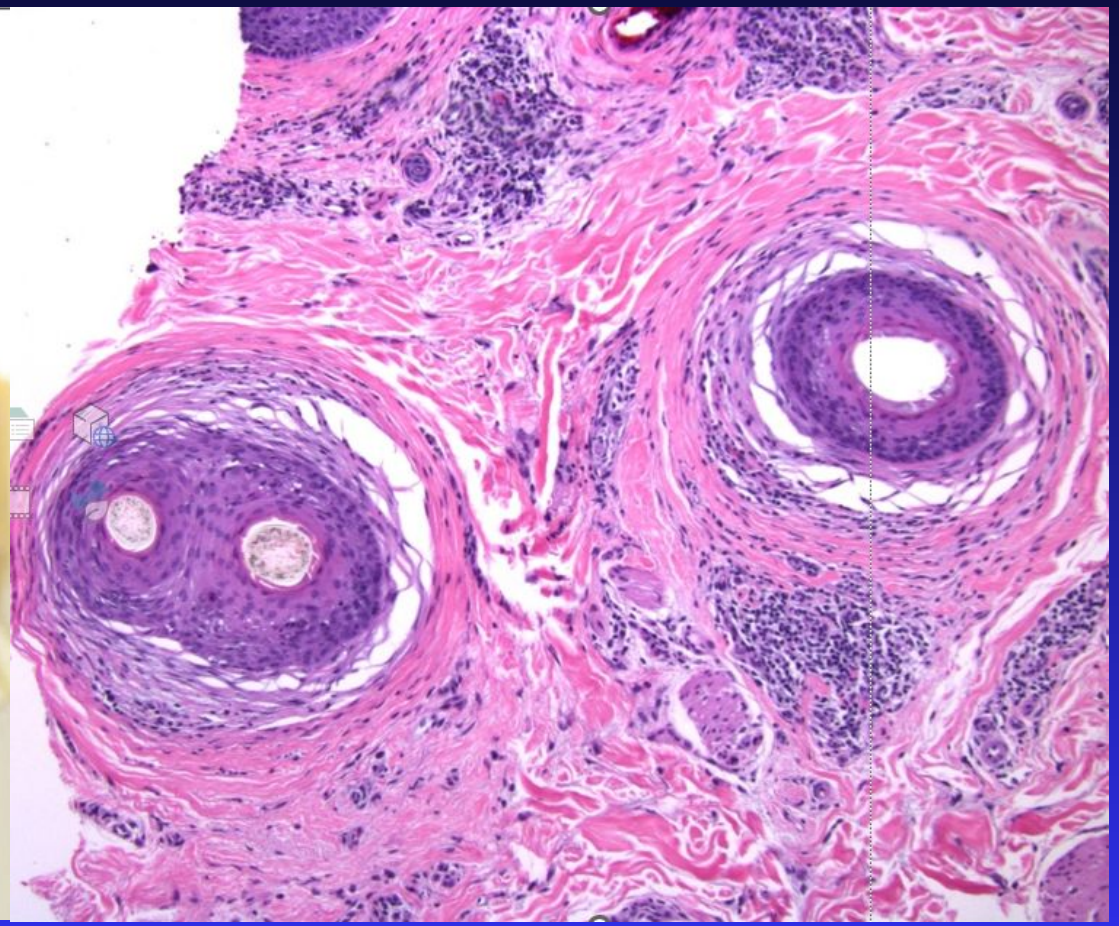
Fibrosing Alopecia in Pattern Distribution

FAPD

OBSERVATIONS: The six postmenopausal women developed a progressive frontal hairline recession that was associated with perifollicular erythema within the marginal hairline, producing a frontal fibrosing alopecia extending to the temporal and parietal hair margins. Scalp biopsy specimens from the frontal hair margin showed perifollicular fibrosis and lymphocytic inflammation concentrated around the isthmus and infundibular areas of the follicles. Immunophenotyping of the lymphocytes showed a dominance of activated T-helper cells. Clinical review of all six cases showed a progressive marginal alopecia without the typical multifocal areas of involvement seen in lichen planopilaris or pseudopelade. None of the patients had mucous membrane or skin lesions typical of lichen planus. Hormonal studies, in five patients, showed no elevated androgen abnormalities.

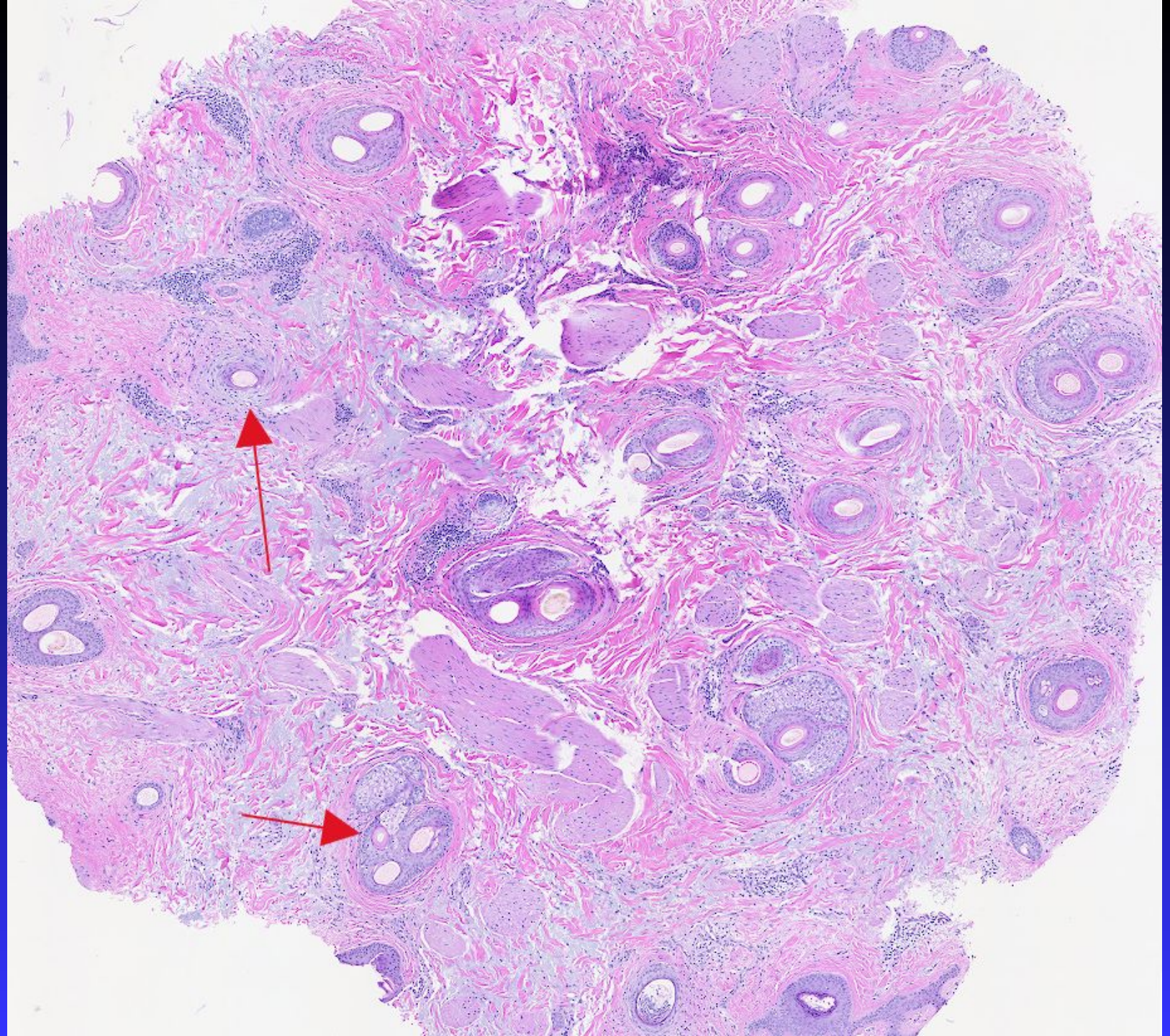
CONCLUSIONS: Progressive frontal recession in postmenopausal women may show clinical features of a fibrosing alopecia. The histologic findings are indistinguishable from those seen in lichen planopilaris. However, the absence of associated lesions of lichen planus in all six women raises the possibility that this mode of follicular destruction represents a reaction pattern triggered by the events underlying postmenopausal frontal hairline recession.

Fibrosing alopecia in a pattern distribution
FAPD



Fibrosing alopecia in a pattern distribution
FAPD

- Lichen Planopilaris (LPP) (Diffuse/pattern distribution)
- Subjacent pattern hair loss (PHL)
  - Androgenetic (<60 years)
  - Senescence (>60 years)



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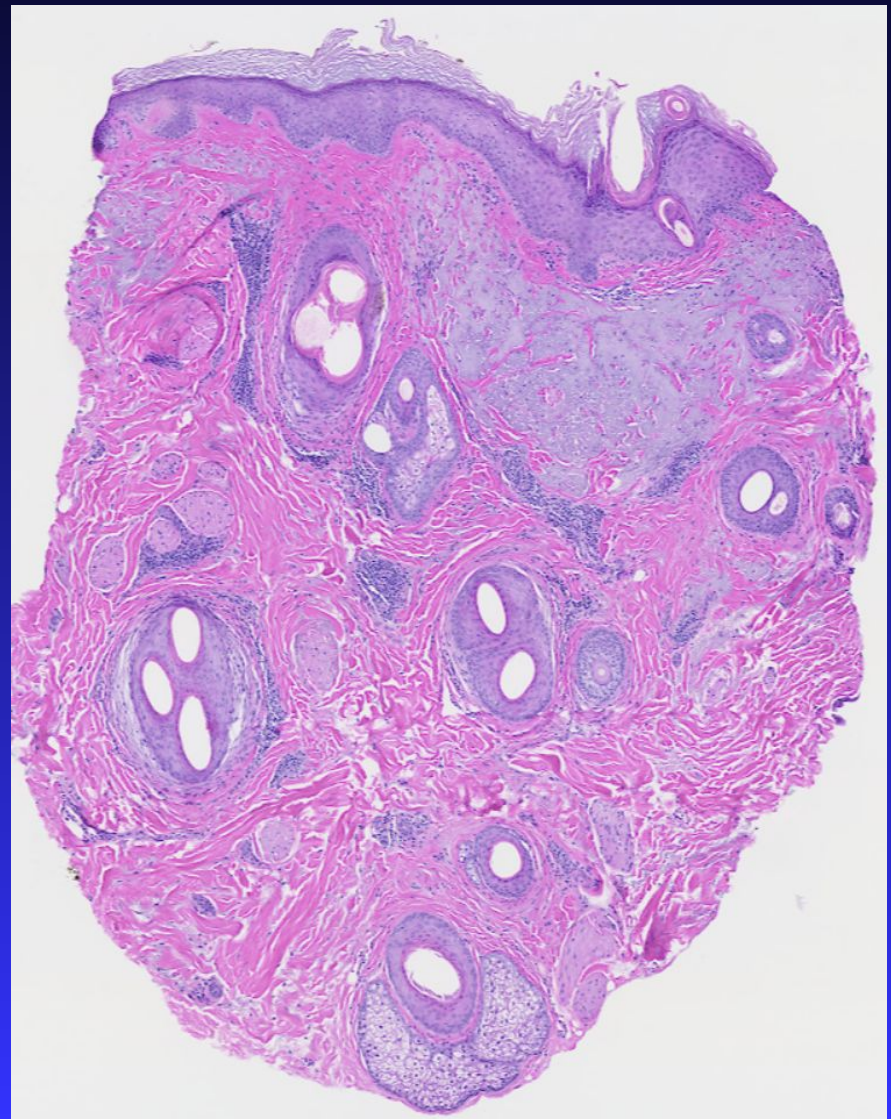
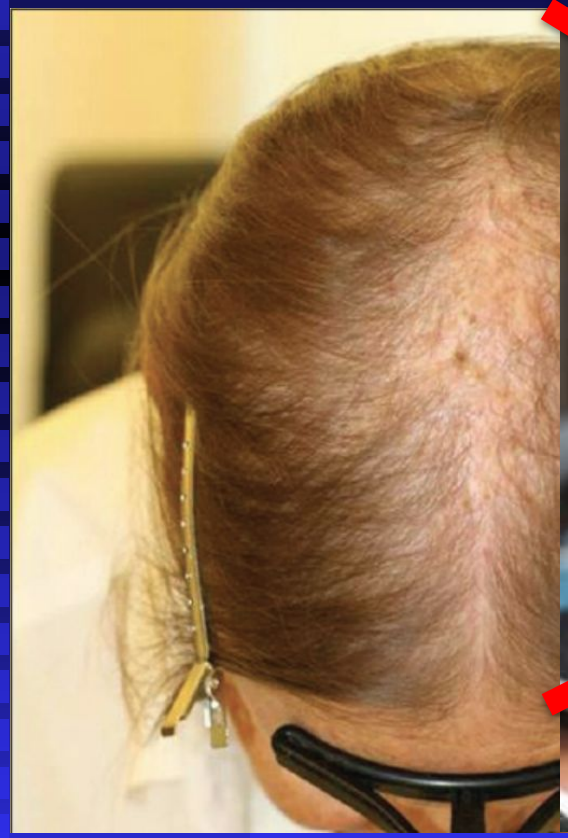
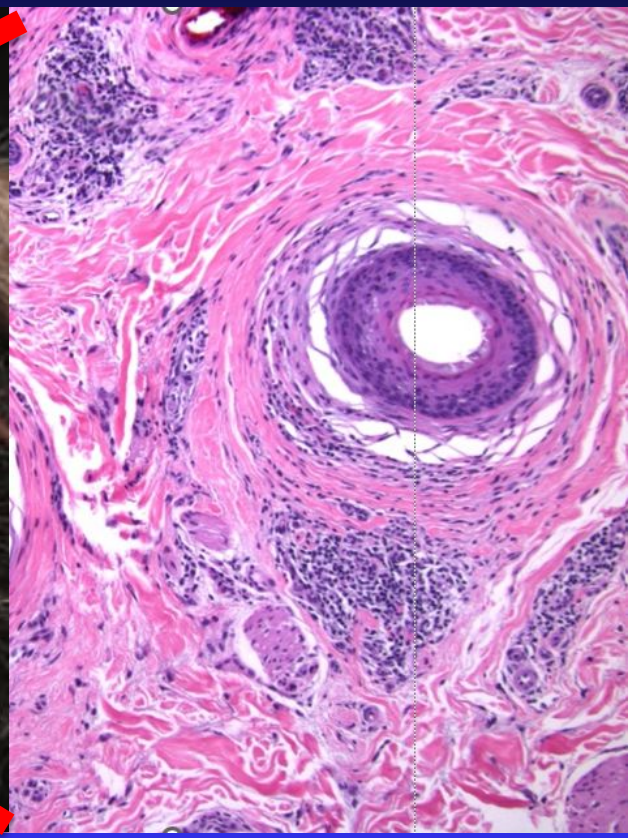
Fibrosing alopecia in a pattern distribution
FAPD

- Lichen planopilaris (LPP)
- Subjacent female pattern hair loss (PHL)



Fibrosing alopecia in a pattern distribution
FAPD





Hair root touch-up dye (home use powder)

5A/MEDIUM ASH BROWN

WATER, C12-15 PARETH-3, AMMONIUM HYDROXIDE, OLETH-10, DILINOLEIC ACID, COCAMIDE MEA, LINOLEAMIDOPROPYL DIMETHYLAMINE DIMER DILINOLEATE, STEARETH-21, BEHENTRIMONIUM CHLORIDE, POLYQUATERNIUM-22, SODIUM SULFATE, FRAGRANCE, RESORCINOL, ERYTHORBIC ACID, p-PHENYLENEDIAMINE, CARAMEL, p-AMINOPHENOL, m-AMINOPHENOL, IRON OXIDES, MICA, SODIUM SULFITE, N,N-BIS(2-HYDROXYETHYL)-p-PHENYLENEDIAMINE SULFATE, 1-NAPHTHOL, SODIUM METASILICATE, EDTA, SARGASSUM FILIPENDULA EXTRACT, HYPNEA MUSCIFORMIS EXTRACT, GELLIDIELA ACEROSA EXTRACT, TITANIUM DIOXIDE.

Product-use and FFA

Meta-Analysis > Arch Dermatol Res. 2023 Oct;315(8):2313-2331.
doi: 10.1007/s00403-023-02604-7. Epub 2023 Apr 4.

Frontal fibrosing alopecia and personal care product use: a systematic review and meta-analysis

Olivia Kam [1], Sean Na [2], William Guo [3], Christina I Tejeda [3], Tara Kaufmann [3]

Summary of 9 studies
1,248 patients with FFA
1,459 negative controls

FFA Association
(9 Studies)

- Sunscreen
  - 4.61 (men)
  - 2.74 (women)
- Facial moisturizer
  - 5.07 (men)
  - 1.58 (women)

Kam O, Na S, Guo W, Tejeda CI, Kaufmann T. Frontal fibrosing alopecia and personal care product use: a systematic review and meta-analysis. Arch Dermatol Res. 2023 Oct;315(8):2313-2331.

Sur

Mirmirani, P., & Vanderweil, S. G. (2020). Frontal fibrosing alopecia with involvement of the central hair part: distribution of hair loss corresponding to areas of sunscreen application. *Dermatology Online Journal*, 26(11).

No association with FFA

- Cleanser, facial tonic, aftershave
- Foundation make-up
- Shampoo, conditioner, gel, dye, hair remover, shaving cream

Kam O, Na S, Guo W, Tejeda CI, Kaufmann T. Frontal fibrosing alopecia and personal care product use: a systematic review and meta-analysis. Arch Dermatol Res. 2023 Oct;315(8):2313-2331.

Meta-Analysis > JAMA Dermatol. 2025 Mar 1;161(3):310-314.
doi: 10.1001/jamadermatol.2024.6434.

Epistasis of ERAP1 With 4 Major Histocompatibility Complex Class I Alleles in Frontal Fibrosing Alopecia: A Genome-Wide Association Study Meta-Analysis

- 6668 patients
  - 1585 FFA (European females)
  - 5083 controls

Genetic predisposition for FFA

- Genome-wide significant associations at 4 genomic loci
  - HLA-A*11:01, HLA-A*33:01, HLA-B*07:02, and HLA-B*35:01.
  - ERAP1 gene mutation at 5q15

Rayinda T, Dand N, McSweeney SM, Christou E, Ung CY, Stefanato CM, Fenton DA, Harries M, Palamaras I, Tidman A, Holmes S, Koutalopoulou A, Ardern-Jones M, Kaur M, Papanikou S, Chasapi V, Vañó-Galvan S, Saceda-Corralo D, Melián-Olivera A, Azcarraga-Llobet C, Lobato-Berezo A, Bustamante M, Sunyer J, Starace MVR, Piraccini BM, Wiss IP, Senna MM, Singh R, Hillmann K, Kanti-Schmidt V, Blume-Peytavi U, McGrath JA, Simpson MA, Tziotzios C. Epistasis of ERAP1 With 4 Major Histocompatibility Complex Class I Alleles in Frontal Fibrosing Alopecia: A Genome-Wide Association Study Meta-Analysis. JAMA Dermatol. 2025 Mar 1;161(3):310-314.

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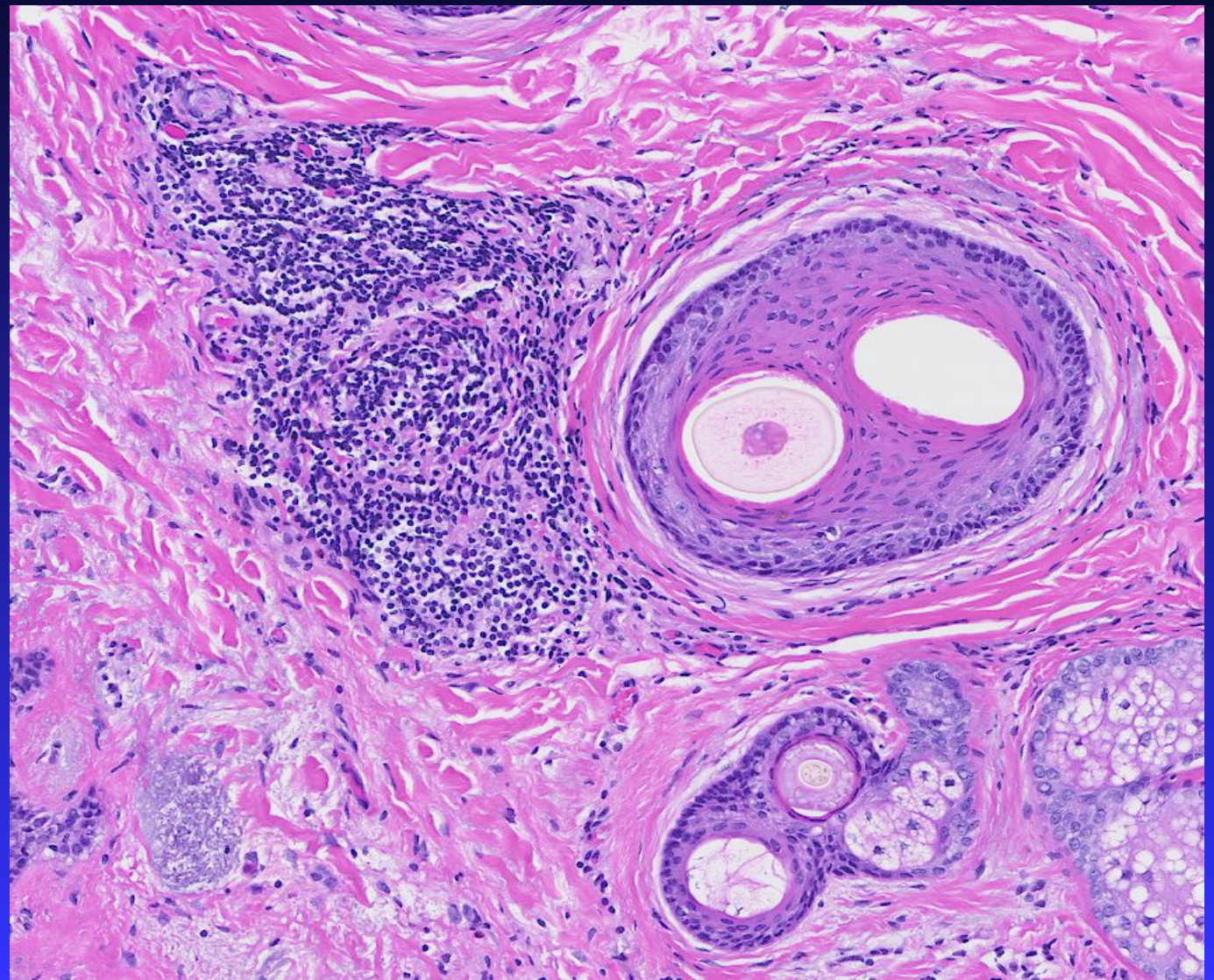
Pseudopelade of Brocq

Pseudopelade of Brocq



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LPP versus CCCA

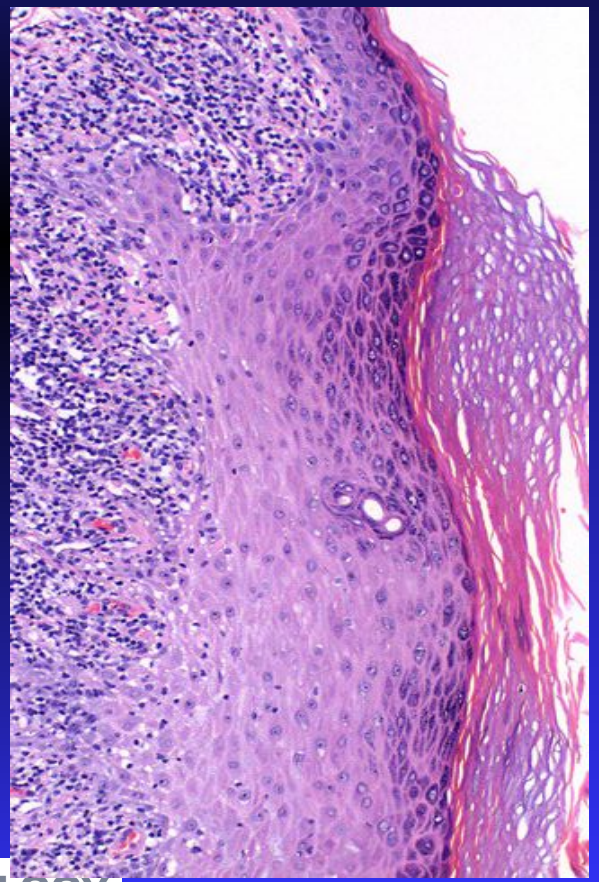
The Question:

Are LPP and CCCA related histopathologically?

Premature desquamation of the inner root sheath (PDIRS)

=

PDIRS exists in both CCCA and LPP



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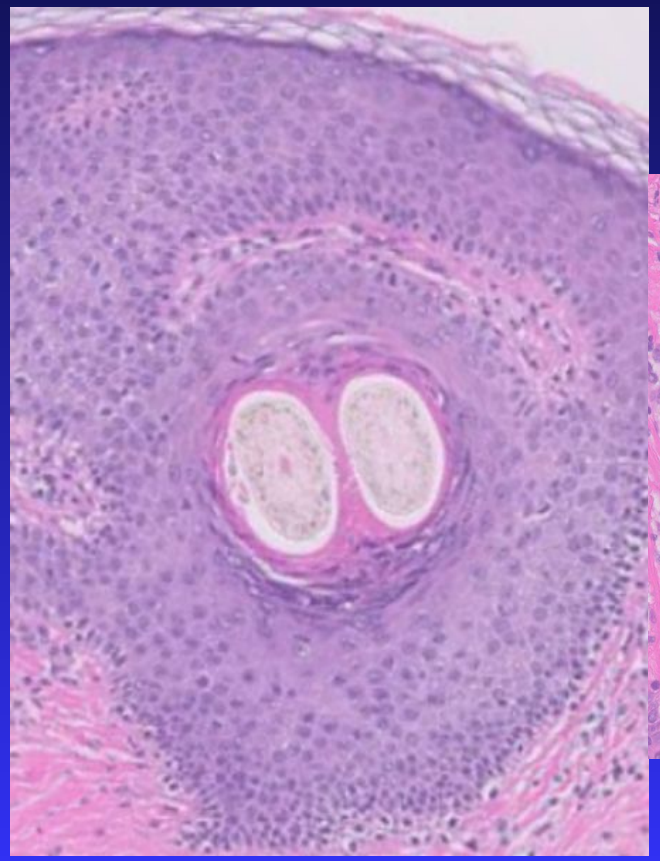

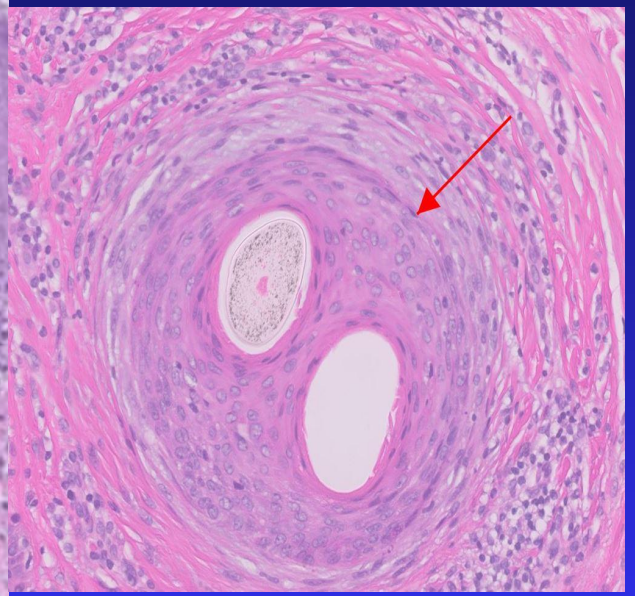

Premature Desquamation of the Inner Root Sheath in Noninflamed Hair Follicles as a Specific Marker for Central Centrifugal Cicatricial Alopecia

Timothy Tan, DO, Joan Guitart, MD,†‡ Pedram Gerami, MD,†‡ and Pedram Yazdan, MD†*

TABLE 2. Cases of PDIRS in Inflamed and Noninflamed Hair Follicles

Type of Alopecia	Total Cases With PDIRS, n	Cases With PDIRS in Inflamed Follicles, n (%)	Cases with PDIRS in Noninflamed Follicles, n (%)
Cicatricial alopecia			
CCCA	111	30 (27)	81 (73)
LPP	44	44 (100)	0 (0)
DLE	3	3 (100)	0 (0)
AKN	1	1 (100)	0 (0)
FD	24	21 (87)	3 (13)
Noncicatricial alopecia			
AGA	1	0 (0)	1 (100)
AA	1	1 (100)	0 (0)
PsA	2	0 (0)	2 (100)

Tan T, Guitart J, Gerami P, Yazdan P. Premature Desquamation of the Inner Root Sheath in Noninflamed Hair Follicles as a Specific Marker for Central Centrifugal Cicatricial Alopecia. Am J Dermatopathol. 2019 May;41(5):350-354..

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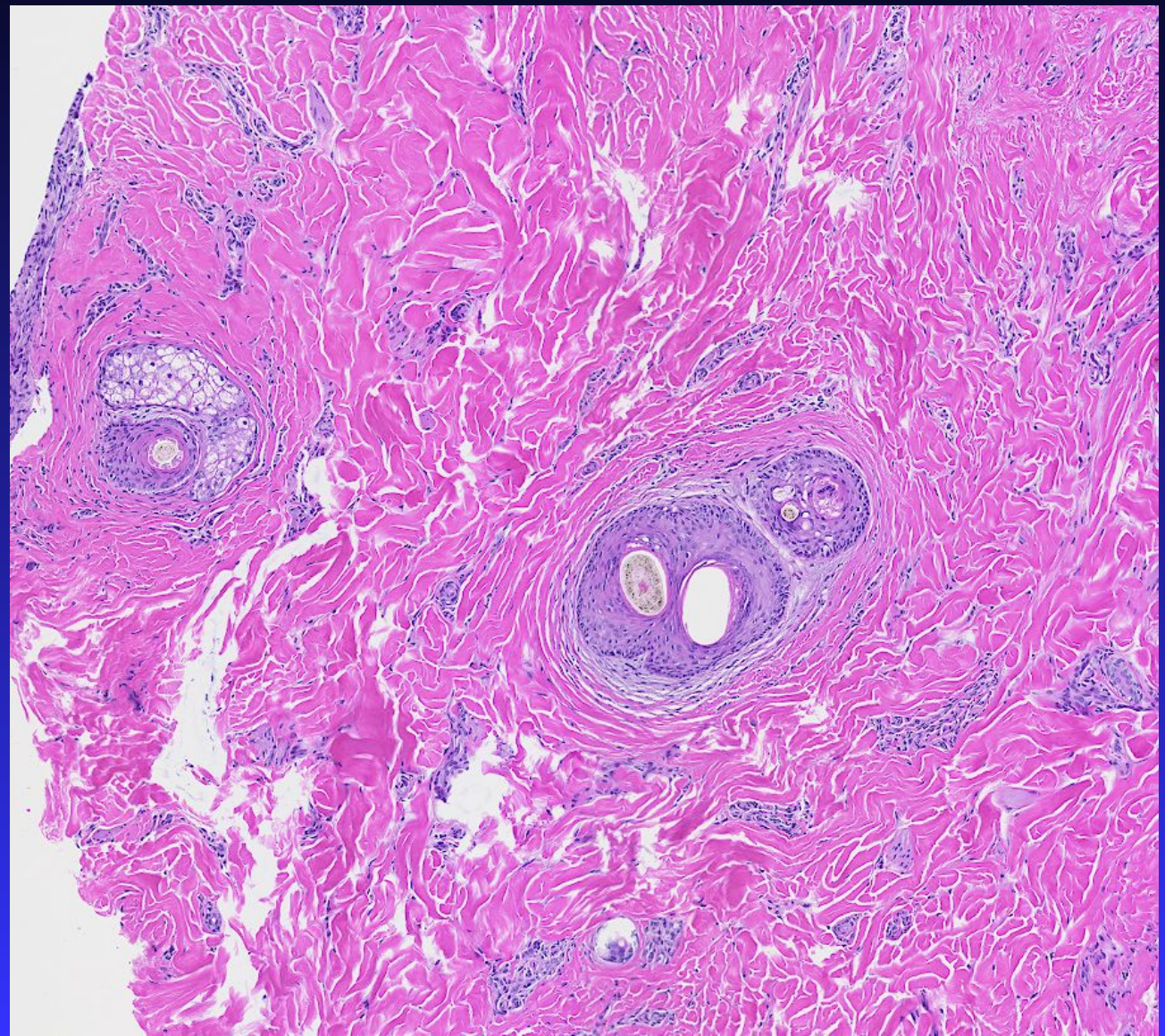
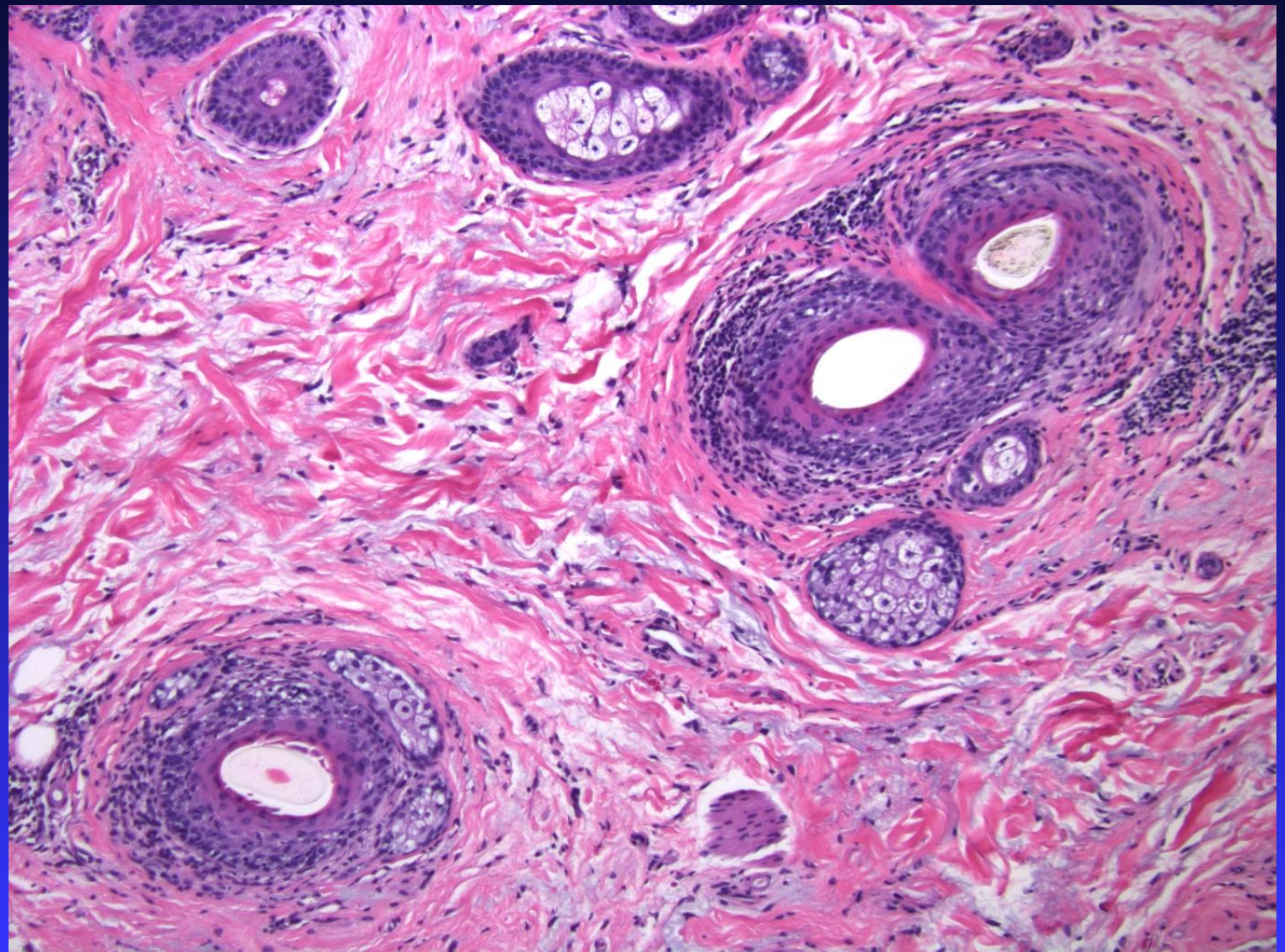
CCCA has perifollicular mucinous fibroplasia (scarring) without inflammation and LPP does not

Tan T, Guitart J, Gerami P, Yazdan P. Premature Desquamation of the Inner Root Sheath in Noninflamed Hair Follicles as a Specific Marker for Central Centrifugal Cicatricial Alopecia. Am J Dermatopathol. 2019 May;41(5):350-354..

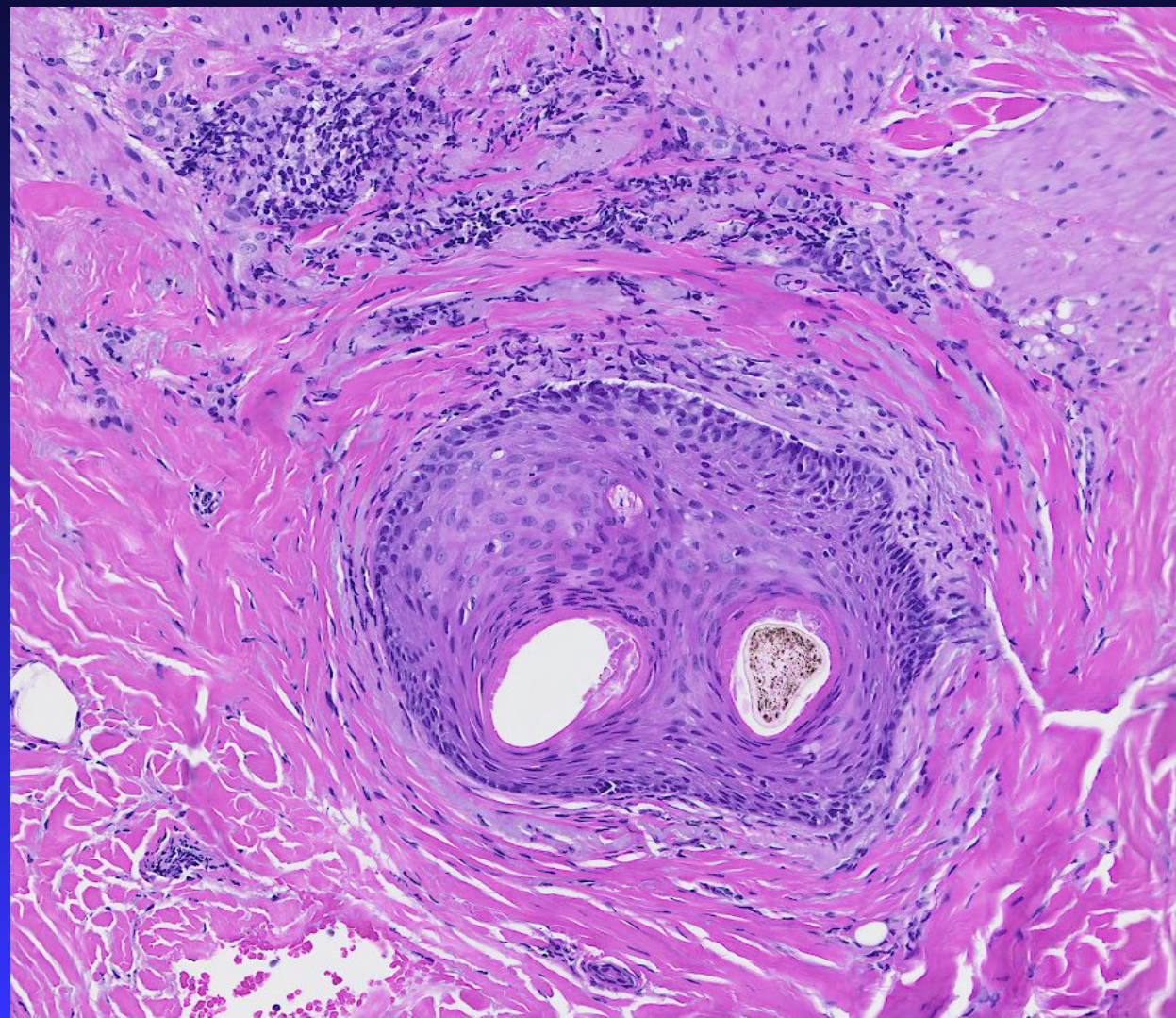
Central centrifugal cicatricial alopecia (CCCA)



In LPP, there is basilar involvement with intraepithelial lymphocytes.



CCCA—Eccentric follicular atrophy



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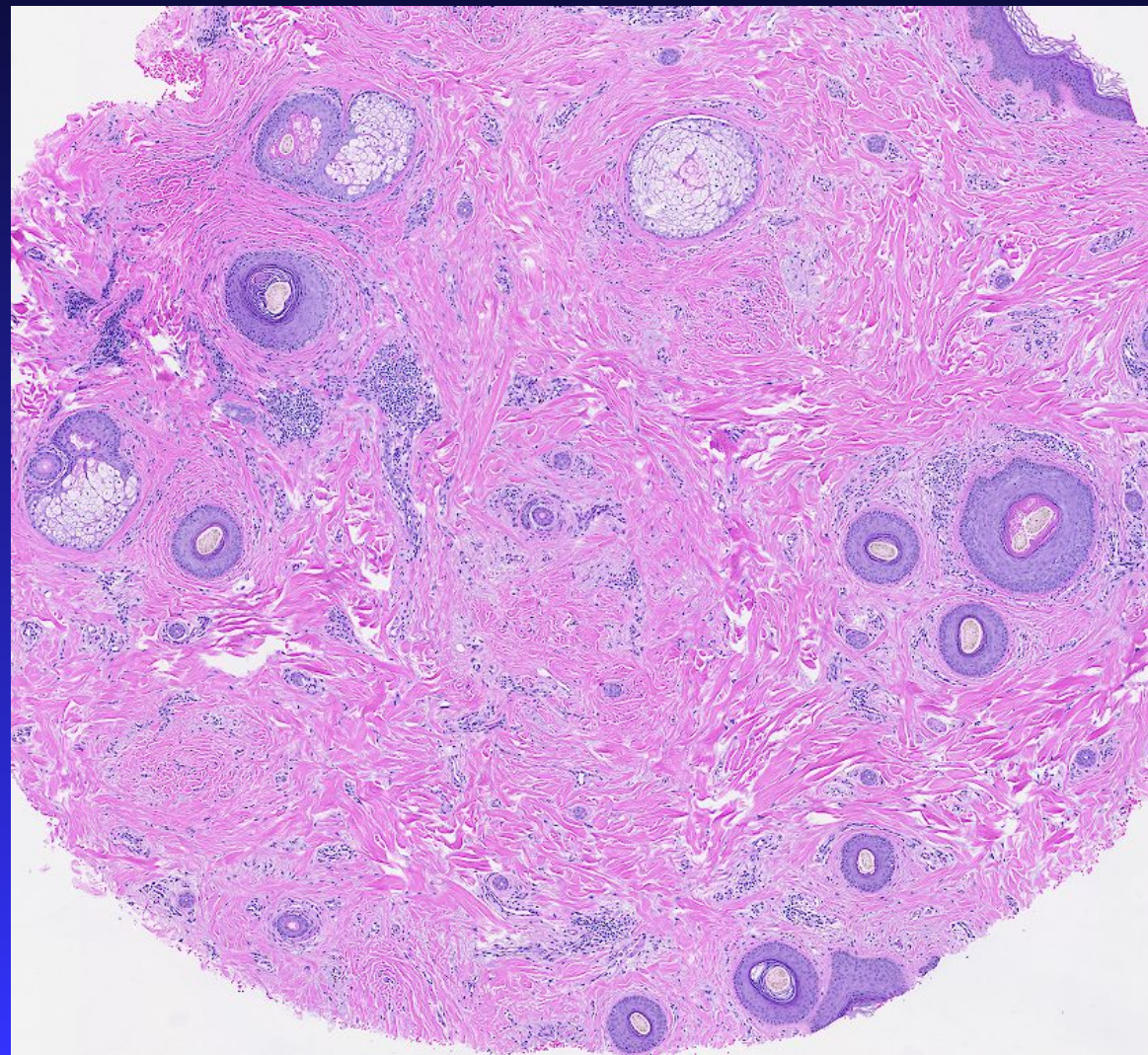
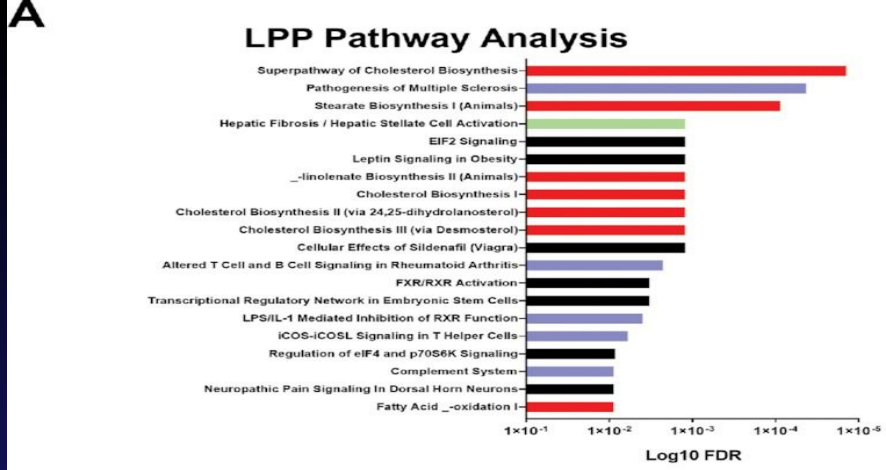
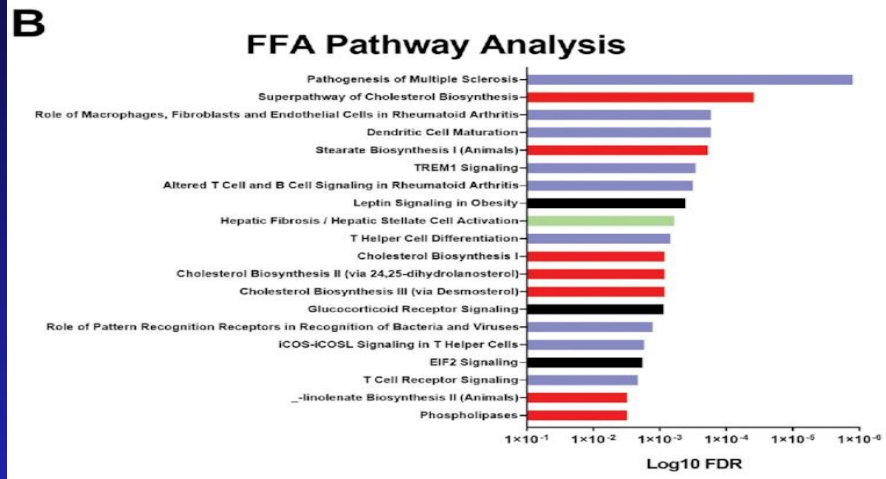
Central centrifugal cicatricial alopecia (CCCA)

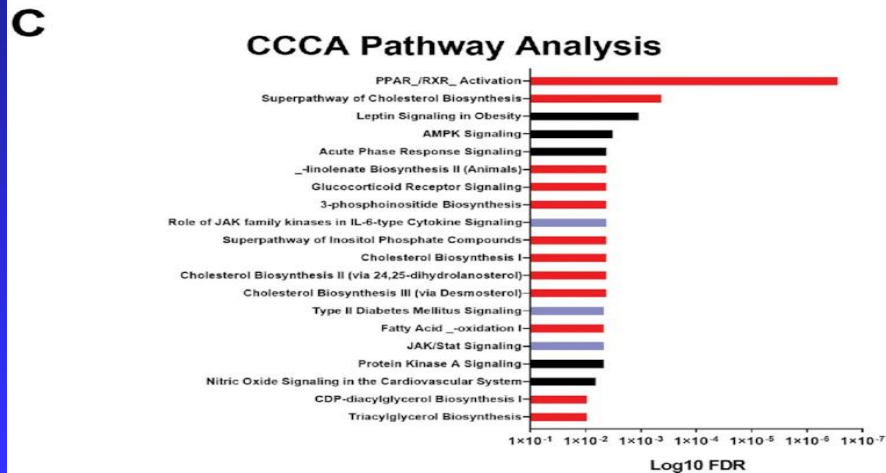
- Less inflammation
- More end-stage than LPP
- African descent



Shared dysregulated pathways in cholesterol biosynthesis and ...







Eddy H C Wang, Isha Monga, Brigitte N Sallee, James C Chen, Alexa R Abdelaziz, Rolando Perez-Lorenzo, Lindsey A Bordone, Angela M Christiano, Primary cicatricial alopecias are characterized by dysregulation of shared gene expression pathways, *PNAS Nexus*, Volume 1, Issue 3, July 2022, pgac111.

LPP versus CCCA

- Experience from Dr. Ngoza Dlova who specializes in hair loss in patients of African descent:
  - Important to confirm the presence of the primary cicatricial (scarring) alopecia;
  - Rule-out other causes (T. capitis, AA, etc.)
  - **There are 3 clinical presentations:**
    - **CCCA**
    - **LPP**
    - **CCCA/LPP indeterminate**

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- Describe Early- and Late-stage phases of the entities

Eliminating entities which are not primary cicatricial (scarring) alopecias

- Congenital
  - Keratosis follicularis spinulosa decalvans
- Aging/sun damage
  - Erosive pustular dermatosis of the scalp
- Acneiform
  - Folliculitis (acne) necrotica
- Lymphoproliferative disorders
  - Alopecia mucinosa (follicular mucinosis)

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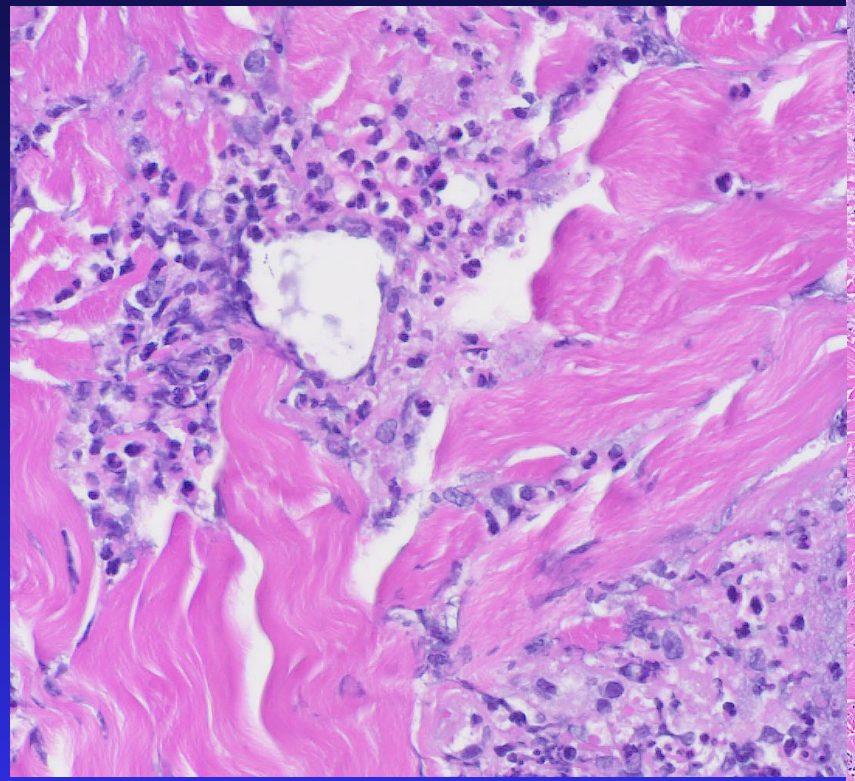
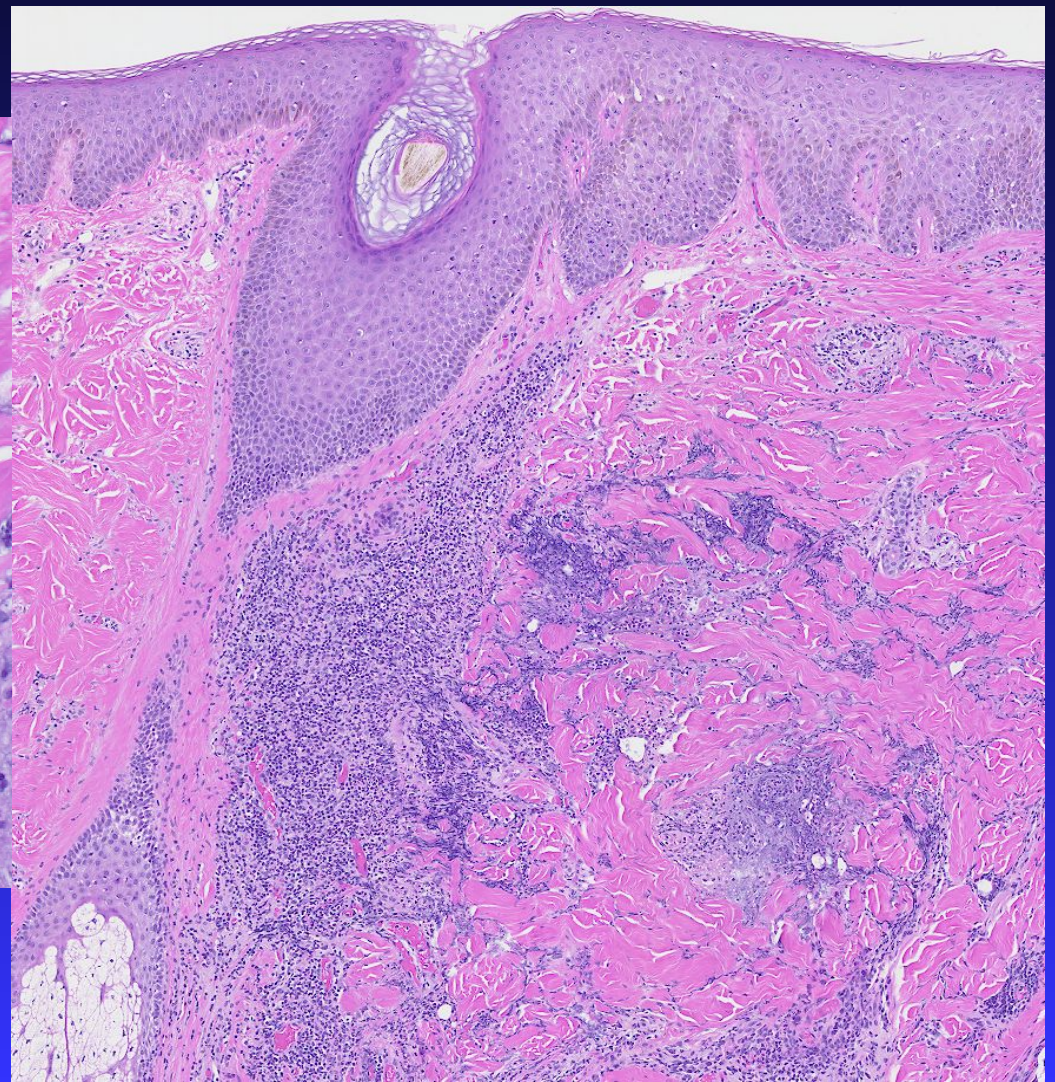
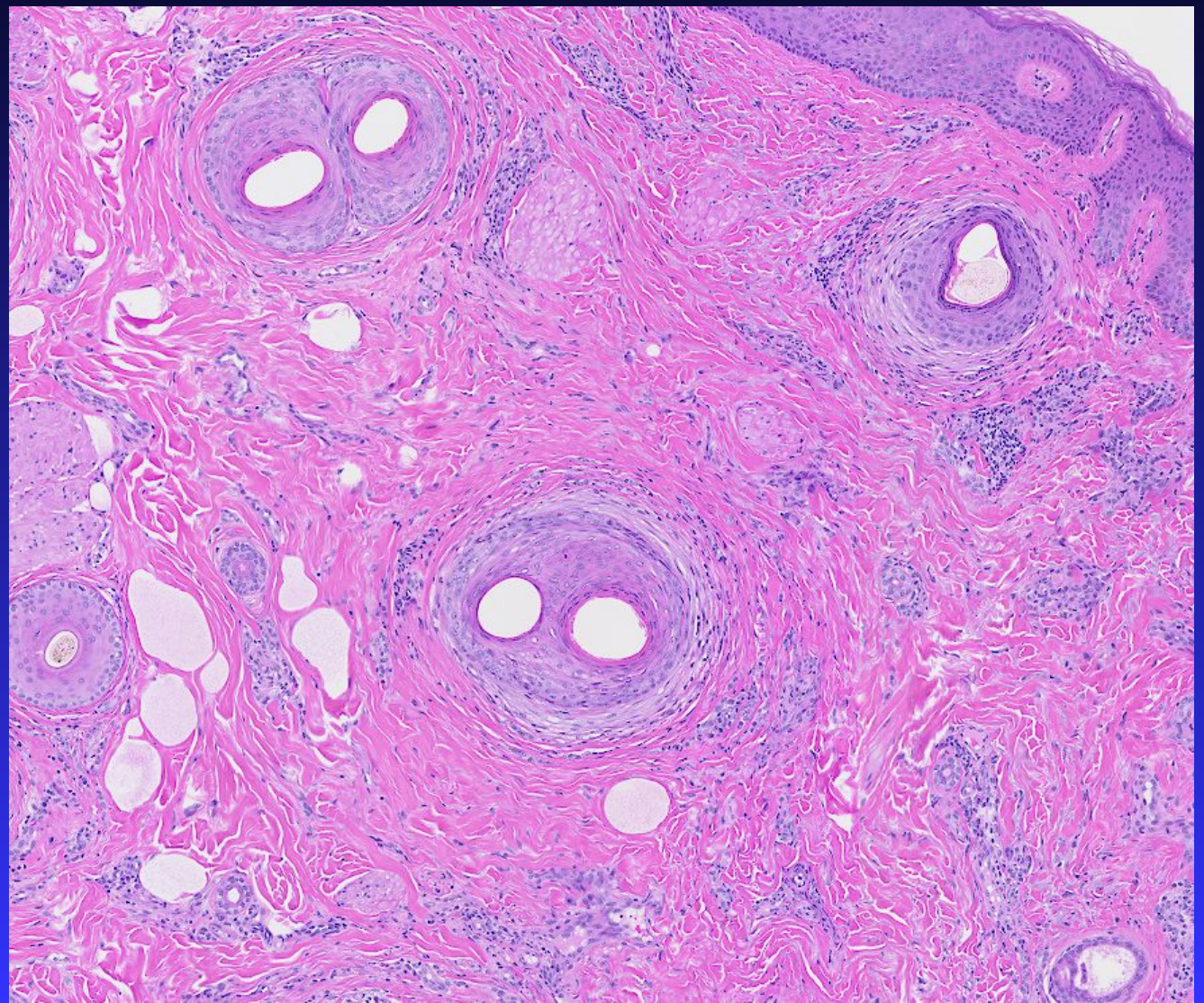
Foliculitis decalvans
Early stage or pustular lesion--neutrophilic

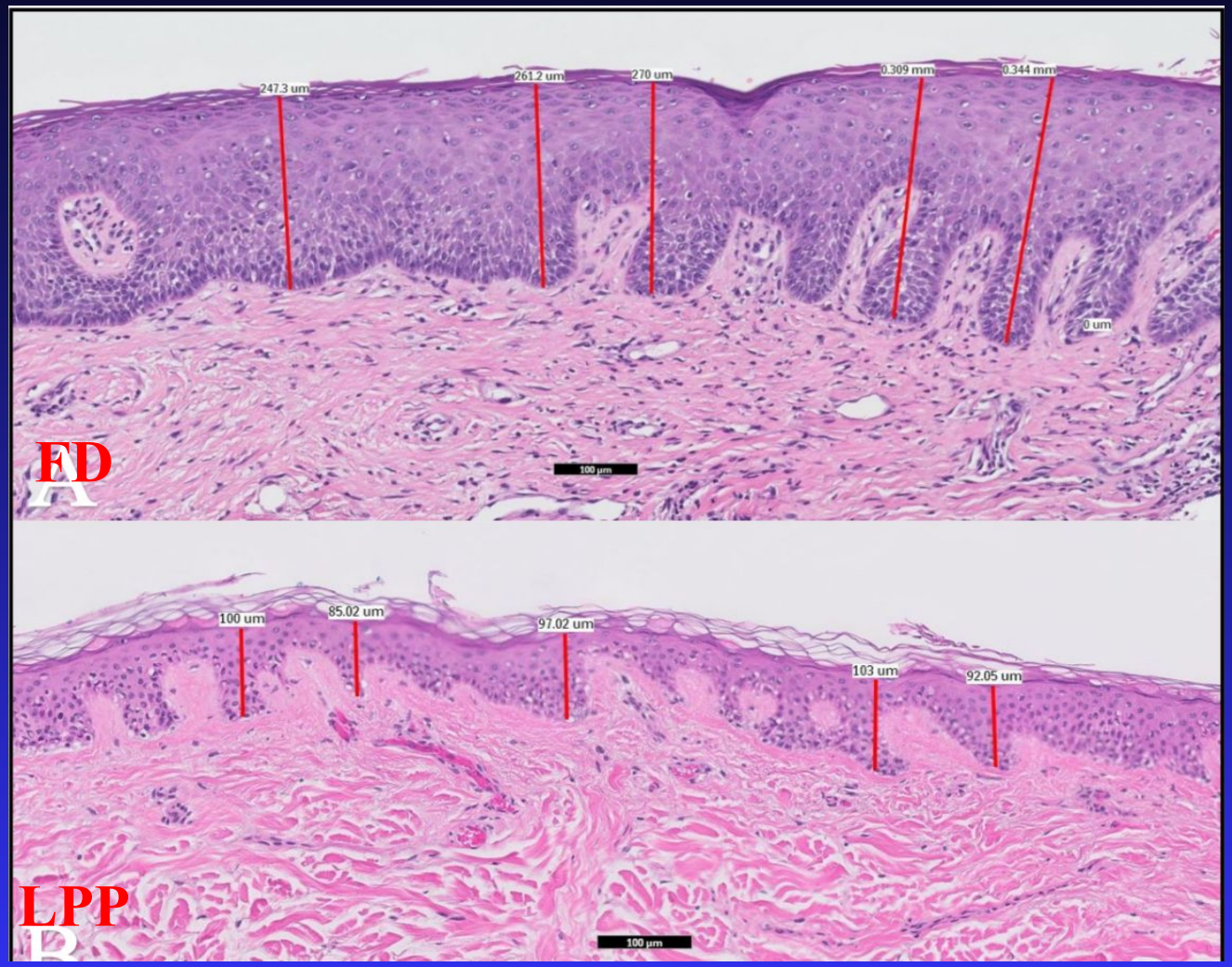




Foliculitis decalvans
Late-stage lesion--lymphocytic



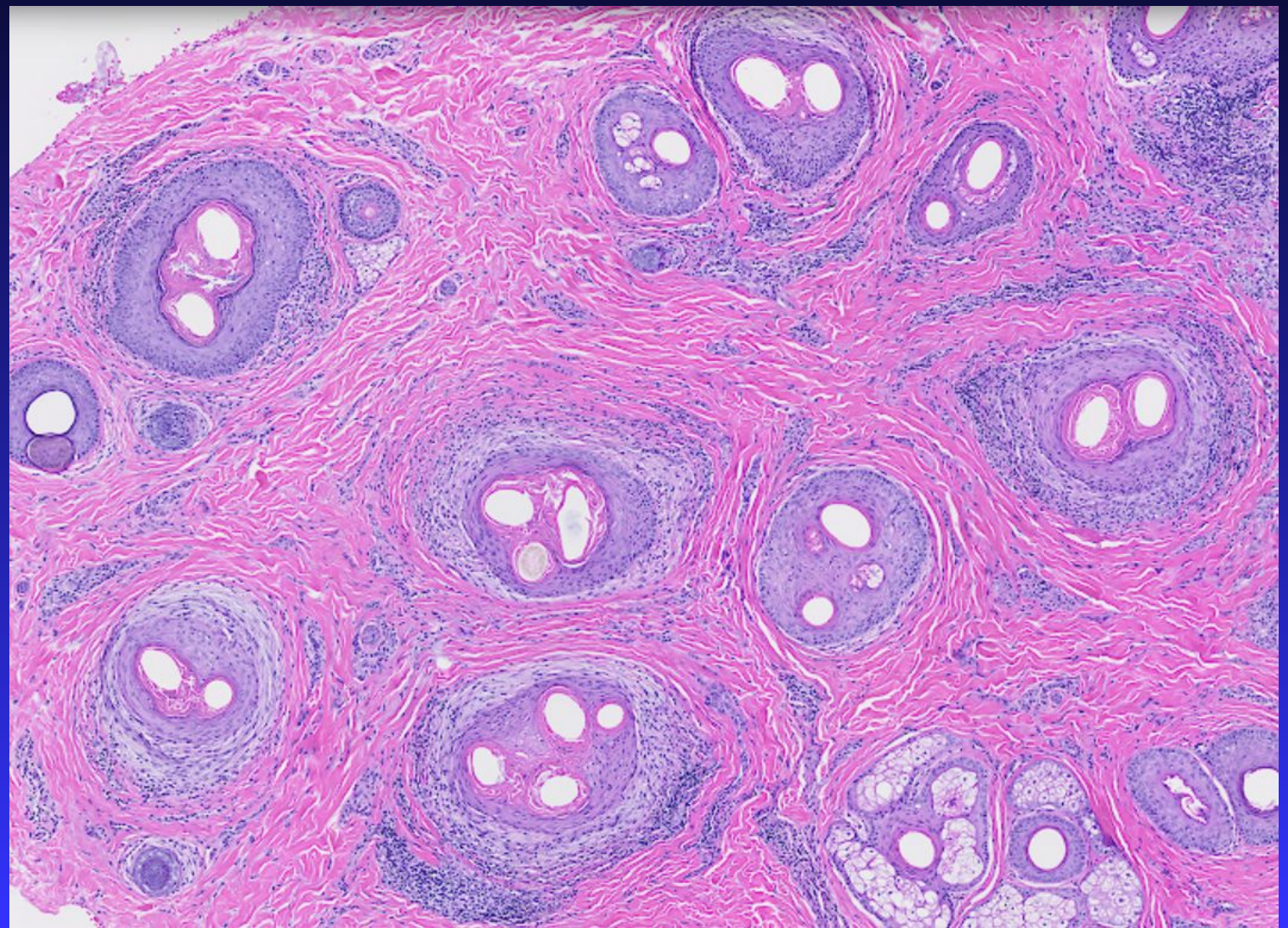
Epidermal thickness
Folliculitis decalvans vs LPP



Bohnett MC, Kolivras A, Thompson AA, Thompson CT. *J Cutan Pathol*. 2021;48(6):816-818.

Foliculitis decalvans versus LPP

Tufted compound follicles (>3 hairs)



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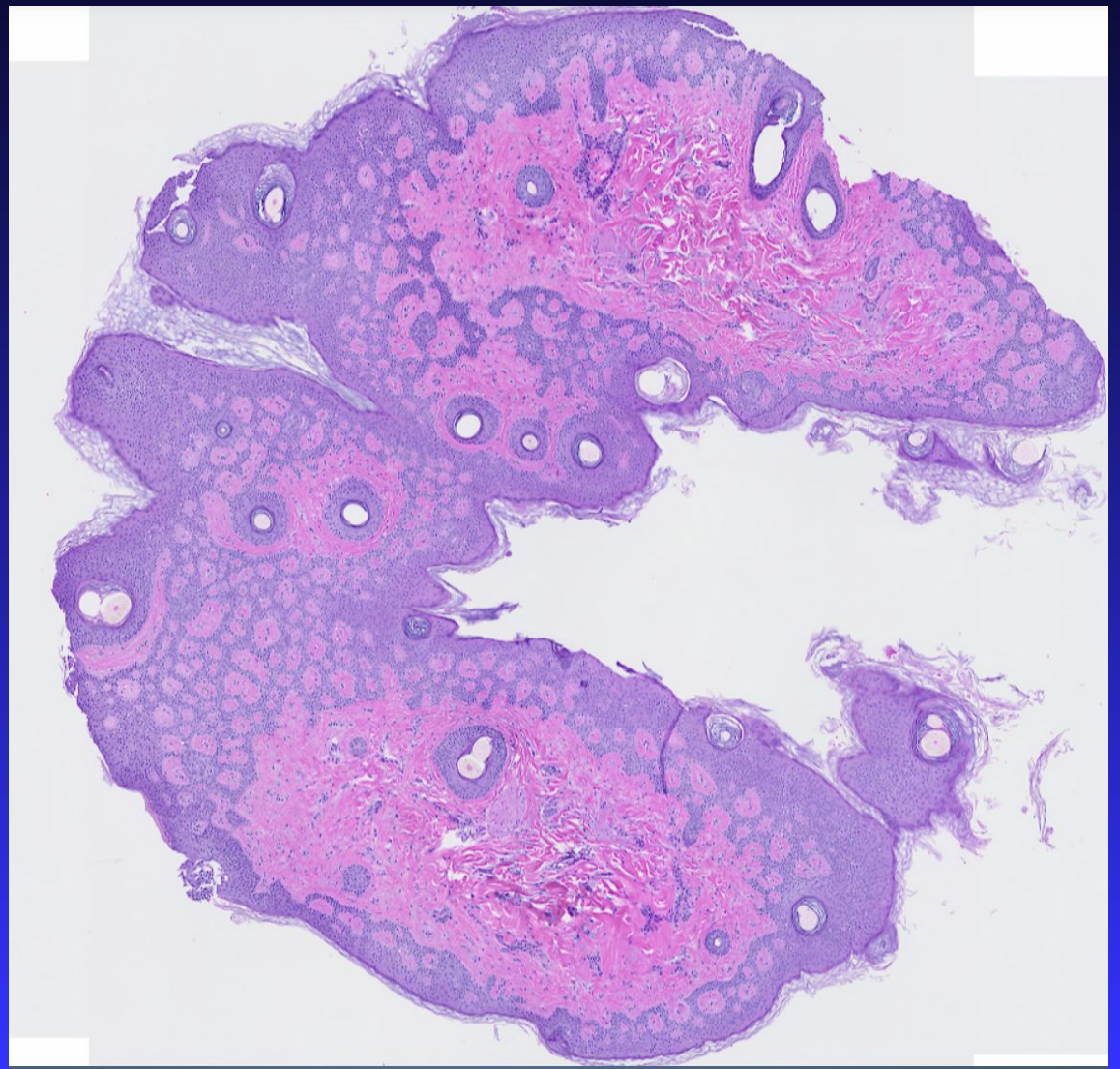
Provisional addition

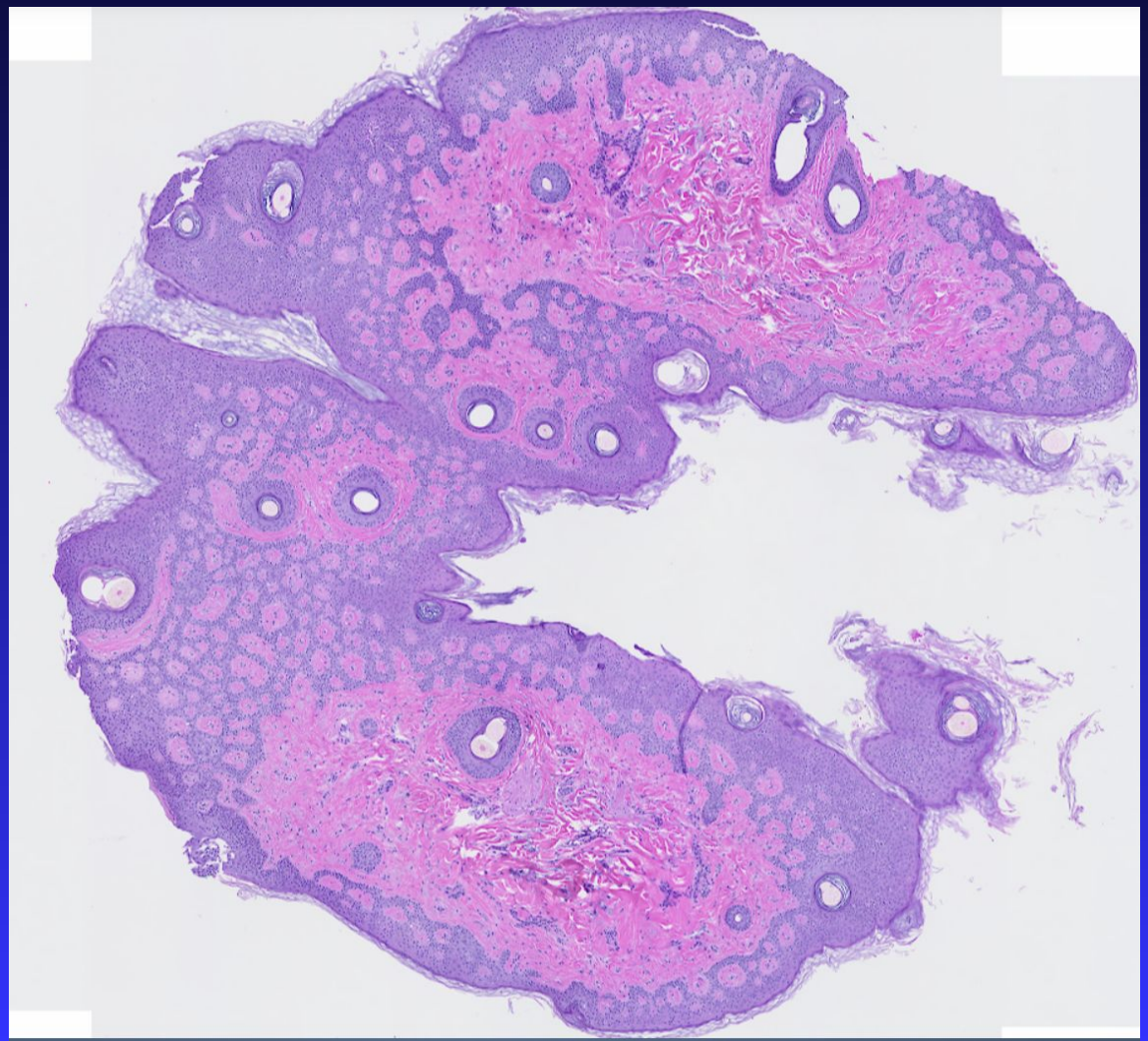
- Cicatricial pattern hair loss (CPHL)
  - End-stage PHL
  - No perifollicular scarring or inflammation

A few diagnostic clues . . .

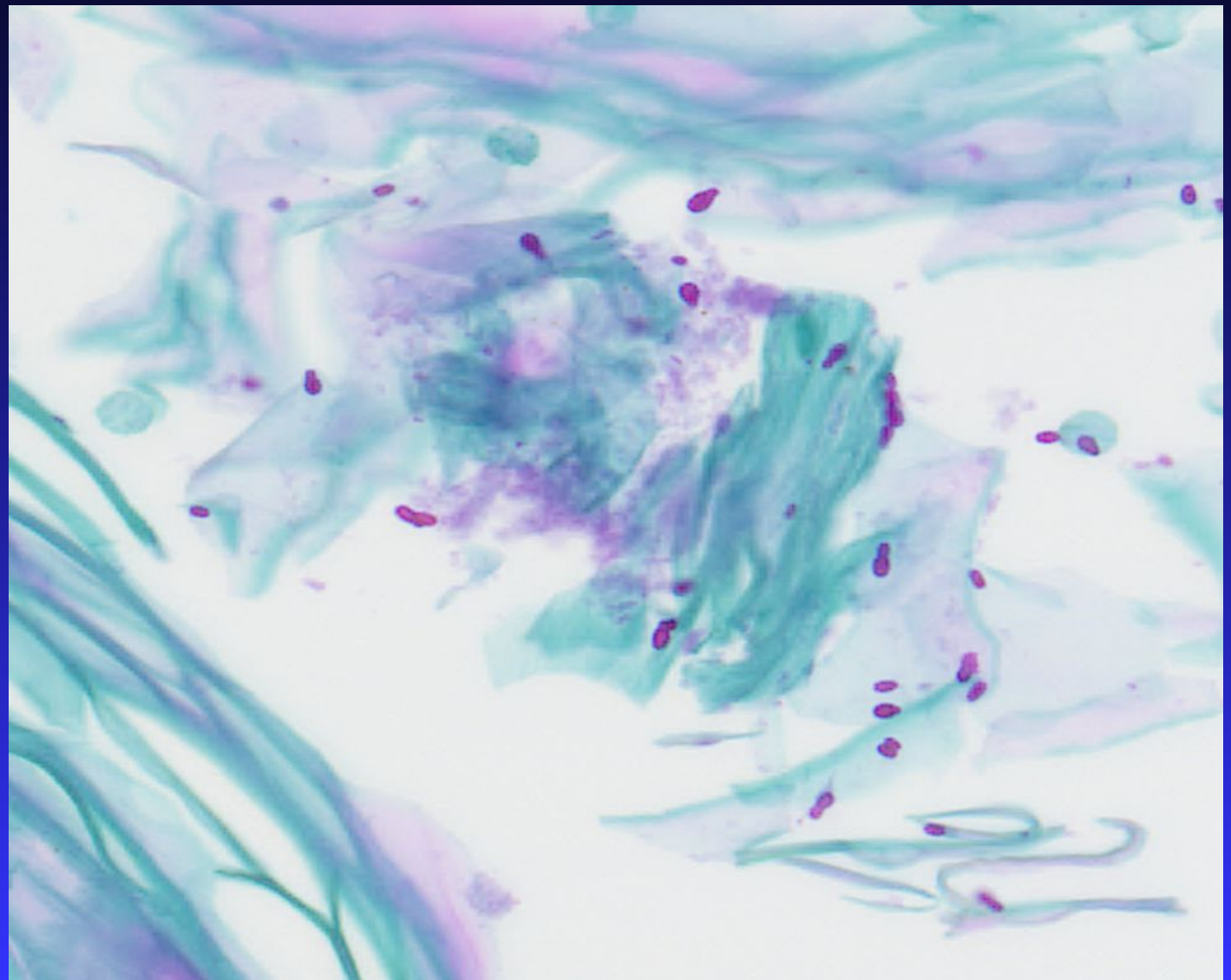


Clue #1

Hyperkeratosis (not parakeratosis) is a diagnostic clue for seborrheic dermatitis.



Yeast



Histologic absence of yeast as a clue for classic lichen planopilaris, fibrosing alopecia in a pattern distribution, and frontal fibrosing alopecia: A cross-sectional observational study

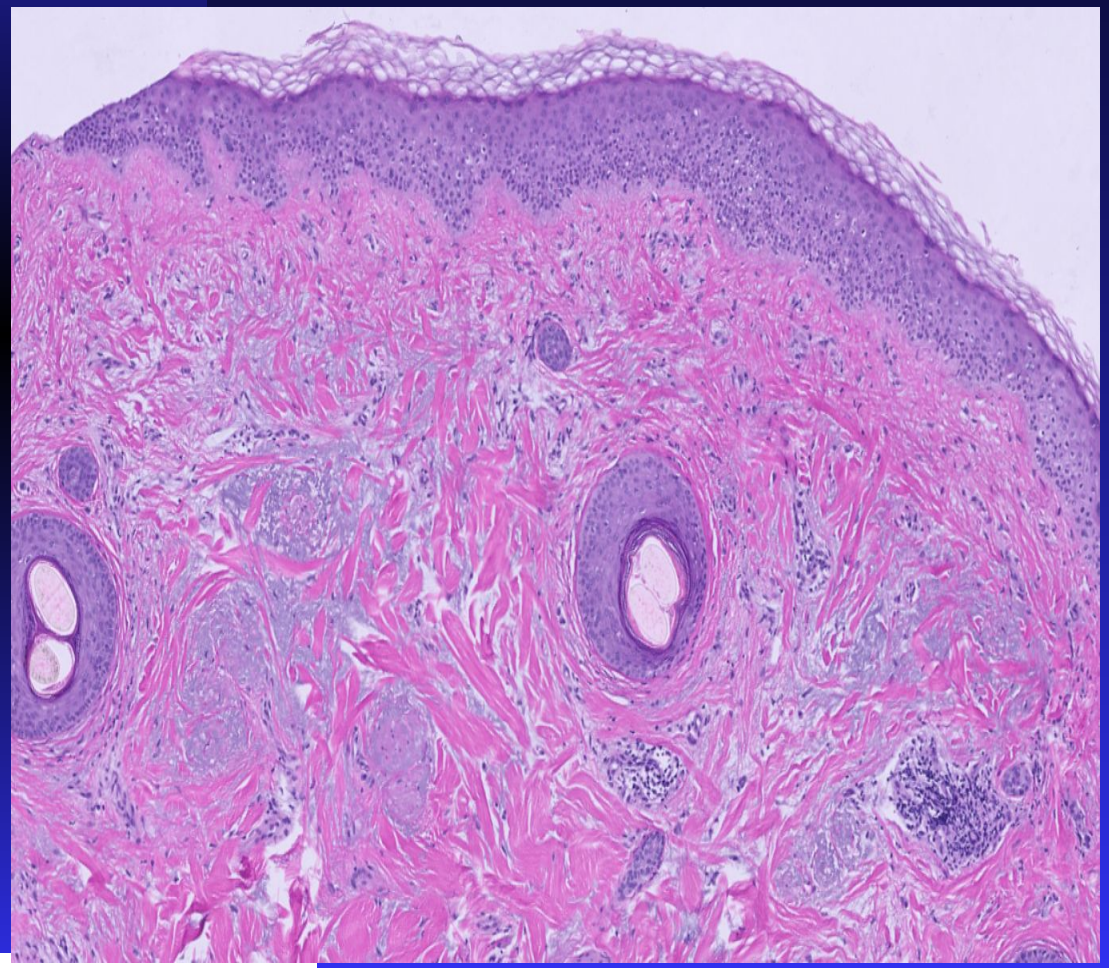
Kimberly Williams, BS [a] · Antonella Tosti, MD [a] · Curtis T. Thompson, MD [b,c]

JAAD International, Volume 19, 10 - 11

There was a distinct difference between the absence and presence of yeast between cases of LPP/FAPD/FFA and FPHL. In LPP/FAPD/FFA, 98.5% (68/69) of cases had no identifiable yeast. In contrast, in FPHL 50% (34/68) of cases had identifiable yeast ($P < .001$).

- >98% of LPP/FAPD/FFA without yeast
- 50% of PHL has yeast

No sebum = No yeast



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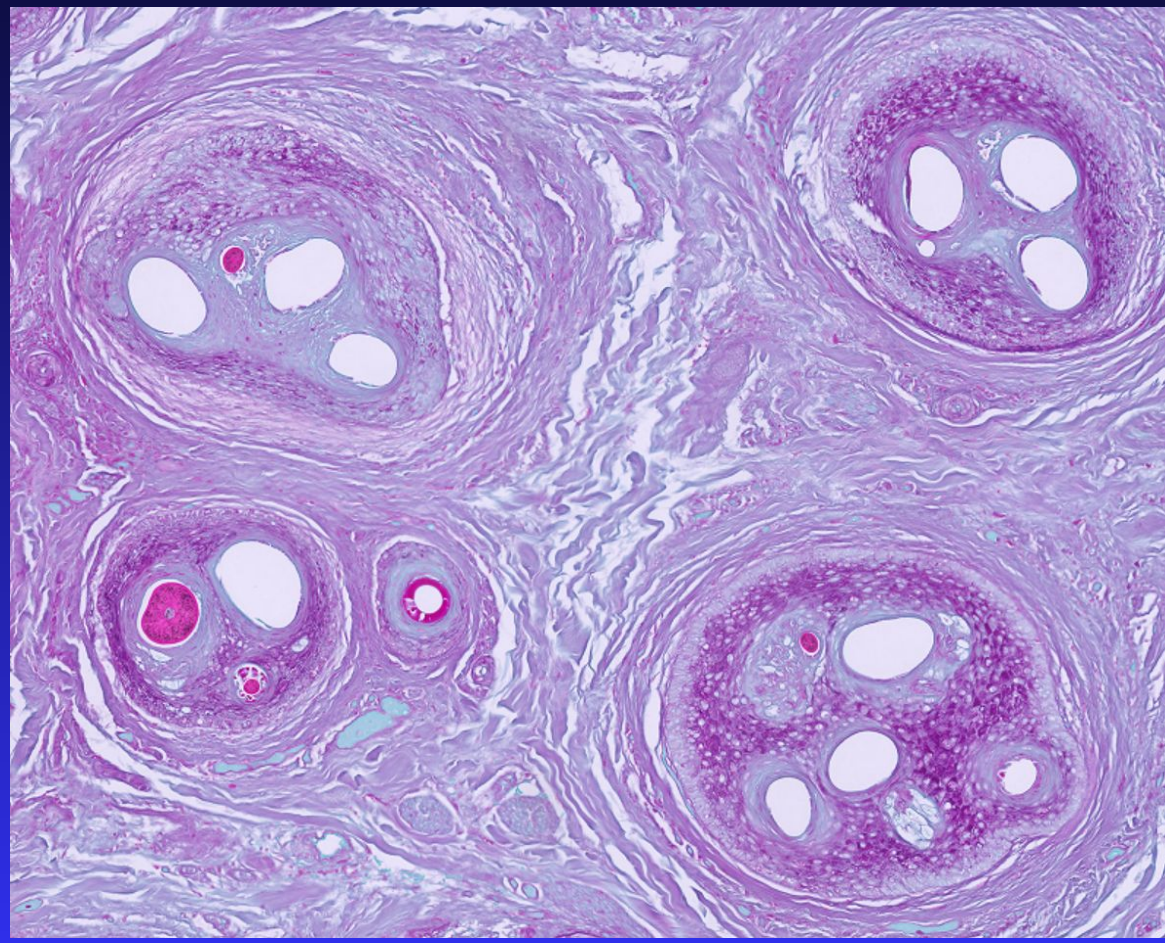
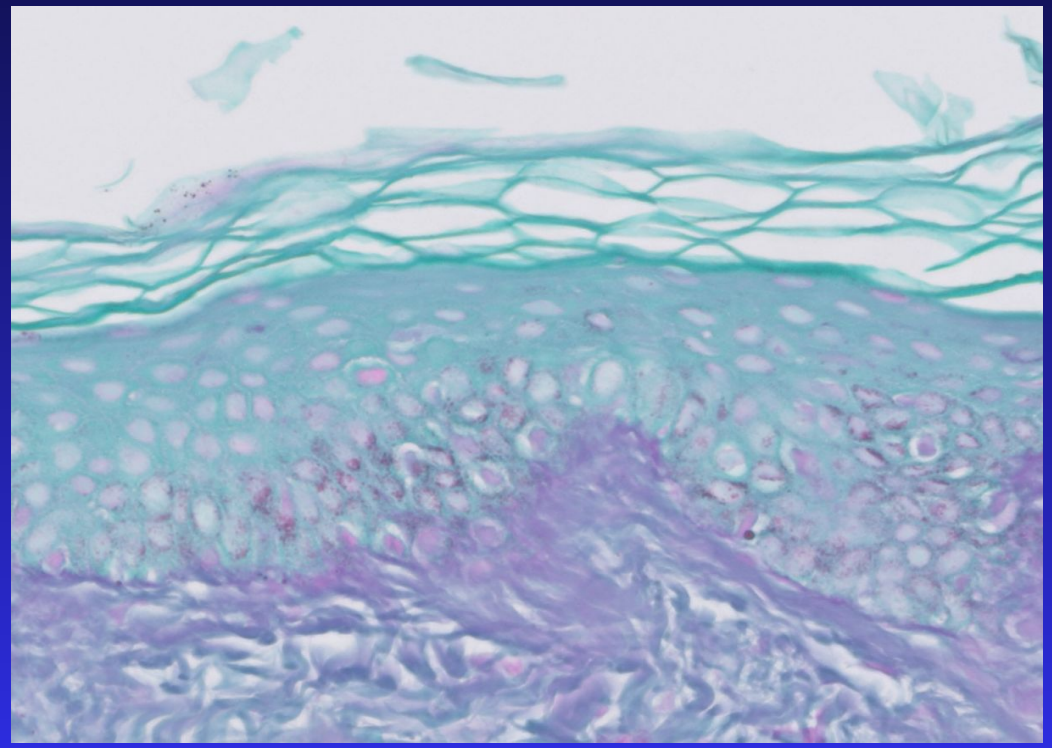


The absence of yeast is a clue to the diagnosis of LPP/FFA/CCCA/FAPD



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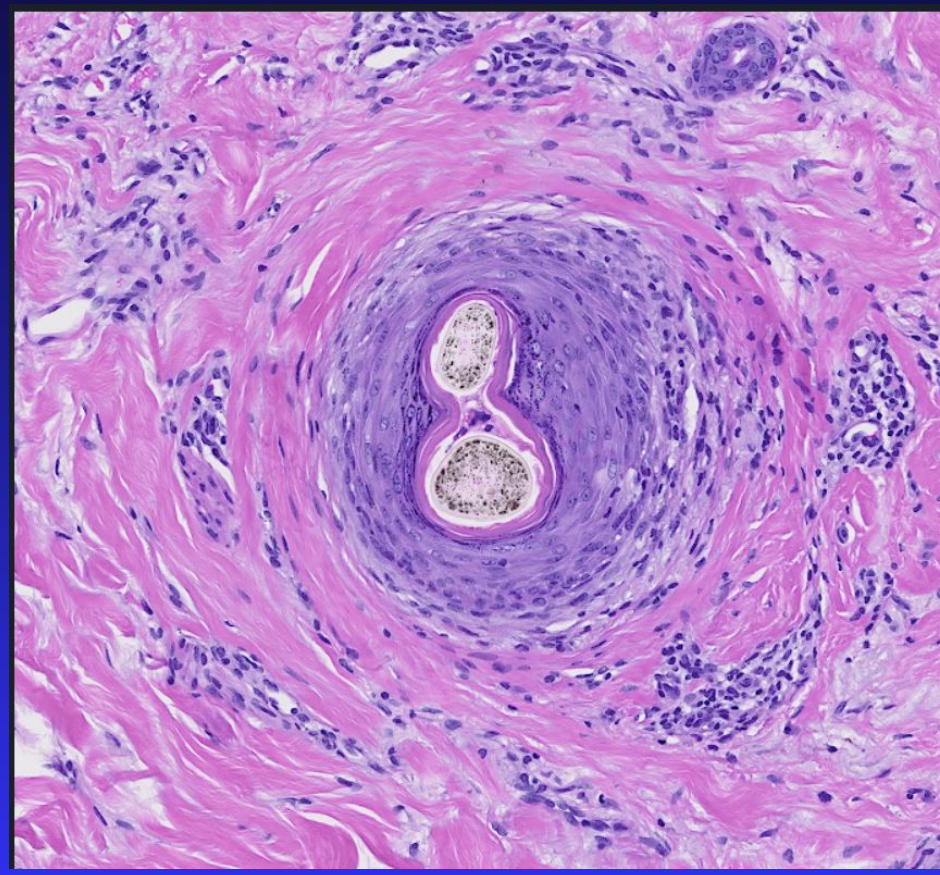
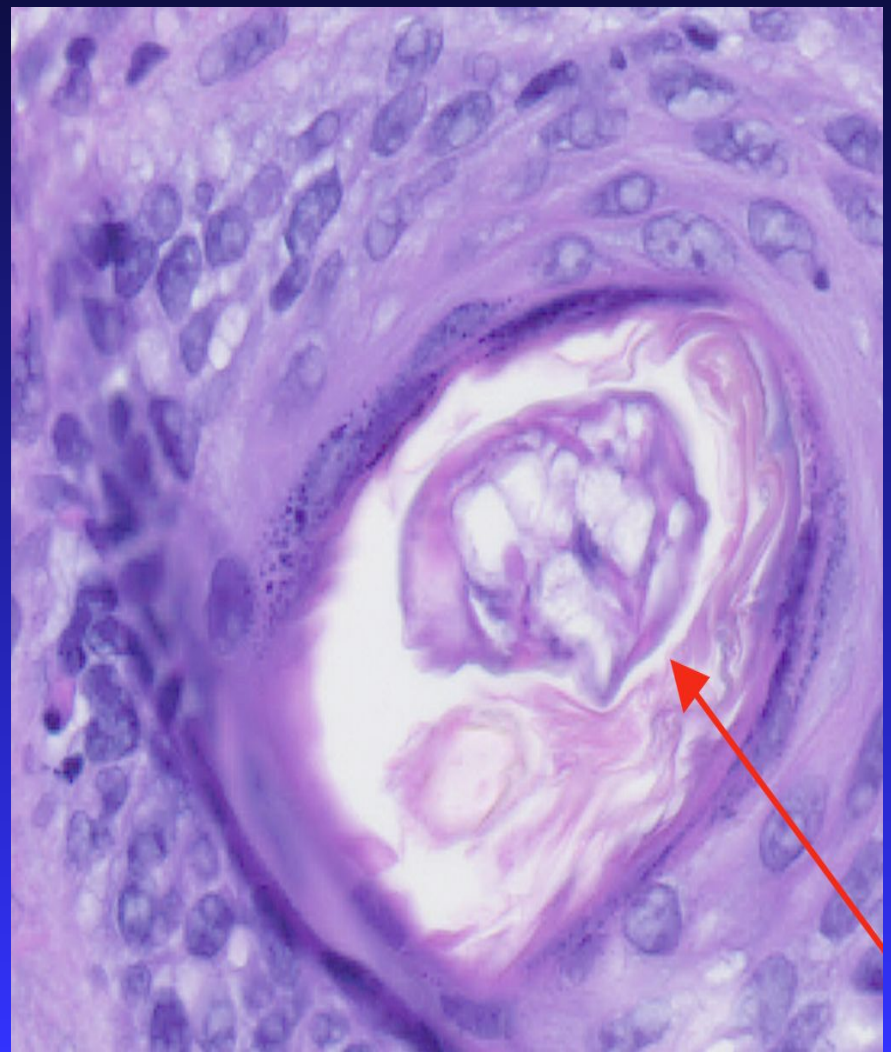
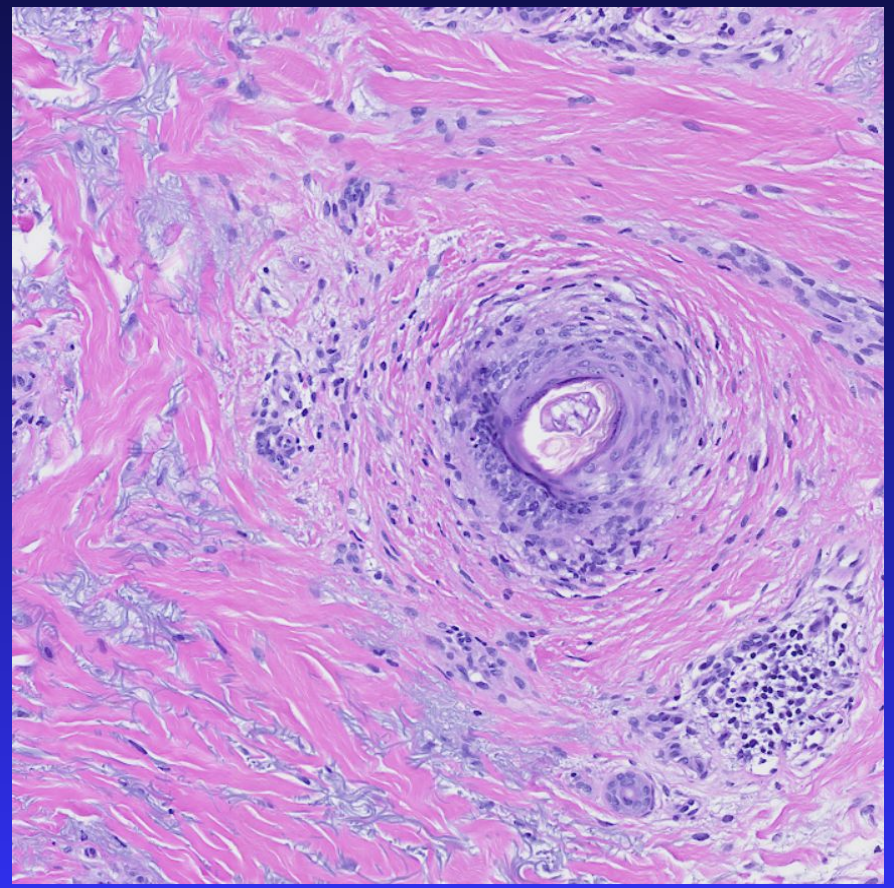


Clue #2

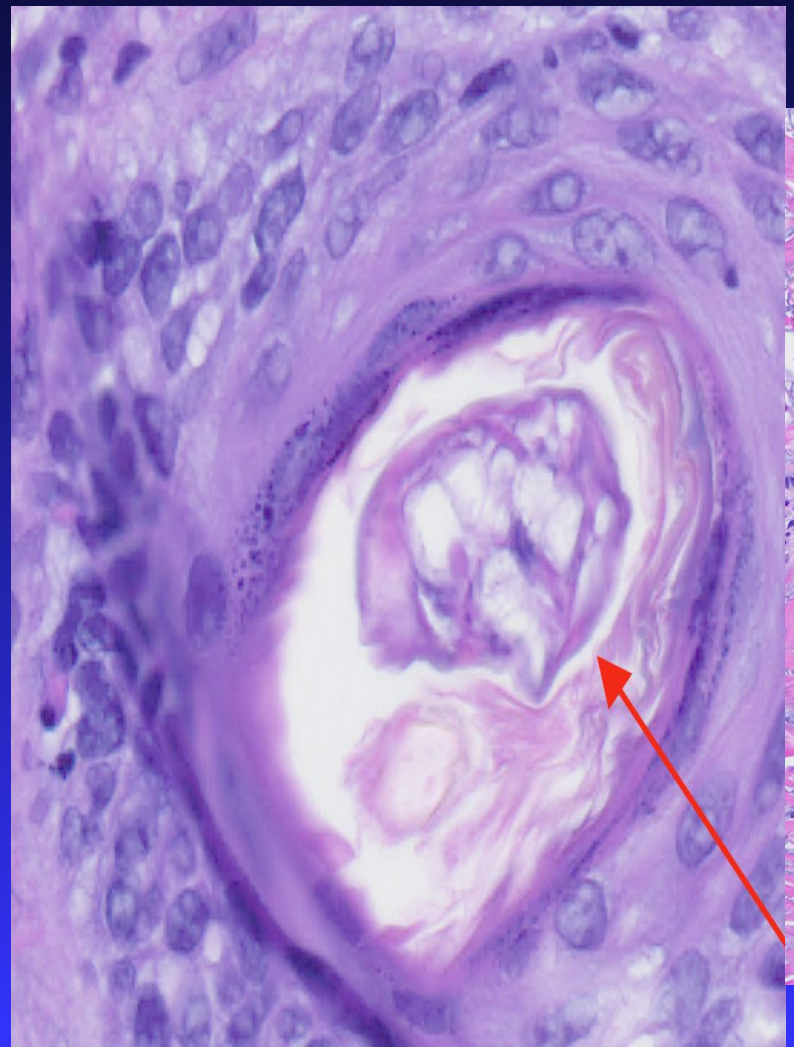
Demodex is a commen cause of inflammation and pruritus

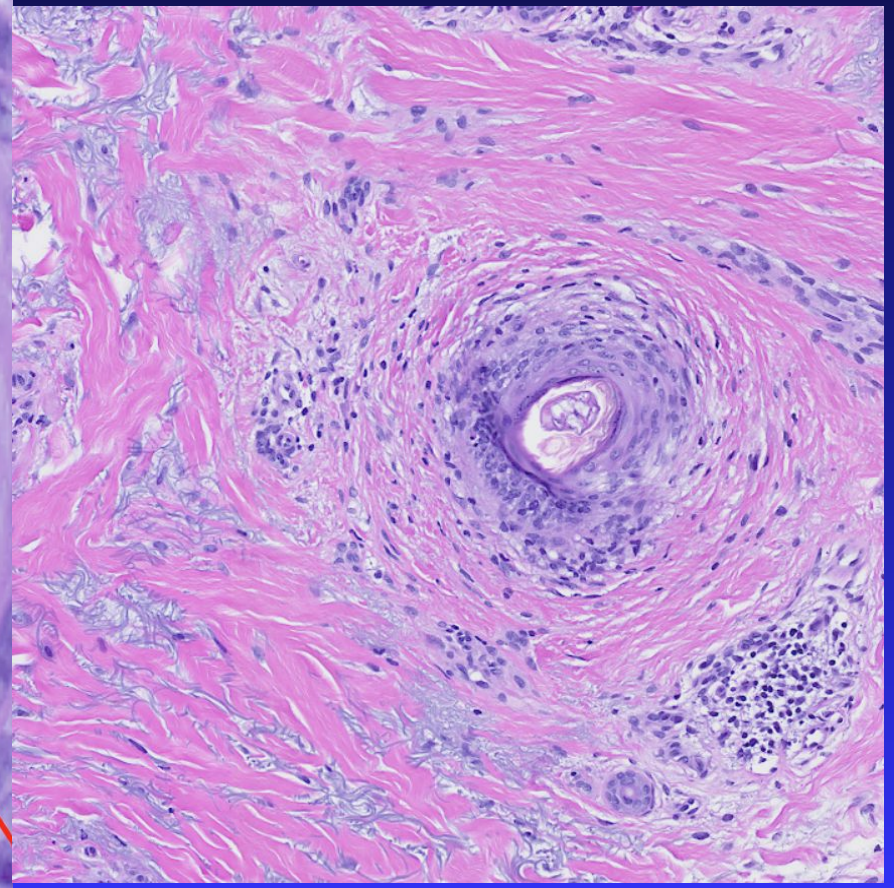




Clue #2

It is necessary to identify the cause of inflammation to prevent an incorrect diagnosis of a subtle primary cicatricial alopecia (esp FFA).

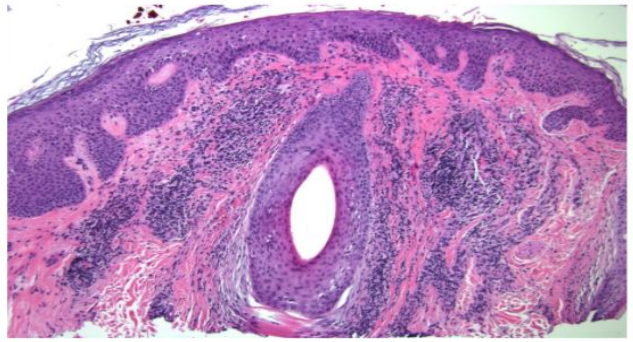


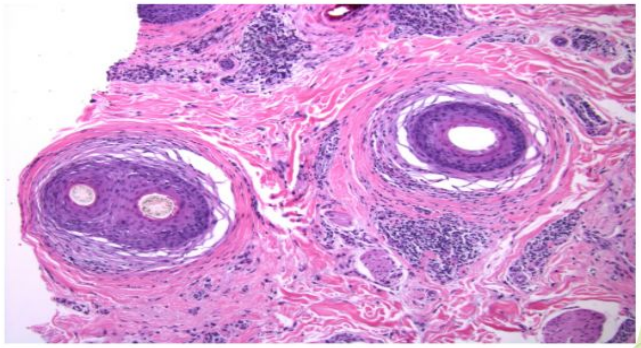


Clue #3

Near total absence of catagen/telogen phase follicles is a clue to LPP/FAPD/FFA/CCCA

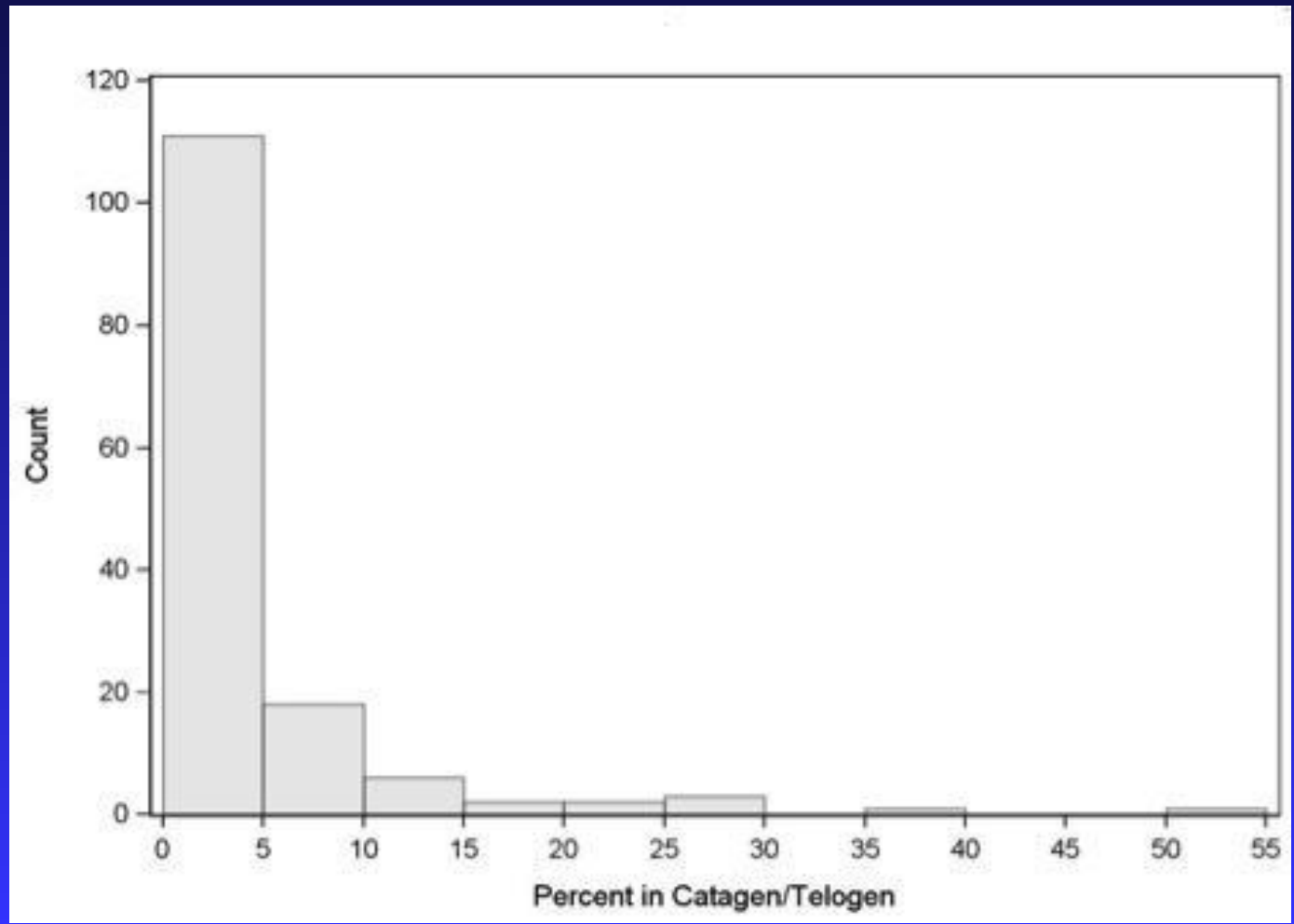
Lichen Planopilaris (LPP)





Loss of catagen/telogen phase follicles

Near total absence of catagen/telogen phase follicles is a clue to LPP



Habashi-Daniel et al. Absence of catagen/telogen phase and loss of cytokeratin 15 expression in hair follicles in lichen planopilaris. JAAD 71:969-72, 2014.

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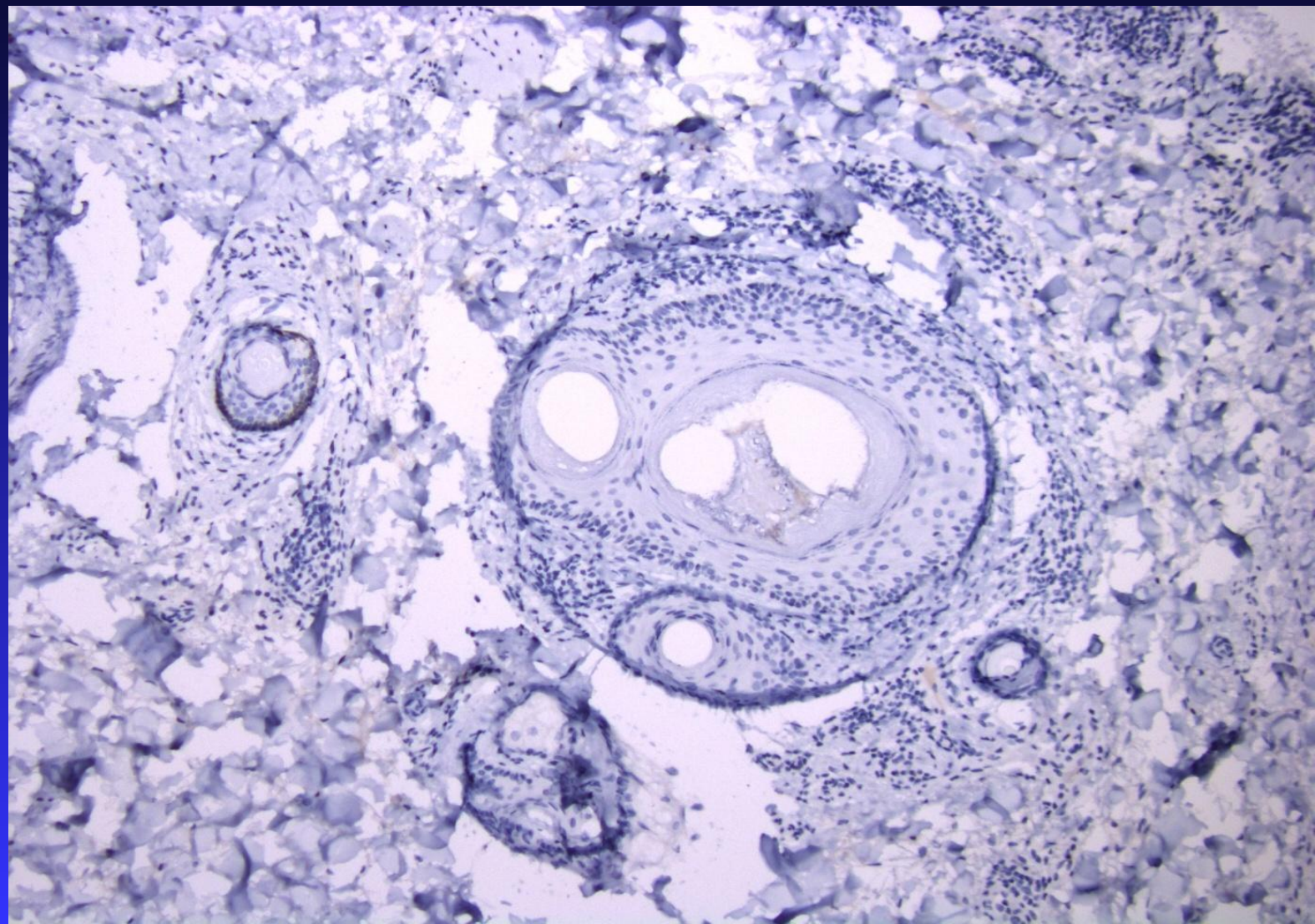
Loss of cytokeratin 15 in follicular stems cells



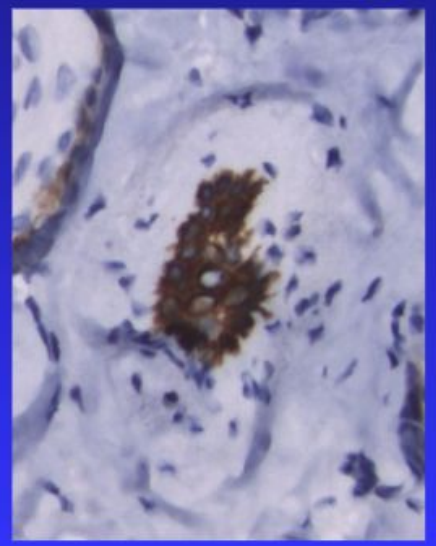
Habashi-Daniel et al. Absence of catagen/telogen phase and loss of cytokeratin 15 expression in hair follicles in lichen planopilaris. JAAD 71:969-72, 2014.

Lichen Planopilaris Progression

Loss of CK15+ stem cells

↓

Disappearance of follicle when cycle into catagen



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Clinical progression despite immunosuppressive treatment

The normal common ostium of the hairs is often overdiagnosed as scarring (LPP/FD/CCCA).

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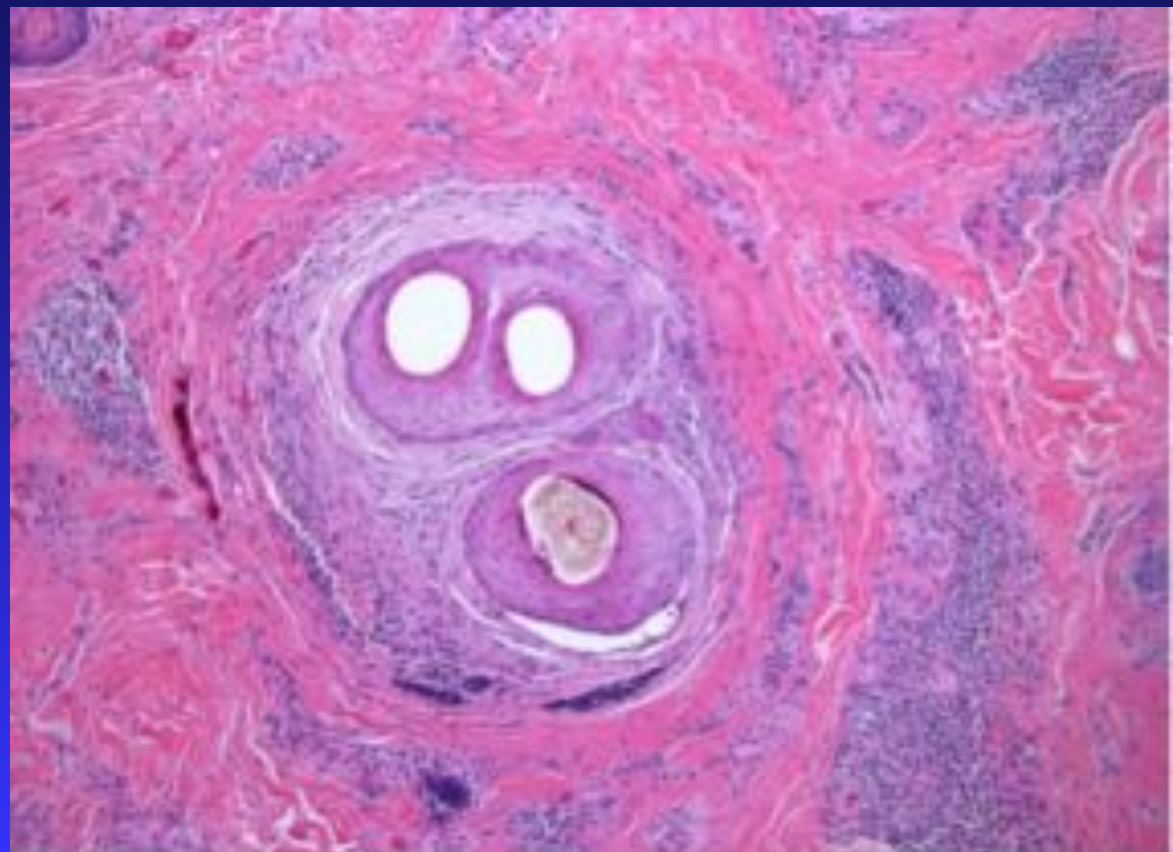
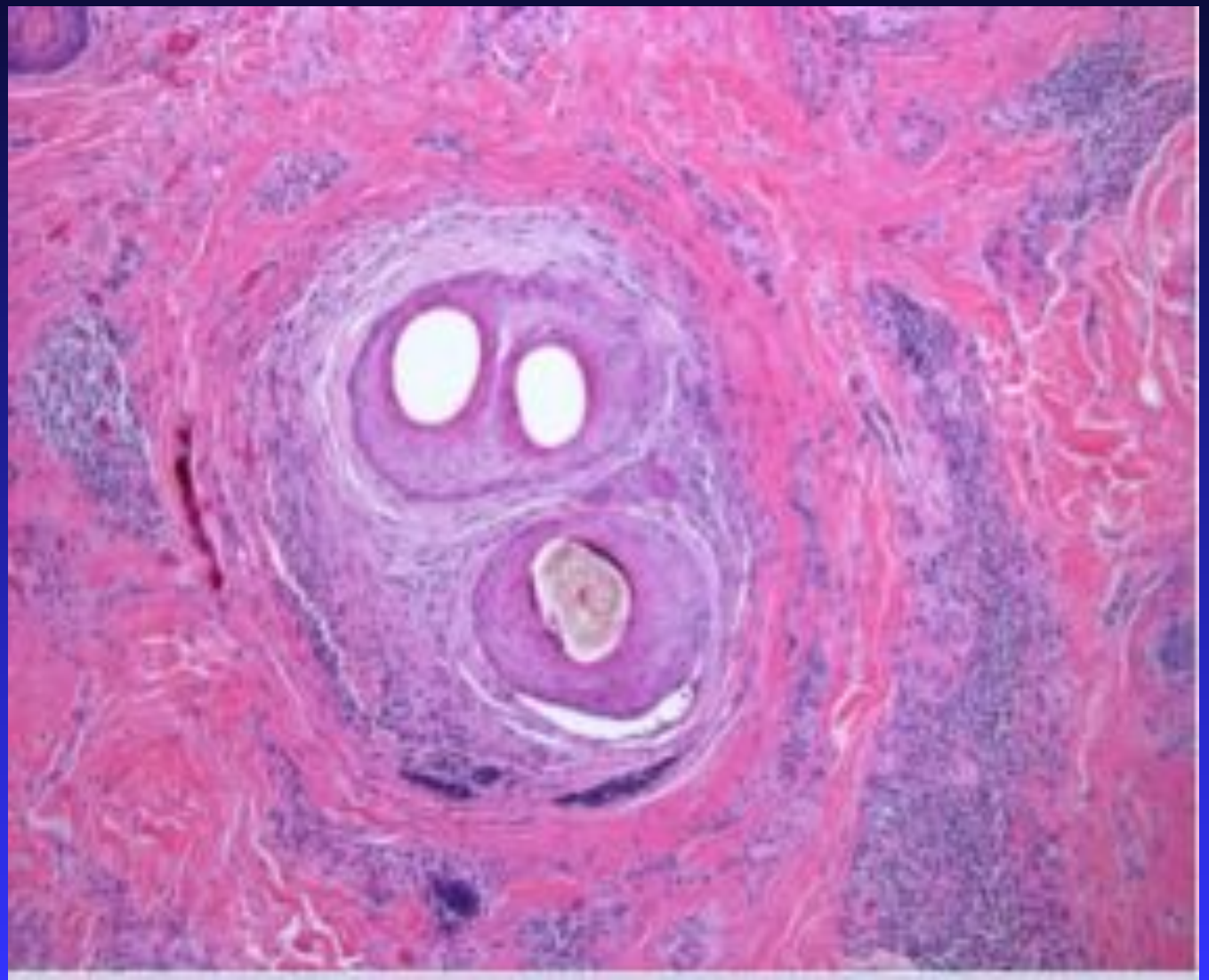
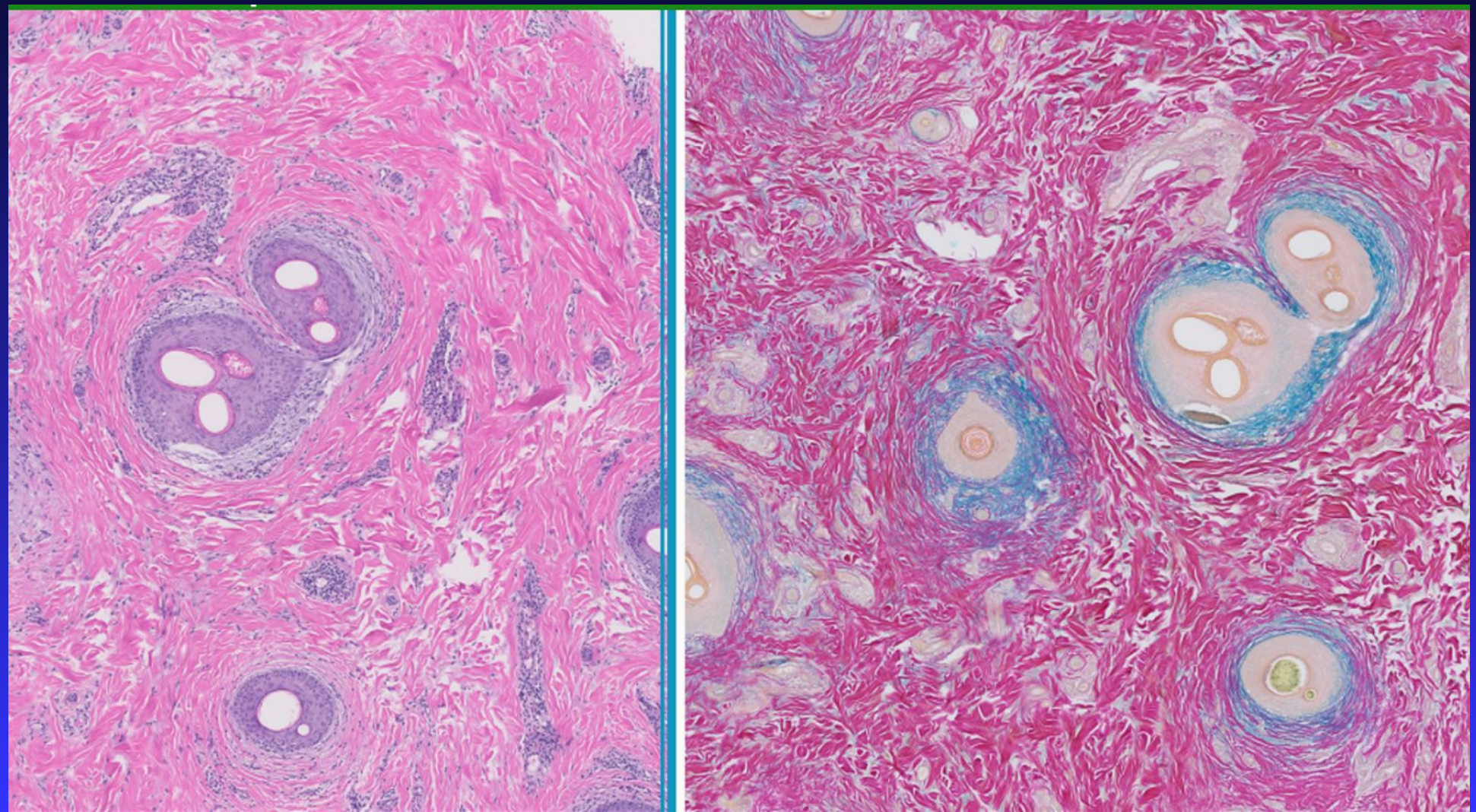


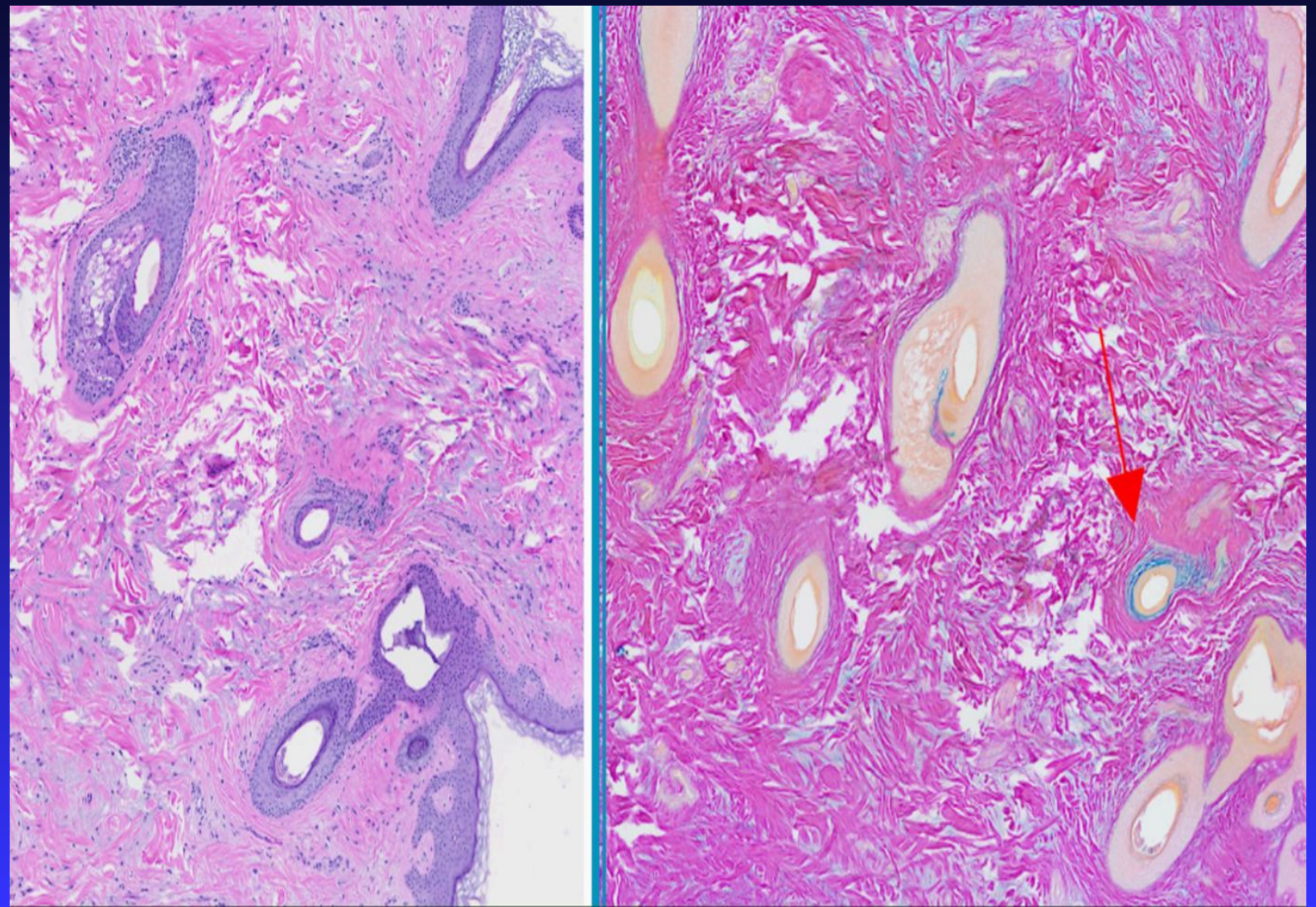
A resolving acneiform lesion looks like LPP or FD.



The Colloidal Iron stain works very well for identifying the perifollicular mucinous fibroplasia seen in LPP/FFA/FAPD/CCCA/FD.



The colloidal iron stain especially helpful with subtle FFA.



Hypothesis:
Are all of these the result of the same chemical?

- LPP
- FFA
- FAPD
- CCCA
- Lichen planus pigmentosus

Another Hypothesis

- Does solar protection allow for the presence of chronic inflammation?
- If so, perhaps different solar protective products all for chronic inflammation which is a fertile environment for the developments of LPP and FFA, especially in people with a genetic predisposition.

Thank you!

- University of Miami
  - Antonella Tosti, Betty Nguyen and Kimberly Williams
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Mahalo!

¡Gracias!

Merci beaucoup!

감사합니다!

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